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Contents

Selected abstracts presented at the XXI Symposium of the International Society of Oncology Pharmacy Practitioners, March 2-4, 2023, Seville, Spain.

Platform Presentations
Plenary

001

Dose intensity of palbociclib and initial body weight dosage: implications on progression free survival in 220 patients with ER+/HER2-negative metastatic breast cancer

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Objective/Purpose: Many novel oral targeted therapies have become available in oncology over the past two decades. In most of cases, as palbociclib, patients are treated at standard fixed dose, resulting in higher variability in efficacy and toxicity profile. The objective of this exposure-response analysis is to evaluate the effect of palbociclib exposure on progression free survival (PFS) in metastasic breast cancer stratified by dose intensity > or < 80% and starting dose of palbociclib > 2mg/kg or < 2mg/kg.

Study Design/Methods: A multicentric retrospective study was conducted for patients with ER+, HER2-negative metastasic breast cancer who started treatment with palbociclib November 2017 and May 2021 at Institut Catala d'Oncologia. Clinical data were obtained from electronical medical records and treatment data were obtained from chemotherapy software. Dose intensity was calculated as a percentage, and was categorized <80% and >80%: amount of milligrams delivered until progression or end of treatment/amount of theoretical milligrams if no reductions needed 125mg/daily for 21 days (28 days was considered one cycle). Kaplan-Meier method was used to generate median PFS. Log-rank test was used to compare differences.

Results/Key Findings: 220 patients were included with median follow up of 22.8 months (interquartile Range: IQR 13.6 – 31.8 months). Median age was 63 years (IQR 54 – 72.7) and Palbociclib was used as first line and second line treatment in 137 (64.3%) and 45 patients (21.1%), respectively. In 215 patients (97.7%), the recommended dose of 125mg/daily was the starting dose, and initial dose on body weight was 1.9mg/Kg (IQR 1.6mg/kg – 2.2mg/kg). Dosing reduction due to palbociclilb toxicity was needed in 94 patients (42.7%). Median dose intensity was 88.7% (IQR 74.8% - 98.1%), 76 and 144 were treated with dose intensity <80% and >80%, respectively. Dose reduction and hematological toxicity (mostly neutropenia grade III-IV) were statistically higher in patients who were treated with dose intensity < 80%: 84.2% vs 20.8%; p<0.001 and 93% vs 55.6%; p<0.001, respectively. At the cut-off analysis, treatment was stopped in 168 patients (76.4%): 140 due to progression (83,9%) and 11 for toxicity (17,7%). Overall response rate was 76.1% vs 70.6% with dose intensity <80% and >80%, respectively, with 55.2% vs 38.8% stabilization disease, 17.9% vs 27.1% partial responses and 3% vs 4.7 complete responses. In our follow-up, there were no differences in PFS in dose intensity of palbociclib <80% vs >80% (18.1 months vs 12.2 months; p=0.193), but surprisingly PFS was statistically higher in patients with dose reductions (18.1 months vs 11.4 month; P=0.02) and in those starting at a dose lower than 2mg/Kg(17.5 months vs 10.5 months; p=0.01).

Conclusion/Recommendations: In our study, dose-reduction of palbociclib occurred in 42.7% of patients, mainly due to hematological toxicity. There was no impact in PFS was observed in patients who were treated with dose intensity <80%. However, starting dose lower than 2mg/Kg was associated with significantly better PFS. Prospective and multivariate analysis are needed to find independent predictive factors associated with better PFS

002

Characteristics of Nirmatrelvir/Ritonavir (Paxlovid) Recipients and Clinical Interventions by Oncology Pharmacists at a Tertiary Outpatient Cancer Centre

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Objective/Purpose: Patients with cancer are at risk of acquiring COVID-19 and progression to severe illness. A five-day course of oral nirmatrelvir/ritonavir (PAX) is the recommended treatment of mild to moderate COVID-19 infection in this patient population in the outpatient setting. The potential for numerous drug interactions with PAX in the context of oncology-related polypharmacy requires careful assessment by oncology pharmacists for drug interaction management. This study aimed to characterize the population of patients requested to receive PAX at a single centre and document the clinical interventions performed by pharmacists with respect to drug-drug interactions.

Study Design/Methods: This was a retrospective analysis of all requests for PAX from April 08, 2022 to July 11, 2022. All requests for PAX were documented in a log for workload tracking purposes. Each PAX order requires clinical assessment by the pharmacist, including dose adjusting for renal function and identifying and managing clinically significant drug interactions (using at least two resources). A retrospective chart review was conducted to extract demographic data and clinical variables. Vaccination status, treatment status and treatment interruptions were recorded. Drug interactions of potential clinical significance were defined as those requiring any clinical intervention due to concomitant medications, including patient counselling and monitoring. Drug interactions were summarized and categorized according to the action taken. Data was summarized using descriptive statistics.

Results/Key Findings: There were 85 requests for PAX during the study period, 47 were for females (55.3%). The median age of the patients was 66 years (range: 22 – 87). Sixty-two patients (72.9%) were receiving anti-cancer therapy, of which 48.4% experienced treatment interruption due to COVID-19 infection and/or PAX treatment. Hematological malignancies accounted for 48.2% of patients. During the study period, health officials recommended 4 doses of vaccine (initial 2-dose series + 2 booster doses of mRNA vaccine) for immunocompromised patients with cancer. The study population had a median number of 3 vaccines at the time of their infection. Seventy-eight of the 85 PAX requests were assessed by cancer centre pharmacists (7 were assessed in the community). Three requests were contraindicated or not eligible, leaving 75 orders included in the final analysis. Out of the 75 PAX order recipients, 57 were associated with clinically significant drug interactions (76.0%). The median number of drug interactions found was 2 (range 1-4) per prescription with a total of 100 drug interactions among the 57 prescriptions. The most common actions required for drug interactions were holding medication (n=51, 51%), patient monitoring (n=20), followed by reducing home medication dose temporarily (n=12). Dose adjustment for renal function was necessary for 17 prescriptions (22.7%).

Conclusion/Recommendations: Clinically significant drug interactions were frequently observed in patients with cancer being treated with PAX. As such, oncology pharmacists play a vital role in the assessment of COVID-19 treatments for this vulnerable population to mitigate harm and monitor outcomes. Future research should evaluate the impact of drug-drug interactions between PAX and anti-cancer therapies, document clinical outcomes of drug interaction monitoring, and contribute to the development and refinement of PAX drug interaction resources for clinicians at the point of care.

003

Safe handling of non-carcinogenic drugs in the Ghent University Hospital: development, implementation and communication of hospital-specific guidelines

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Objective/Purpose: Guidelines for safe handling of hazardous drugs are well known, generally in place and with a high degree of adherence to the guidelines. On the other hand, the awareness of possible health risks of other drugs, less known to be potentially hazardous, is often very low. The use of these drugs is sometimes widely spread across the hospital without any safety warnings in terms of handling. Many of these drugs, might have the potential to have negative effects for example, on the reproductive system. To create awareness and to inform the healthcare workers in our hospital about potentially hazardous drugs. Guidelines for personal protective equipment and handling were developed and communication tools as well as electronic warnings were put in place.

Study Design/Methods: The National Institute for Occupational Safety and Health (NIOSH) list of hazardous drugs in healthcare settings 2020 was used as a base to develop a hospital-specific list of hazardous drugs, aligned with drugs available in the hospital formulary. In collaboration with the hospital safety advisors, personal protective equipment guidelines were developed for handling less known hazardous drugs. These measures were summarized in a poster as educational tool and were communicated hospital wide. An electronic alert, embedded in the clinical patient management system, was implemented to inform healthcare workers about the drugs that might need extra precautions.

Results/Key Findings: In agreement with the NIOSH list version 2020, classifying hazardous drugs in 2 groups, our list was built up in the same way. Molecules of group 1 included drugs with antineoplastic, carcinogenic and/or immunosuppressive properties. Precautions, guidelines and identification for this type of drugs have been in place for a long time in our hospital and are generally very well known. The second group of drugs included those that are linked with developmental or reproductive toxicity (for example spironolactone, fluconazole, …). The awareness of possible toxicities with this group of drugs was very low and no safety guidelines were in place so far. In the clinical patient management system, an extra symbol was added to identify this group 2 therapeutics. A blue exclamation mark was introduced in the medication administration schedule of the electronic patient's medical record. Second, guidelines for safe handling of hazardous drugs (personal protective equipment, cleaning,…) were developed to reduce exposure to both types drugs from group 1 and group 2. Specific actions were defined according to the kind of exposure, manipulation and type of dosage formulation (tablets, suspensions,…) of the drugs used. A hospital-wide information campaign was set up to inform all healthcare workers of this new tool by means of online communication, posters as well as newsletters

Conclusion/Recommendations: Updated scientific insights have led to the development and implementation of a tool for safe handling of non-typical hazardous drugs manipulated by healthcare workers. All information is now electronically provided via a unique symbol in the electronic prescription system, guiding healthcare workers to take correct protective measures depending on the pharmaceutical properties of the prescribed drug and hence reduce the risk for occupational exposure.

004

Infusion of Busulfan solution through closed safety connectors Qimomale© and Qimofemale©

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Objective/Purpose: Among all the injectable anticancer drugs used, drug containing busulfan (Active Pharmaceutical Ingredient, API) is certainly one of the most at risk of interaction with the preparation and infusion medical devices (MD) due to the presence of large quantities of DiMethylAcetamide (DMA) necessary for the solubilization of the active ingredient but aggressive on certain plastics. The Summary of Product Characteristic (SmPC) specifies: “Due to incompatibility, do not use infusion material containing polycarbonate (PC) with busulfan”. Nevertheless, the question of the use of PC-containing MD arises when they have no strict alternatives (Closed Safety Connectors) and allow nurses to secure the disconnection steps by highly limiting the exposure to cytotoxics. This is the case for the QIMONO devices (Vygon).

Study Design/Methods: A 0.5mg/mL busulfan solution (Busulfan Fresenius Kabi 60mg/10ml diluted in NaCl 0.9%) was infused through the QIMO connectors (male and female) at a flow rate of 0.17mL/min for 3h (situation in accordance with the SmPC and observable in pediatrics). An assay at T0 and T3h, at the tubing outlet, was performed by a stability-indicating HPLC/MS method. pH analyses and visual aspect control were evaluated as follows:

- Visual observation (particles, colour change or turbidity) and presence of cracks/degradation on the connectors
- Visual observation of the membranes and the membranes closure at disconnection
- Sealing under gravity (1 m of water) Tests were performed on three samples of Qimomale® and Qimofemale® pairs

Results/Key Findings: The chemical stability of the solution in terms of busulfan concentration determined by HPLC/MS was validated (average 104%). There were no change in the pH analysis (pH=5.5) and in the visual observation:

- No degradation, no crack in housings and connector locks.
- During a disconnection, the connectors (and the membranes) have the same behaviour as the sample control. No leakage was observed

Conclusion/Recommendations: The concentration of the API remains unchanged, The contact of Qimomale® and Qimofemale® connectors has no impact on the pH of the solution. Contact between Qimomale® and Qimofemale® connectors has no impact on the visual appearance of the solution, which shows no particles, no colour change or turbidity. No visual or mechanical degradation of the devices were observed after their prolonged exposure to Busulfan solution. Busulfan (diluted to 0.5 mg/mL) is stable when infused through Qimomale® and Qimofemale® connectors for 3 hours. Similarly, Qimono® connectors do not deteriorate mechanically under the conditions of the test.

Concurrent Session: Research 1

005

Case series: use of olaparib in uncommon locations in patients with impaired homologous recombination.

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Objective/Purpose: The objective of this study is to describe the effectiveness and safety of olaparib in patients with homologous recombination deficiency (HRD) with different solid tumors than those considered in the product data sheet.

Study Design/Methods: Single-center, observational, retrospective study including patients with tumor sites other than those authorized in the data sheet who initiated olaparib between June 2019 and April 2022. The variables collected were: age, sex, Eastern Cooperative Oncology Group performance status (ECOG), mutation, initial dosing, line of treatment, dose reductions, discontinuations, adverse events (AEs), best overall response (BOR), progression-free survival (PFS) and overall survival (OS). Data were obtained from the clinical history and the outpatient dispensing program. Quantitative variables are expressed as median (range) and qualitative variables as (cases/total).

Results/Key Findings: Four patients were included, three of them female, with a median age of 55 (29-71) years and a baseline ECOG of 1. The tumor sites and mutations found were: intrahepatic cholangiocarcinoma with PALB2, non-small cell lung adenocarcinoma with ATM, EGFR wild-type BRAF wild-type colorectal cancer with BRCA2g and breast neuroendocrine tumor with BRCA2g. All patients had metastases. Initial dosing was 300mg/12h tablets in 3/4 patients while 400mg/12h capsules were used in 1/4 patient. Olaparib was used as maintenance therapy in cholangiocarcinoma and neuroendocrine patients while in lung and colon patients it was used as 5th and 3rd line treatment respectively. The BOR of patients with cholangiocarcinoma and lung was stability while that of the remaining 2 patients was progression. The PFS obtained according to the order of tumor sites described above were: 3.4 months; 5.6 months; 1.4 months; 1.3 months. Regarding OS data, at the time of follow-up, 2 patients had died, with cholangiocarcinoma and lung, after 0.7 and 4.6 months, respectively, from the start of treatment. AEs of any grade were reported in 3/4 patients: asthenia (2/4), anemia (2/4), nausea and vomiting (1/4); no treatment reductions or interruptions were required.

Conclusion/Recommendations: The results of our case series study show moderate effectiveness, probably related to the fact that these patients are in advanced lines of treatment. Tolerance to treatment has been adequate. Further studies are needed to assess the effectiveness and safety of olaparib use in patients with HRD in tumor sites other than those evaluated by regulatory agencies.

006

Real-world data evaluation of medicines used in special situations in oncohematology: a retrospective study from a comprehensive cancer institution

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Objective/Purpose: Medicines in Special situations (MSS) refer to marketed drugs used outside the conditions described in the product information (off-label) or to unlicensed drugs under investigation (compassionate use). MSS are common in oncology, triggered especially by unmet clinical needs and due to lengthy and cumbersome marketing and post marketing authorisation process. However, little information is known about MSS results in real world practice.

Study Design/Methods: Retrospective cohort study to evaluate characteristics and clinical outcomes of MSS requested from 2011 to 2020, at a comprehensive cancer institution and followed-up until April 2022. We aimed to estimate overall survival (OS), progression-free survival (PFS), treatment duration (TD), and percentage of patients with TD <6 months. Reasons for MSS discontinuation or for not starting treatment, demographic, clinical, tumour and drug data were described.

Results/Key Findings: A total of 2,377 MSS episodes were included (2,189 patients): 49% women, median age of 61 years (range: 17-92), 17.4% with ≥75 years. Two thirds of the requests were for solid tumour (ONC) and 32.8% for haematological (HEM) cancer treatment, mostly in refractory/relapsed (R/R) or advanced/metastatic (A/M) stage (83.1% HCL and 86% ONC). In 285 episodes (11.4%), treatment was not finally administered, mostly due to approval denial by the MSS committee (40%) or to patient status deterioration (24%). The most frequent pathologies for oncology were thoracic (n=361) and breast (n=227) cancer and for haematology non-Hodgkin lymphoma (n=201) and myeloid leukemia (n=86). Most frequently administered drugs in ONC were antiPD-L1/PD-1 (nivolumab 7.4%, pembrolizumab 6.1%) and targeted therapies: antiEGFR (osimertinib, 2.9%), PARP inhibitors (olaparib, 2.7%, niraparib, 2.2%), abiraterone (2.6%); for HCL, monoclonal antibodies (brentuximab 2.4%, rituximab 2.1%) and JAK inhibitors (2.2%). Median OS (months) was 34.2 (95%CI 26.6-40.2) for HCL and 18.1 (95%CI 16.6-20.0) for ONC. For HEM, OS (months) was statistically significant according to ECOG 1 (48.7 (95%CI 37.6-65.3)) vs ECOG ≥2 (8.6 (95%CI 6.6-12.3)) and for ONC as well (ECOG 1: 18.7 (95%CI 17.1-21.1) vs ECOG ≥2: 4.4 (95%CI 3.7-5.6)). OS also differed by treatment setting: initial stages (53.7 (95%CI 26.6-NR) months) vs R/R disease (31.9 (95%CI 24.9-38.8) months) for HCL and between adjuvant/localized disease (42.1 (95%CI 23.1-NR) months) and A/M disease (14.3 (13.0-16.3) months) for ONC. Median PFS (months) was 6.0 (95%CI 5.1-7) for HCL and 6.8 (95%CI 6.2-7) for ONC. At the end of the study period, 91% of MSS had been discontinued, mostly due to disease progression (HCL: 51.2%; ONC: 72.2%) and toxicity (HCL: 18.3%; ONC: 13.1%). Median TD was 5.55 (95%CI 5.1-6) months. TD was <6 months in 61.3% of HCL patients and 56.0% of ONC patients; 40% of patients underwent a new treatment after the MSS and 15% ≥2 treatments.

Conclusion/Recommendations: We provide a comprehensive assessment of MSS in a multicentre cancer institution. MSS is commonly practiced across almost all cancer types. Although some patients received off-label agents as part of frontline therapy, most received this as therapy for advanced disease. This, along with ECOG PS≥2, was related to a worse survival outcome. Information about clinical outcomes in our cohort is valuable and contributes to better decision-making regarding MSS.

007

Dostarlimab in the treatment of recurrent endometrial cancer: real life experience

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Objective/Purpose: Dostarlimab is a monoclonal antibody that blocks the programmed cell death protein 1 (PD-1) receptor. The European Medicines Agency approved its use in 2021 for the treatment of patients with advanced endometrial cancer (EC) with loss of base-pairing repair mechanism (dMMR) or microsatellite inestability high (MSI-H) who have progressed during or after prior platinum-based treatment. Thus, dostarlimab represents a therapeutic alternative that changes the treatment paradigm for this disease. This medicine is hasn't been commercialised in Spain yet, so the access to it is done through the "Medicines in Special Situations" application of the Ministry of Health. The objective is to analyze the effectiveness and safety of dostarlimab in patients diagnosed with recurrent CS in a tertiary hospital.

Study Design/Methods: Observational, retrospective, single-center study that included all patients (n=4) with SC who were authorized for treatment with dostarlimab in our center. The follow-up was carried out until July 2022. Socio-demographic, clinical and treatment-related data were collected using the hospital's electronic medical record program and the Farmis-Oncofarm® onco-hematological patient management software

Results/Key Findings: Two patients achieved complete response and currently continue with the treatment after a follow-up of 15 and 17 months, respectively. Another patient experienced progression after two cycles and died 4 months after starting with dostarlimab. The fourth patient did not start treatment due to a rapid clinical deterioration that required admission to the Palliative Care Unit. In terms of toxicity, an elevation of transaminases grade 1 (G1) was recorded in one of the patients, as well as asthenia and anorexia G1 in another one. None of the adverse effects involved treatment delays or interruptions.

Conclusion/Recommendations: Dostarlimab is a new therapy for EC with good results based on our limited experience. The toxicity profile was manageable, with all adverse events being G1.

008

Medication-related osteonecrosis of the jaws and CDK4/6 inhibitors in breast cancer

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Objective/Purpose: medication-related osteonecrosis of the jaw (MRONJ) is a relatively uncommon but serious complication of osteoclast inhibitors therapy with intravenous bisphosphonates and denosumab. Dose, schedule, and duration of inhibition are associated with MRONJ risk. Marcianò et al.[1] launched an alert about a possible association between MRONJ and cyclin-dependent kinase (CDK)4/6 inhibitors in breast cancer patients with osteoclast inhibitors therapy. This study aims to evaluate the use of CDK4/6 inhibitors as a risk factor for MRONJ in our cohort of patients with metastatic breast cancer and denosumab.

Study Design/Methods: retrospective observational study. All patients with denosumab for breast cancer (January 2011-February 2022) were included. Cases of MRONJ found were described. Relationship between CDK4/6 inhibitors and MRONJ was analysed with a Chi-square analysis.

Results/Key Findings: 223 patients were included. 12 cases of MRONJ were detected: 91.7% (11/12) women. 41.7% (5/12) with extraosseous metastases. Median treatment duration for denosumab was 19 months (1-25). 6 with a CDK4/6 inhibitors (3 palbociclib, 1 abemaciclib and 2 ribociclib). Median treatment duration with CDK4/6 inhibitors was 22.5 months (17-29). The mean time from the start of denosumab to the appearance of the event was 19.5 months (1-32). Incidence of this complication in patients treated with denosumab but without CDK4/6 inhibitors was 4.65% (6/129) and 6.38% (6/94) in patients with denosumab and a CDK4/6 inhibitor. Although the group with CDK4/6 inhibitors had a higher incidence of MRONJ cases, the difference was not significant (0.07).

Conclusion/Recommendations: The incidence of MRONJ in our cohort of patients with metastatic breast cancer and denosumab was higher in the group of patients with CDK4/6 inhibitors. However, this difference was not significant. Our data is higher than those reported in the literature according to which the risk of MRONJ with denosumab is 1.1% during the first year, 3.7% the second year and 4.6% per year thereafter. Studies with more patients would be necessary to confirm the relationship between the use of CDK4/6 inhibitors and MRONJ.

009

Efficacy and safety outcomes of generic imatinib in adults with chronic myeloid leukaemia (CML) following the switch from branded imatinib

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Objective/Purpose: Since 2017, generic formulations of imatinib from different manufacturers have become available in the UK. The use of generic imatinib created concern within the CML community, including patients and physicians. The aim of this study was to investigate the efficacy and safety outcomes of generic imatinib after the switch in adults with CML at Oxford University Hospitals (OUH) reviewing real-world UK practice.

Study Design/Methods: This is an observational retrospective study of anonymised data from medical records of patients with CML from diagnosis until December 2019 for whom the treatment was switched from brand to generic imatinib in 2017. To assess efficacy laboratory results were reviewed for disease status with molecular response using BCR-ABL1 international scale (IS) polymerase chain reaction (PCR) values before and after the switch. Survival was also assessed. To assess safety patients' notes and laboratory results were reviewed for documentation and comparing the numbered (%) of adverse events (AEs) on original imatinib with persistent, worsening and newly reported AEs of generic imatinib after the switch.

Results/Key Findings: For 42 patients included, the median value of the 3 BCR-ABL (IS) PCR performed before the switch was 0.0096 with the median value after the switch 0.00205. Median PCR values after the switch had reduced by 0.00755 in favour of generic imatinib when using descriptive statistics. When doing the Wilcoxon test statistic analysis, the p-value of 0.070 showed that there is not a statistically significant difference between branded imatinib and generic imatinib. When the Wilcoxon rank test was done with the 40 patients on complete cytogenetic response (CCyR) and the 34 patients on major molecular response (MMR) statistically there is a significant difference in favour of using the generic. Adverse effects (AEs) reported were similar when comparing pre- and post- switch periods with only a significant difference in favour of generic for thrombocytopenia (p=0.039). After switching 9 patients had worsening AEs: 5 (12%) anaemia, 2 (5%) muscle cramps, 1 (2%) fatigue and 1 (2%) periorbital oedema. New AEs were reported after the switch in 25 patients with the most reported: 4 (9%) with nausea, 3 (7%) with diarrhoea and 3 (7%) with neutropenia.

Conclusion/Recommendations: Results show that generic imatinib is the same as branded imatinib in terms of efficacy so it does not affect the effect on patients' CML and the safety profile is the same or better than branded imatinib. An interesting result to consider is when I only included the patients on CCyR or MMR before the switch the analysis showed that the generic did better. AEs are well-tolerated after the switch due to patients managing the AEs or less reporting of them. This finding shows that it is effective and safe to switch to generic imatinib then to support its continued use. More patients with a longer follow-up are required to confirm this conclusion.

Funding: Oxford University Haematology fund

010

Reproducibility analysis of PRONTO, chemotherapy order verification checklist

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Objective/Purpose: To evaluate the reproducibility of PRONTO (Patient, Regimen, Organ Function, Numbers, Toxicity, Order Verification), a checklist was created to assist young and/or non-specialist oncology pharmacists to review chemotherapy orders.

Study Design/Methods: Retrospective cross-sectional study where one hundred chemotherapy orders of adult patients in cancer treatment were checked by two pharmacists that used a checklist composed of 30 questions grouped in 06 domains (Patient, Regimen, Organ Function, Numbers, Toxicity, Order Verification). For Intraobserver Analysis, pharmacist #1 checked all the prescriptions twice with an interval of 15 days between them. For Interobserver Analysis, pharmacist #2 checked all the prescriptions once. Descriptive statistics of sample and Intraclass Correlation Coefficient were performed using the software IBM SPSS Statistics for Windows, version 19 (IBM Corp., Armonk, N.Y., USA).

Results/Key Findings: Women were the majority of patients (61%) and the mean age was 61 years (SD ± 14,93). Gastrointestinal (29%), breast (25%), and genitourinary (10%) were the primary sites of cancer. On the day of infusion, patients used a mean of eight medicines [IQR 4-12] including drugs for other reasons than cancer. 794 were prescribed to all patients and 84 medication errors were detected (10,57%). Intraobserver reproducibility were classified as excellent (ICC > 0,75; p< 0,001) in 07 questions and were classified as regular to good (ICC 0,40-0,75; p< 0,001) in 13 questions. Interobserver were classified as excellent in 02 questions and as regular to good in 06 questions.

Conclusion/Recommendations: PRONTO checklist demonstrated good to excellent intraobserver reproducibility in the majority of domains and low interobserver reproducibility, showing differences in medication error detections when performed by different pharmacists. This could be explained by differences in the educational background of pharmacists and the systematization-checking process of chemotherapy orders. More studies about checklists elaboration for chemotherapy order review should be performed in the future.

Posters
Clinical Science (CS)

011

Real-world data with pembrolizumab plus chemotherapy in the first line treatment of non-squamous metastatic non-small cell lung cancer

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Objective/Purpose: Due to the strict eligibility criteria of clinical trials, there is often uncertainty about the applicability of their results in the real-world setting. The main objective of this study was to evaluate the effectiveness of pembrolizumab combined with chemotherapy in the first-line treatment of patients with metastatic non-squamous non-small cell lung cancer (NSCLC). Secondary objectives were to analyze the clinical characteristics of treated patients and their mutational profile, in order to figure out if there was any correlation with overall survival (OS).

Study Design/Methods: Observational retrospective study that included patients with metastatic non-squamous NSCLC in first-line treatment with pembrolizumab plus platinum-based chemotherapy (cisplatin/carboplatin+pemetrexed) from January-2020 to December-2021. Patients with EGFR-activating mutations (exons 18-21), ALK and ROS1 genomic aberrations were excluded. Variables collected were: age, sex, history of smoking, PD-L1 expression levels, baseline Eastern Cooperative Oncology Group Stage Performance Status (ECOG PS), brain metastasis, comorbidities and cancer mutations determined by Next Generation Sequencing (NGS). Effectiveness was measured in terms of response according to RECIST 1,1 criteria, progression free survival (PFS) and OS. Kaplan–Meier analysis was performed through long-rank test to assess the relationship between variables and OS.

Results/Key Findings: 71 patients fulfilled the inclusion criteria. Main characteristics were: 77.5% men, the mean age (±SD) 62 years (±7.7), 90% current/former smokers, 25% had brain metastasis, 82.5% ECOG 0-1, 95.7% PD-L1<50% (9.8% negative, 32.4% <1% and the rest 1-49%), mean Charlson Comorbidity Index (CCI)=0.53 (range:0-2), 52.1% CCI=0, 43.2% CCI=1 and 5.6% CCI=2. 81.7% of patients had NGS available of which the 68,9% (n=40) had some mutation. More than one mutation was identified in 10 patients (14.1%). The most frequently mutations were KRAS (n=24), BRAF non-V600E (n=6), PIK3CA (n=4), ERBB2 (n=4), EGFR non exons 18-21 (n=3), MET (n=3). Proportion of women with mutations was significantly higher (87.5% vs 47.3%; p= 0.017).42.5% of patients had partial response, 27.5% stable disease, 15% progression disease, and non-evaluated the rest. At the cut-off date (September 30, 2022), 73.2% and 50.7% of patients had progressed and dead, respectively. 19.7% continued in treatment and the rest discontinued for several causes. Median OS and PFS were 15 months (95% CI, 6.6-23.4) and 5.0 months (95% CI, 3.4-6-5), respectively. There were statistically significant differences in OS according to sex and ECOG. Median OS in men was 9 months (95% CI, 5.6-12.4) vs. not reached in women, p=0.018. Median OS in patients with ECOG ^{3};2 was 2 months (95% CI, 0-5.4) vs. 17 months (95% CI, 0-0) in patients with ECOG<2, p=0.001. No differences were found related to KRAS mutations.

Conclusion/Recommendations: PFS and OS outcomes in our cohort were inferior to those obtained in the pivotal trial (KEYNOTE-189). In terms of OS, the benefit observed was significantly higher in women and patients with good PS. The proportion of patients with oncogenic mutations was high, being of a very heterogeneous nature. No mutations with a significant effect on survival were identified.

012

Are antiemetic prophylaxis regimens of Hematopoietic Stem Cell Transplantation in hematologic malignancies patients appropriate?

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Objective/Purpose: To assess the appropriateness of antiemetic prophylaxis regimens (APR) for conditioning protocols in hematopoietic stem cell transplantation (HSCT) in hematologic malignancies patients at our institution, based on the emetogenic risk chemotherapy and best clinical evidence available.

Study Design/Methods: Nine conditioning HSCT protocols (BUCY, BEAM, Melphalan 140, Melphalan 200, Cyclophosphamide ICT, low intensity FLUBU, myeloablative FLUBU, TBF, thiotepa-carmustine) were reviewed at a third hospital level in Seville, Spain, in October 2022. The audit focused on (1) To review the best clinical-evidence related to APR for conditioning protocols in HSCT. (2) To describe the emetogenic risk of conditioning protocols based on drugs, doses and days of chemotherapy. (3) To assess the APR appropriateness to best available evidence. (4) To establish an APR proposal based in best evidence, if need it. (5) To check for potentials interactions between APR and concomitant medication in each conditioning protocol.

Results/Key Findings: Evidence in APR for conditioning protocols in HSCT is scarce. 6/9 conditioning protocols were classified as highly emetogenic (BUCY, BEAM, Melphalan 140, Melphalan 200, Cyclophosphamide ICT, Thiotepa-Carmustine). Neurokinin 1 (NK1) P receptor antagonists are not currently used in our protocols. In highly emetogenic regimens the current APRs are based on ondansetron 8 mg/8 h, dexamethasone 4 mg/12 h, with a length depending on the scheme. Metoclopramide was used as a rescue therapy. In moderately emetogenic regimens APR is based on ondansetron 8 mg/8h. Therefore, the APRs used in our institution doesn't follow evidence-based recommendations (NCCN, ASCO PETHEMA guidelines and RCT phase 3 FONDO). Based on these recommendations, the APR proposal for highly emetogenic regimens is based on +/- olanzapine 10mg oral on all chemotherapy days plus 3 additional days after chemotherapy in addition to receiving standard triplet therapy (ondansetron 8 to 16 mg p.o. /i.v. and dexamethasone 8 to 20 mg p.o. /i.v. on each day of chemotherapy and fosaprepitant 150 mg IV on 1 day. After assessing the potential risk of interactions between APR proposal and concomitant treatment, the only drug contraindicated was phenytoin in HSCT protocols carrying busulfan. Phenytoin reduce also olanzapine levels so it could be necessary to increase olanzapine dose. There is also a contraindication of fosaprepitant and ondansetron with azoles due to increased concentrations of fosaprepitant and increased risk of prolonged QT interval respectively. Olanzapine may also prolong QT interval in combination with azoles, although this interaction is considered moderate to severe depending on the interaction-database. However, since our protocols incorporate micafungin as antifungal rather than azoles, the only clinically relevant interaction in our protocols is with phenytoin, which could be modified by levetiracetam to over the potential interaction.

Conclusion/Recommendations: Evidence in APR for conditioning protocols in HSCT patients is scarce. But according to best clinical-evidence a consensus was reached to optimize APR at our institution and to replace phenytoin for levetiracetam to over the potential interactions.

013

Anticancer drug utilization and adverse drug reactions (ADRs) in patients receiving chemotherapy in a tertiary hospital, Abuja

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Objective/Purpose: Identification of the various cancer types managed with chemotherapy to determine the pattern of anticancer drugs prescribed with the aim of studying the anticancer drug utilization pattern, the prevalence and management of adverse drug reaction in patients receiving chemotherapy. The study outcome like several drug utilization studies helps to facilitate rational drug use which in turn improves therapeutic efficacy and reduces cost.

Study Design/Methods: Observational follow-up study of newly diagnosed patients, (age 14 years and above) receiving chemotherapy at the Chemotherapy ward of National Hospital Abuja (a 450 bedded tertiary health institution, located in the central part of the country –Nigeria), between January 2021 and December 2021. Data were collected from consented patients' medical record folder, prescription and interview and documented in a suitably designed proforma over a period of six months. Descriptive statistical tools were used to analyze the data and results presented in figures, tables and graphs.

Results/Key Findings: Among the 269 patients involved in the study comprising of male (26%) and female (74%). Breast cancer was the commonest (44.1%) cancer type observed, while the age range with the highest case is 36 to 45 years (31.9%). The average number of drugs per prescription is 8.56, with Carboplatin (18.2%) being the most prescribed anticancer medicine and dexamethasone (13.34%) was the most prescribed adjuvant medicine. About 98.8% of the prescribed medications were from the National Hospital formulary while 93% were prescribed in generic names. Hypertension was the commonest comorbid condition amongst the 107 patients observed with comorbidity with about 59.8% followed by diabetes. ADRs were observed in a number of patients as 91.5% of the studied patients had side effects, which include GIT manifestations, hypersensitivity reactions, myelosuppresion, Alopecia and others, with varying severity, management and outcomes.

Conclusion/Recommendations: This study shows that the management of cancer in the facility in question is individualized and rationale. Although, not in consonance with the World Health Organization (WHO) core prescribing indicators, however, it is consistent with the recommendations of the National Comprehensive Cancer Network (NCCN) Guidelines. It is advocated by WHO that such drug evaluation studies should be encouraged in other healthcare settings.

014

Effectiveness of irinotecan-bevacizumab scheme in second-line treatment of gliomas

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Objective/Purpose: Malignant glioma represents the most frequent form of primary brain tumors. Glioblastoma multiforme is included in glioma classification as the most aggressive central nervous system tumor with a median overall survival of 5 to 12 months. The standard first-line treatment for these tumors consists of surgical excision followed by radiotherapy and adjuvant chemotherapy. Currently, there are no drugs in Europe authorized as a second-line treatment. However, it is common to use off-label schemes which try to combat angiogenesis and vascularization of these tumors, such as the combination of irinotecan and bevacizumab. The aim of this study is to evaluate the effectiveness of irinotecan-bevacizumab scheme in second-line treatment of patients diagnosed with glioma, based on progression-free survival (PFS) and overall survival (OS) results.

Study Design/Methods: Observational, retrospective and descriptive study in patients diagnosed with glioma and treated with irinotecan-bevacizumab scheme in the last two years [from April 2020 to April 2022]. The following data were recorded from the electronic medical records: sex, age, diagnosis, date of treatment initiation, discontinuation and/or death. Kaplan-Meier statistical method was used for the estimation of PFS and OS and were compared with the results of published trials.

Results/Key Findings: The study population consisted of 17 patients (N=17) with a median age of 50,7 years [27-61], 58,8% (n=10) were men and 41,2% (n=7) were women. As first-line treatment, 88,3% (n=15) had been treated with temozolomide in combination with radiotherapy, while 11,7% (n=2) were treated with procarbazine, lomustine and vincristine. The median PFS for the study regimen was 3,2 months, (30% PFS at 6 months) and the median OS of this sample was 7,2 months (56% OS at 6 months).

Conclusion/Recommendations: The available phase II trials studying this combination obtain better results than those in our population, with a median of 6 months PFS and 10,5 months OS. The difference in results may be due to a smaller sample size and the characteristics of the patients included in our study, being less strict with inclusion criteria than trials and giving us real world evidence.

015

Safety of tyrosine kinase inhibitors in chronic myeloid leukemia

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Objective/Purpose: Since the discovery of imatinib in the mid-1990s, tyrosine kinase inhibitors (TKIs) have been the first line of treatment in chronic myeloid leukemia (CML), obtaining unprecedented results in disease control. Although they are safe drugs, they are not exempt from toxicity, so their continued use is conditioned by their tolerance. Each molecule has different pharmacodynamic characteristics that determine its safety profile and open up the possibility of selecting the most appropriate treatment according to the clinical history of each patient. The aim of this study is to analyze the adverse effects related to ITKs and their implication in treatment changes.

Study Design/Methods: Retrospective descriptive study in which CML patients' treatment with ITKs from November 2020 to April 2022 were included. Database was created with the following variables: sex, age, ITK, line of treatment, start and end date, and adverse reactions described in the electronic medical record. Statistical analysis was performed using Rcommander® software. To establish the incidence of adverse reactions by drug group, not only the current treatment was taken into account, but also the existence of this type of reaction in previous treatments. The classification was based on the Common Terminology Criteria for Adverse Events (CTCAE).

Results/Key Findings: This study included 31 patients with a mean age of 54,3 years [23-85], 58% of whom were men (n = 18). Imatinib was the most commonly used drug as first line treatment in 80,6% (n=25) of patients, followed by nilotinib 12,9% (n=4) and dasatinib in 6,5% (n=2) (Table 1). Among the group of patients initially treated with imatinib, 40%(n=10) are currently in a second or third line of treatment. Half of them (n=5) had to switch ITK as a consequence of imatinib toxicity, related to grade II-III gastrointestinal and musculoskeletal reactions. In contrast, in the nilotinib group, there was no discontinuation of treatment due to adverse reactions and, among patients treated with dasatinib, there was one change of treatment as a consequence of pleural effusion (n=1). No statistically significant differences were detected between the three treatment groups (p=0,43).

Conclusion/Recommendations: Imatinib, being the most widely used ITK in routine clinical practice, is characterized by gastrointestinal and muscular toxicities, which are limiting treatment continuation. New generation ITKs, with different safety profiles, show adverse reactions whose incidence and severity can be higher than those with imatinib. It is necessary to know the incidence of these reactions in routine clinical practice and to continue increasing the study population with the aim of detecting clinical and genetic factors which predispose to these reactions.

016

Incidence and management of neutropenia during treatment with palbociclib

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Objective/Purpose: Cyclin-dependent kinase inhibitors (iCDK4/6) have consistently proven themselves as first- and second-line treatment for locally advanced or metastatic hormone receptor-positive, HER2-negative breast cancer. The aim of this study is to evaluate the incidence of neutropenia during treatment with palbociclib its management and clinical impact on the patient.

Study Design/Methods: Observational and retrospective study. All patients who received treatment with palbociclib in the previous 5 years were included. The toxicity was evaluated in accordance with the Terminology Criteria for Adverse Events (CTCAEC4.0) and its management was obtained from the medical records program.

Results/Key Findings: 26 patients were included in the study. All of them were women, mean age 57 years. 39% started it as first-line treatment for metastatic disease. 24 (92%) patients started with a dose of 125 mg.12 (57%) patients presented neutropenia, being grade 3 in 11 patients, whereas grade 2 appeared just in one patient. The pharmacological management was a temporary suspension of treatment in 87% of the cases and the dosage adjustment in 80%. Half of the patients requiring a first dose adjustment (100 mg) needed a second dose reduction (75 mg) Treatment suspension occurred in 19 patients. In 90% of these, the reason for discontinuing was disease progression, while in the rest (2 patients) it was due to the presence of side effects. Switching to another cyclin inhibitor was undertaken in only one patient.

Conclusion/Recommendations: More than half of the patients treated with Palbociclib have presented neutropenia, however, in most cases it has been possible to continue treatment by adjusting the dosage without having to suspend the drug.

017

Real-world effectiveness of short-course radiation therapy followed by preoperative chemotherapy in locally advanced rectal carcinoma

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Objective/Purpose: To evaluate the effectiveness of the Rectal cancer And Preoperative Induction therapy followed by Dedicated Operation (RAPIDO) trial's treatment in real clinical practice. According to the RAPIDO clinical trial, patients diagnosed with locally advanced rectal carcinoma received short-course radiotherapy (5 days × 5 Gray) followed by 6 cycles of CAPOX (capecitabine 1000 mg/m^2 twice daily on days 1–14, oxaliplatin 130 mg/m^2 on day 1, and a chemotherapy-free interval between days 15–21) or 9 cycles of FOLFOX (oxaliplatin 85 mg/m^2 on day 1, leucovorin 200 mg/m^2 on days 1 and 2, followed by bolus fluorouracil 400 mg/m^2 and fluorouracil 600 mg/m^2 for 46h, and a chemotherapy-free interval between days 3–14) followed by total mesorectal excision.

Study Design/Methods: Retrospective observational study that included all patients diagnosed with locally advanced rectal cancer from a third-level hospital, who had been treated with the treatment of the RAPIDO clinical trial (NCT01558921) from May 2020 to April 2022. Data was obtained from electronical medical history and the oncology software Farmis-Oncofarm. Variables included were: sex, age, distance from the tumor to the anal margin, TNM clinical stage, number of hospital admissions, chemotherapy cycles received, dose reduction and discontinuation of treatment. Effectiveness was assessed in terms of number of events of disease-related treatment failure defined as the first occurrence of locoregional failure, distant metastasis, new primary colorectal tumour, or treatment-related death. Descriptive statistical analysis was performed using SPSS v25.0.

Results/Key Findings: 25 patients were selected, 80% men, median (IQR) age: 62 years (53-70). At the time of analyses, median follow-up was 16.23 months (IQR 13.27–16.28). The location of the tumor according to the distance to the anal margin was divided into <5cm (56%), 5-10 cm (20%) and >10 cm (24%). The clinic of the patients at diagnosis was rectorrhagia (36%), rectal tenesmus (20%), constipation (20%), weight loss (16%), fecal occult blood (12%) and diarrhea (12%). Stage T at diagnosis was T3 (68%), T4 (32%) and nodal was N0 (4%), N1 (32%) and N2 (64%) while stage T after surgery was T0 (56%), T2 (12%), T3 (32%) and nodal was N0 (52%), N1 (12%), N2 (8%) and Nx (28%). Regarding chemotherapy tolerance, 60% (n=15) of patients completed all scheduled cycles and 36% (n=9) patients required hospital admission during the treatment period. Dose reduction of chemotherapy occurred in 40% (n=10) of patients and 36% (n=9) of patients prematurely stopped preoperative chemotherapy due to relevant toxicity. At 1 year follow up after the end of preoperative treatment, 84% (n=21) of patients remains without tumour progression and only 16% (n=4) of patients have experienced disease-related treatment failure.

Conclusion/Recommendations: The baseline characteristics of patients treated with the RAPIDO clinical trial's treatment in our hospital was very similar to the participants selected in the original clinical trial, specifically the TN stage at diagnosis and after surgery. The effectiveness results observed in real clinical practice appear to be inferior to those obtained in the RAPIDO clinical, although our sample size and design are limited.

018

Evaluating the workload of pharmacist assessments of Nirmaltrelvir/Ritonavir (Paxlovid) prescriptions by oncology pharmacists at a tertiary outpatient cancer centre

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Objective/Purpose: Polypharmacy is common in oncology patients due to complicated anti-cancer therapy regimens, use of supportive medications, and treatment of comorbid conditions. Patients on chemotherapy may be taking CYP3A4 substrate anti-cancer drugs with a high toxicity profile susceptible to interactions with nirmatrelvir/ritonavir (Paxlovid). Assessing these types of interactions is time consuming and challenging in the community pharmacy setting. The purpose of this study was to exhibit the intensive time involvement of dispensing a Paxlovid prescription, evaluate time spent during the pharmacist assessment process and demonstrate the necessity for clinical pharmacy services for oncology patients.

Study Design/Methods: This was a study analyzing the Paxlovid requests at our academic tertiary cancer centre. Outpatient oncology patients at the center who received a Paxlovid prescription and pharmacist referral from the physician between April 6 2022 and August 19 2022 were prospectively allocated and extracted through a retrospective chart review through electronic health record software. After receiving a referral, the pharmacy team logged the time spent on each step in prescription processing. Prescription processing was categorized by the following steps: (1) order review of the computerized provider order entry (CPOE), (2) assessing dosing for kidney function, (3) obtaining a Best Possible Medication History (BPMH), (4) assessing and managing drug-interactions and (5) counselling. The number of drug interactions per prescription and determining the prescriptions dispense location were extracted. Available data was then descriptively summarized. The time for each prescription processing step and number of drug interactions were reported as a median.

Results/Key Findings: A total of 122 Paxlovid prescriptions were identified, 58% were for females (n=70). Of the steps in prescription review, the most time consuming step was assessing and managing of drug-interactions at 15 minutes (n=59, range: 0-100) followed by patient counselling and obtaining a BPMH, taking 10 minutes (n=40, range: 0-25) and (n=48, range: 0-35) each, respectively. The least time consuming steps were reviewing the CPOE and assessment of renal function at 5 minutes (n=56, range: 0-45) and (n=57, range: 0-15) each, respectively. The highest number of Paxlovid referrals in one day was six (range: 0-6). Of the prescriptions requesting a pharmacist referral, they were only dispensed at the Odette Cancer Centre 59% of the time. The other 41% of the time they were either transferred to a different pharmacy to be dispensed or deemed ineligible for treatment after assessment. The average number of clinically significant drug interactions per prescription was one (n=107, range: 0-5).

Conclusion/Recommendations: The processing of Paxlovid prescriptions was highly time consuming and the majority of assessments revealed at least one clinically significant drug interaction requiring intervention. These types of assessments are often not possible in the community pharmacy setting due to lack of resources and access to pertinent clinical information. A large percentage of Paxlovid prescriptions were never dispensed through the centre, suggesting there is a large portion of time-intensive oncology pharmacist assessment that goes without remuneration. This study demonstrates there is a need for clinical pharmacy services to ensure the safety of prescribed medication therapy for oncology patients.

019

Effectiveness and safety of CAR T-cell in acute lymphoblastic leukemia pediatric. Real-life data

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Objective/Purpose: To evaluate the effectiveness and safety of tisagenlecleucel (tisa-cel) in acute lymphoblastic leukemia (ALL) in post-transplant relapse or in second or subsequent relapse in pediatric patients and to compare with the Pivotal Clinical Trial ELIANA.

Study Design/Methods: Retrospective observational study that included all patients treated with tisa-cel (October2019-September 2021) in a reference tertiary level hospital. The following variables were recorded: sex/age, previous chemotherapy regimens, dose of tisa-cel, infiltration by blasts or minimal residual disease (MRD) prior to infusion, complete response (CR/CRi) at 3-months, progression-free survival (PFS) and overall survival (OS) at 6-months, adverse events reported (AEs) and need for corticosteroids or tocilizumab or second line therapies (siltuximab or anakinra). Complete response (CR/CRi) at 3 months was used as the main endpoint to assess effectiveness, and event-free survival and overall survival as secondary endpoints. To assess safety, the rate of occurrence of adverse events described in the label was used, especially grade 3-4 (according to CTCAE "Common Terminology Criteria for Adverse Events version5" and ASBMT "American Society for Transplantation and Cellular Therapy"). We obtained data from the electronic-prescribing-system (Athos®), electronic-medical-record (Diraya®) and processed with Excel-Microsoft-Office-2010®.

Results/Key Findings: 9 patients (56% girls) were analyzed. Median age was 8 years (IQR: 4-14). The baseline characteristics of our group of patients were different from those of the Pivotal Clinical Trial (PCT:ELIANA) in terms of previous treatments: allogeneic Hematopoietic Stem Cell Transplantation (allo-HSCT: 100% *vs* 61%) and use of Blinatumomab (22% *vs* 0%). Median dose of tisa-cel: 2,4 cel/kx10^6 (IQR: 1.85-3.1). 66.7% patients had infiltration by blasts or MRD prior to infusion (56% patients>50% lymphoblasts: high disease burden *vs* 68% in PCT). Regarding CR/CRi at 3-months: 66% were in complete response *vs* 81% in the PCT. PFS rate at 6-months: 37.5% *vs* 73% in PCT; Median PFS: 5 months (IQR: 2.5-8.5). OS rate at 6-months: 62.5% *vs* 90% in PCT; Median OS: 8.5 months (IQR: 4.5-9); 44% had a survival of less than 9 months. Regarding relapses, as in PCT most (74%) were CD19- and occurred in the context of B lymphocyte aplasia, in our patients they accounted for 50% of relapses. Regarding safety, 33% of the patients developed grade-2 cytokine release syndrome (CRS) and 22% grade-3, all receiving tocilizumab. 33% of patients also presented macrophage activation syndrome (MAS) and 22% disseminated intravascular coagulation (DIC). 33% of the patients received corticosteroids (mean duration 4 days). 22% of the patients suffered neurotoxicity, one grade-2 and the other grade-3. 44% had persistent cytopenias and 33% of the patients grade 3-4 infections.

Conclusion/Recommendations: In our study, the effectiveness is lower than that obtained in PCT; it could be explained by differences in the basal characteristics of our patients, however the safety is better. The evaluation of effectiveness and safety in real world data of advanced therapies is an essential tool to complete the information obtained from clinical trials and patient follow-up. The low number of patients is an important limitation to draw conclusions, which makes it advisable to add the available data in real world data in different healthcare centers.

020

Hospital pharmacist´s role in the management and care process of CAR-T cell therapies

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Objective/Purpose: Chimeric antigen receptor T-cell (CAR-T) are medicines for human use, which belong to the group “Advanced therapy medicinal products”. Our objective is to describe the role of the oncohematology pharmacist in the different phases of the pharmacotherapeutic process involving CAR-T.

Study Design/Methods: Observational, retrospective, single-center study. Patient’s data were collected in a tertiary hospital using the Farmis-Oncofarm® software for onco-haematological patient management.

Results/Key Findings: Twenty patients received CAR-T cell therapies in our hospital: 11 commercial, 5 clinical trials and 4 academic cells. The oncohematology pharmacist is part of a multidisciplinary clinical team, and participates in the assessment of patients who are candidates for CAR-T treatment, as well as in their follow-up. One of their key roles is the management of the adverse effects related to this therapy: the pharmacist must ensure the availability of supportive therapy (tocilizumab and siltuximab) in hospital wards. He is also in charge of doing all reports in Farmacovigilance and toxicity matters. On the other hand, the pharmacist is responsible for the management of these medicines, from acquisition and reception (temperature and transport conditions, traceability and correct labeling), custody and storage (ensuring the temperature of the nitrogen tank), to defrost, dispensation and administration. Prior this last step, the pharmacist validates, prepares and dispenses the lymphodepletion chemotherapy and also validates the CAR-T protocol, which includes its premedication. Finally, the pharmacist reviews and reconciles the patient’s medication at discharge. Out of the twenty treatments, one incidence was found in the labelling process.

Conclusion/Recommendations: Hospital pharmacist is an essential professional within the multidisciplinary clinical team for the correct management of CAR-T cells, taking a lead role in the management of these medicines and in the traceability, quality and safety of the entire pharmacotherapeutic process.

021

Effect of oral antineoplastic drugs on fertility, pregnancy and driving ability

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Objective/Purpose: Influence on fertility, pregnancy and driving ability are very relevant aspects of treatment with cytostatics that are not usually addressed in the medical visit. The objective was to collect information on the effect of oral antineoplastic agents (OAA) on fertility, pregnancy and the influence on driving ability.

Study Design/Methods: All oral antineoplastic drugs authorized by the European Medicines Agency (EMA) until November 2021 were identified. Information about how OAA could affect female and male fertility, as well as recommendations for contraceptive measures and their duration over time were reviewed. British Columbia Cancer Agency database (BC Cancer), Spanish Medicines Agency and Health Products (AEMPS) and FDA label were reviewed. Potential risks during pregnancy were classified following FDA: category C (no satisfactory studies in pregnant women, but animal studies demonstrated a risk to the fetus), category D (studies in pregnant women have demonstrated a risk to the fetus, but potential benefits of the drug may outweigh the risks) or category X (contraindicated in pregnancy). In addition, effects on the ability to drive were reviewed following the classification of the European DRUID project (Driving Under the Influence of Drugs, Alcohol and Medicines) with a scale ranging from 0 (no or negligible influence) to III (mayor influence on driving fitness).

Results/Key Findings: A total of 68 OAA were reviewed. In the FDA classification regarding the influence on pregnancy, 2 had category C, 25 had category D, 6 had category X and 35 didn't have any category assigned.24 (35%) OAA could affect female fertility, one of which could cause irreversible infertility and two reversible. On the other hand, 38 (56%) could affect male fertility, 3 irreversible and 7 reversible. Ovules and/or sperm preservation are recommended in 11 drugs. There is not information in 38 drugs about their influence on fertility. For all of them, contraceptive measures were recommended during and after treatment, both in male and female, but their duration was variable. According to their influence on driving ability, 13 were in category 0, 43 in category I, 11 in category II and 1 in category III.

Conclusion/Recommendations: Influence on fertility, pregnancy and driving skills is relevant and frequent with OAA. These topics should be always addressed before starting a new treatment. Contraceptive measures should be used during and after treatment. OAA affect more frequently male than female fertility. A high percentage of OAA lack information on the effect in pregnancy and fertility.

022

Real world dose evaluation of Cyclin-kinase 4/6 inhibitor treatment in women treated for advanced breast-cancer

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Objective/Purpose: The aim of this study is to analyse initial dose, dose reduction and adverse events of CK 4/6 inhibitors in our population.

Study Design/Methods: Retrospective pharmacy electronic chart review of patients in treatment with Abemaciclib, Palbociclib or Ribociclib at a tertiary University Hospital. All patients on active treatment with CK4/6 inhibitors during the last two months (August-September 2022) were included. Drug selection depended on date of commercial availability, adverse effect profile and drug interactions. Variables were retrieved from the Electronic Health-Care Record and information system that managed the dispensation for Outpatients Unit at de Pharmacy Department. Variables analysed were: age, drug, initial dose, actual dose, reason to reduce dose and adverse events (AE) severity graded with CTCAEv5. Dose reductions were analysed by drug and age. For quantitative variables mean or median were calculated, and for categorical variables frequencies. The statistical program SPSS was used.

Results/Key Findings: 69 patients were included. Mean age was 63.0 (95%CI: 60.0-66.0), 33/69 (47.8%) of the patients were ≥ 65 years old. 12/69 (17.4%) patients were treated with Abemaciclib, 49/69 (71.0%) with Palbociclib and 8/69 (8.6%) with Ribociclib. All patients started at European Medicines Agency (EMA) recommended full dosing. Dose was reduced in a total of 26/69 (37.7%) patients (5/26 Abemaciclib (19,2%), 18/26 Palbociclib (69,2%), 3/26 Ribociclib (11,5%)) following recommendations for dose adjustment in EMA drug labels. By age, dose was reduced in 14/33 (42.4%) of elderly patients (2/14 Abemaciclib (14,3%), 12/14 Palbociclib (85,7%)). Among all patients treated with Palbociclib, the dose was reduced in 6/18 (33%) patients under 65 years old and 12/18 (66%) patients over 65 years old, p=0.0509. Actual reduced doses: Abemaciclib: 2 patients with 150 mg/day (50% of initial dose) and 3 with 200 mg/day (66% of initial dose); Palbociclib: 4 patients with 75mg/day (50% of initial dose) and 14 with 100 mg/day (80% of initial dose); Ribociclib 3 patients with 400mg (66% of initial dose). AEs were the only reason to dose reduction. Theses AEs were with Abemaciclib: Grade 3 neutropenia in 2 patients and G3 diarrhoea in 3 patients; Palbociclib: 18 patients with G3 neutropenia in 18 patients, 1 besides with G3 thrombocytopenia and another patient also with G3 asthenia; Ribociclib: G3 neutropenia in 3 patients.

Conclusion/Recommendations: About 40% of the patients in treatment with CK4/6 inhibitors needed a dose reduction for AE management, 80% of initial dose for Palbociclib and lower to 66% for others CK4/6 inhibitors. Palbociclib was involved in 85,7% of AES who needed dose reduction, 66% of these patients were elder than 65 years old. In our patients haematological AEs were the reason to dose adjustment in 88% of the cases, however gastrointestinal AEs were as well relevant for Abemaciclib

023

Effect of trastuzumab treatment interruption on survival of HER2-positive metastatic breast cancer patients

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Objective/Purpose: Female breast cancer (BC) is the most frequently diagnosed in all regions of the world and a major concern for health systems. Trastuzumab, first monoclonal antibody targeting the HER2 receptor, presented a significant impact on the overall survival (OS) and progression-free survival (PFS) of patients who overexpress this receptor. The OS mean for patients with stage IV BC at diagnosis varies between 2 and 3 years, and long-term survival (>5 years) is still uncommon. We aimed to analyze the effect of interrupting trastuzumab treatment on OS and PFS, in two years, of patients with HER-2 positive metastatic breast cancer.

Study Design/Methods: Retrospective cohort of women diagnosed with HER2-positive metastatic BC, treated with trastuzumab between 2013-2017. Sociodemographic, clinical and therapeutic variables were collected. Trastuzumab treatment interruption was defined as discontinuation of more than six weeks. The estimates of OS and SLP in two years were performed by the Kaplan-Meier method and Log-rank test, with $p<0.05$ for significance. The univariate analysis was performed for all the study variables, those with significance ≤ 0.20 were included for the multivariate analysis. Proportional risk analyses were performed using the Cox Regression model.

Results/Key Findings: Of all the 107 patients included in the cohort, 56 interrupted their trastuzumab treatment at some moment. The mean OS was 20.4 months (95%CI 19.4 – 21.4). The mean PFS was 13 months (95%CI 11.5 – 14.4) and 84 patients had disease progression within two years. OS was higher and statistically significant in patients that had their trastuzumab treatment interrupted when compared to those who underwent the treatment without interruptions (p=0,000). In the univariate risk analysis, uninterrupted treatment was considered a risk factor for death (HR=3.94). The final risk model adjusted for endocrine therapy, *KPS* and number of metastatic sites at diagnosis showed that non-interruption of the treatment presented an independent effect on the risk of death (HR=3.14).

Conclusion/Recommendations: In our cohort, women who had treatment interruption had longer overall survival compared to those who had treatment without interruption. Studies indicate that continued exposure to antineoplastic treatment in patients with metastatic breast cancer may increase the risk of severe toxicities, compromising survival. In addition, future study, including molecular and genetic alterations, could be developed to identify their influence on prognosis of the patients.

024

Characterization of skin toxicity with anti-PD-1/PD-L1 treatment

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Objective/Purpose: To describe the occurrence of skin adverse events (AEs) during the treatment with immune checkpoint inhibitors against programmed cell death protein 1 and its ligand (anti-PD-1/PD-L1).

Study Design/Methods: Retrospective observational study carried out in all patients who had started treatment with an anti-PD-1/PD-L1 between 2015 and 2018 for Oncology indications. Sex, age, drug used and duration of treatment were collected. Regarding the appearance of skin AEs, skin and subcutaneous tissue disorders and their severity were collected according to the CTCAE v.5 as well as the median time until the onset of the AEs (weeks) and their duration (days).

Results/Key Findings: A total of 249 patients were included with a median age of 63.0 years [p25:56.0 – p75:70.0]. There were 195 men (78.3%). These patients had received: 193 nivolumab (77.5%), 46 pembrolizumab (18.5%), 9 atezolizumab (3.6%), and 1 avelumab (<1.0%) with a median duration of treatment of 23.4 weeks [p25:10.6 – p75:54.9]. There were identified 177 skin AEs: 93 grade 1 (52.5%), 65 grade 2 (36.7%) and 19 grade 3 (10.7%). Grade 3 AEs were: 7 cases of pruritus, 2 eczemas, 1 urticaria, 1 hyperhidrosis, 1 rash acneiform, 1 dry skin, and 5 other alterations (Fournier's gangrene, lichen planus, psoriasis, bullous pemphigoid, and psoriasis). All grade AEs were reported in 82 patients (32.9%) while grade 3 AEs in 15 patients (6.0%). The median time to onset for all AEs was 23.0 weeks [p25:8.0 – p75:50.4] and their median duration was 21.0 days [p25:14.0 – p75:56.0].

Conclusion/Recommendations: There is a high rate of patients with skin AEs during the treatment with anti-PD-1/PD-L1. However, most of the skin AEs were mild or moderate in severity according to CTCAE v5. Pruritus is the most common skin AE with grade 3.

025

Impact of the administration of prior targeted treatment for the BRAF V600 mutation on overall survival of patients with advanced melanoma treated with immunotherapy

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Objective/Purpose: To evaluate the impact of the administration of prior targeted therapy in the overall survival of patients with advanced melanoma and BRAF V600 mutation which are treated with an immune checkpoint inhibitor (CPI).

Study Design/Methods: Retrospective observational study in patients diagnosed with advanced melanoma and BRAF V600 mutation which had started treatment with CPI between 2015 and 2018. It was collected: sex, age, CPI, line of treatment and administration of a targeted therapy prior the CPI. The effectiveness was evaluated as overall survival after the beginning of the administration of systemic treatment for advanced disease (OST) using the Kaplan-Meier method. OST was defined as the time elapsed from the start of the first line therapy until death or censoring. The impact on effectiveness was analyzed using Cox regression and Hazard-ratio (HR).

Results/Key Findings: Fourteen patients with a median age of 64.5 years [p25:58.8 - p75:70.0] started treatment with a CPI in this period, 6 of whom were women (42.9%). These patients were treated with nivolumab (11 patients, 78.6%), pembrolizumab (2, 14.3%), and ipilimumab (1, 7.1%). The treatment indication was first line in 7 (50.0%), second in 6 (42.9%) and third line of treatment in 1 (7.1%). Six patients had received targeted therapy for BRAF V600 mutation (3 patients dabrafenib and trametinib, 2 patients vemurafenib and cobimetinib, and 1 patient vemurafenib monotherapy). The OST of patients who received prior targeted therapy was 15.1 months (95% CI: 2.4 – 27.8); however, this median OST was not reached in those who did not receive prior targeted treatment, log Rank 0.045. The rate of OST at 12 and 24 months was 66.7% and 33.3% in those who received prior targeted therapy while OST rate at 12 and 24 months in those who did not receive targeted treatment before the CPI was of 100.0%. Administration of prior targeted treatment had a HR for OST of 3.670 (95% CI: 0.951 – 14.169), p 0.059.

Conclusion/Recommendations: Patients treated with targeted treatment to BRAFv600 prior to immunotherapy have shown worse results in terms of OST than those who receive immunotherapy as initial lines of treatment. However, treatment failure may be affected by other factors.

026

Influence of brain metastases on the effectiveness of immunotherapy in patients with non-small cell lung cancer

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Objective/Purpose: To analyze the influence of brain metastases on the effectiveness of immunotherapy treatment in patients with non-small cell lung cancer (NSCLC).

Study Design/Methods: Retrospective observational study in patients diagnosed with NSCLC who started treatment with immune checkpoint inhibitors between 2015 and 2018. The following data were collected: sex, age, drug, treatment indication and presence of brain metastases at the start of treatment. Treatment effectiveness was evaluated as overall survival (OS) after starting the administration of immunotherapy using Kaplan-Meier survival curves. It was also calculated the HR for OS by Cox regression.

Results/Key Findings: A total of 165 patients were included. There were 24 women (14.5%). The median age was 64.0 years [58.0 – 70.0]. These patients were treated with: nivolumab (128 patients, 77.6%), pembrolizumab (30, 18.2%) and atezolizumab (7, 4.2%). Nineteen patients (11.5%) showed brain metastases at the start of treatment. Among patients with brain metastases, 2 (10.5%) were treated as first line therapy, 7 (36.8%) as second, 6 as third (31.6%) and 4 (21.1%) as fourth or later while those without brain metastases received these drugs 12 (8.2%) as first line, 92 (63.0%) as second, 31 (21.2%) as third and 11 (7.5%)) as fourth or later. Patients with brain metastases showed a median OS of 13.1 months (95% CI: 0.0 – 28.0) versus 12.3 months (95% CI: 10.4 – 14, 1) of those without them, log-Rank 0.587 (Figure 16). The OS rate at 12 and 24 months was 57.9% and 28.9% in patients with brain metastases and 50.9% and 30.8% in patients without them. The value of HR for OS for presence of brain metastases was 1.157 (95% CI: 0.683 – 1.959), p 0.587.

Conclusion/Recommendations: A considerable number of patients with NSCLC have brain metastases at the start of treatment with immunotherapy. No statistically significant differences were detected in terms of the impact of these brain metastases on the effectiveness of treatment, despite the fact that a greater number of patients with brain metastases were treated as third line treatment or later.

027

Prophylaxis with oral clonazepam in adult patients conditioned for stem cell transplant with high dose busulfan

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Objective/Purpose: The incidence of seizures due to high-dose busulfan was about 10% in patients with no prophylaxis, and decreased to 0.5-5% after the introduction of phenytoin prophylaxis. Seizures have been described during busulfan administration or within 24 hours after the last dose. Due to their favorable toxicity profile and lack of interactions, benzodiazepines have been proposed as prophylaxis of busulfan induced seizures. Although they are broadly used in pediatric patients, the experience in adults is limited. The objective of this study is to describe the safety and effectivity of a fixed dose of oral clonazepam (1 mg every 8 h, [q8h]) in adult patients receiving intravenous high dose busulfan (IVBU), as part of a hematopoietic cell transplant conditioning regimen.

Study Design/Methods: This prospective, observational study, was performed from May 2014 to June 2022. Inclusion criteria included: age over 18 years, patients that had received IV high dose busulfan (at least 3.2 mg/kg/day for 2 days), and prophylaxis with oral clonazepam 1 mg q8h starting 12 h before IVBU, until 24 h after the last dose of IVBU. The primary endpoints were the occurrence of seizures until 72 h after finishing busulfan administration, and adverse events associated with the use of clonazepam. The following covariates were recorded: age, sex, diagnosis, type of transplant and conditioning regimen used. Ethical approval for this study was obtained from the Institutional Review Board. Written informed consent was obtained from all participants.

Results/Key Findings: Fifty-nine patients, 23 female and 36 male, median age 51 years [range 22-69], were included. Most frequent diagnosis was acute myeloid leukemia (31 patients), followed by myelodysplastic syndrome (8), multiple myeloma (5), myelofibrosis (4), diffuse large B cell lymphoma (2), mantle cell lymphoma (2), acute lymphoblastic leukemia (2), chronic myeloid leukemia (2), chronic myelomonocytic leukemia (2) and follicular lymphoma (1). Autologous transplant was performed in 11 patients, and allogeneic transplant in 48 (17 related donor, 13 unrelated donor, 18 haploidentical). Busulfan dose was 3.2 mg/kg every 24 h with a variable duration of 2–4 days. The drugs which were associated with IVBU in the conditioning regimen were: fludarabine (21 patients), fludarabine-thymoglobulin (12), fludarabine-thiotepa (10), etoposide-cytarabine (6), melphalan (4), fludarabine-cyclophosphamide (3), cyclophosphamide (2) and fludarabine-thiotepa-thymoglobulin (1). No seizures were recorded. The drug was well tolerated. The adverse effects possibly or probably associated with clonazepam were somnolence (39%; in 6.8% dexchlorpheniramine was administered simultaneously), instability/dizziness (23.7%), disorientation (1.7%) and cognitive disturbances (1.7%); all of them were of grade 1-2 and resolved without intervention. The 100% effectiveness data is in agreement with our previous study using the same clonazepam regimen but administered intravenously. Also, with the study of Carreras et al., 2010, that used clonazepam 0.025-0.03mg/kg/day as a continuous infusion.

Conclusion/Recommendations: Clonazepam at an oral fixed dose of 1 mg q8h is easily administered and very effective for the prevention of high dose busulfan induced seizures in adult patients. The toxicity associated with the drug was mild and transient, mainly somnolence and instability/dizziness.

028

Safety of adjuvant trastuzumab emtansine for the treatment of HER2-positive early breast cancer with invasive residual disease

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Objective/Purpose: Trastuzumab emtansine (T-DM1) was approved by the European Medicines Agency (EMA) based on the results of the pivotal trial (PT) “KATHERINE”, for use in the adjuvant treatment of adult patients with HER2-positive early breast cancer (EBC) who have invasive residual disease, in breast and/or lymph nodes, after neoadjuvant taxane-based treatment and HER-2 targeted therapy. T-DM1 demonstrated a significant benefit achieving an 11% reduction in relapse at 3 years compared to trastuzumab. Our aim is to describe the use of TDM-1 in patients with HER2-positive EBC, evaluating its safety profile in clinical practice and comparing it with PT results.

Study Design/Methods: Retrospective descriptive study that included patients with HER2-positive EBC on neoadjuvant T-DM1 treatment from 01/2021 to 10/2022. The following variables were collected from the clinical history and the onco-haematology prescription programme: age, Eastern Cooperative Oncology Group (ECOG), hormone receptor (HR) status, Ki67, neoadjuvant chemotherapy schedule, T-DM1 cycles received and end of adjuvant therapy. To assess the safety profile, the occurrence of adverse events (AE), use of filgrastim, dose reductions, delays and treatment interruptions were collected. AE were classified according CTCAE scale v5.0.

Results/Key Findings: 14 women with a median age of 55 years (36-83) were included. ECOG: 0 (78,6%) and 1 (21,4%). HR was positive in 71,4% with a mean Ki67 value of 21%. 50% received neoadjuvant treatment based on Trastuzumab+Docetaxel+Carboplatin (TCH), 14,3% TCH+Pertuzumab, 21,4% Doxorubicin+Cyclophosphamide followed by Paclitaxel with Trastuzumab+Pertuzumab. Of the remaining patients one received Trastuzumab+Pertuzumab and the other Nab-paclitaxel+Carboplatin+Trastuzumab. Median of T-DM1 cycles received: 9,5 (1-14). At the time of analysis 4 patients had completed adjuvant therapy. AE were observed in 85,7% of patients, all grade 1-2. Most commonly: fatigue 42,9%, increased transaminases 42,9%, anemia 35,7%, platelet count decreased 35,7%, nausea 28,6%, althralgia 28,6%, hypertension 21,4%, headache 14,3%, neutrophil count decreased 14,3%, dyspnea 14,3%, dysphagia 14,3%, dizziness 14,3% and abdominal distension 14,3%. No AE grade ≥ 3 was observed. 28,6% patients received filgrastim, 28,6% had dose reduction, 28,6% experienced delays due to toxicities and no one had treatment discontinuation. In the PT, AE were observed in 98,8% of patients, the most frequent were: fatigue 49,5%, nausea 41,6%, platelet count decreased 28,5%, AST increased 28,4%, headache 28,4%, althralgia 25,9% and ALT increased 23,1%. AE grade ≥ 3 was experienced by 25.7% of patients. 10,4% had dose reduction and 18% treatment discontinuation. Delays in treatment were not recorded in the PT.

Conclusion/Recommendations: The AE profile of T-DM1 in our study was similar to that reported in the PT, however these results should be interpreted with caution considering our limitations of small sample size and short time period; they could be complemented with results obtained in other real-world cohorts and their comparison with the PT.

029

Real-world effectiveness and safety of second-line atezolizumab in advanced bladder cancer

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Objective/Purpose: To evaluate the effectiveness and safety of second-line atezolizumab in patients with advanced bladder cancer, given its controversial clinical trial methodology with its predefined hierarchical analysis.

Study Design/Methods: Observational, retrospective, single-center study which included patients diagnosed with advanced bladder cancer, and pre-treated with first-line chemotherapy treatment. Patients started atezolizumab treatment between June 2014 and September 2021, and they were followed until September 2022. These patients from our center are also part of a multicentric study. The following variables were recorded: demographical (sex, age), clinical (Eastern Cooperative Oncology Group (ECOG)), presence of autoimmune diseases, disease stage, number and locations of metastases, chemotherapy used in first-line (and second-line, if applicable), and time between last chemotherapy administration and first atezolizumab infusion, and analytical (hemoglobin < or > 10 mg/dL). Variables are presented in median and interquartile range (IQR)The effectiveness variables recorded were: best response reached, progression-free disease (PFS), and overall survival (OS). The safety variable recorded was the presence of adverse effects (AE) according to Common Terminology Criteria for Adverse Events (CTCAE v. 5.0).

Results/Key Findings: 32 patients were included (28 men). The median age was 71 years [range: 48-80]. 50% of patients (n=16) had an ECOG=0 at the beginning of atezolizumab treatment, while the 50% left were ECOG=1. None of them had autoimmune diseases diagnosed. Patients' disease stages were 3A (3.1%), 3B (21.9%), 4A (21.9%) and 4B (53,1%) and the number of metastases ranged from 0 to 3. being extrapelvic node and visceral the two most frequent metastases (28.1% each), followed by liver (21.9%), bones (15.6%), and retroperitoneal (9.4%). First-line chemotherapy used was platinum plus gemcitabine in 90.2% of patients, gemcitabine in 3.1%, cisplatin plus radiotherapy in 3.1%, and gemcitabine plus radiotherapy in 3.1% of patients (two patients were treated with second-line chemotherapy: gemcitabine plus radiotherapy and paclitaxel plus gemcitabine). The median time from the last chemotherapy to the first atezolizumab infusion was 105 days [IQR 40.0 - 182.3]. Hemoglobin levels were <10mg/dL in 18.8% of patients (n=6). Best response reached was complete response in 3.1% of patients (n=1), partial response in 3.1% (n=1), stable disease in 31.3% (n=10) and progressive disease in 46.9% (n=15) of patients. A response could not be evaluated in 15.6% (n=5) of patients because of the worsening health conditions. PFS was 4.4 months (CI95%: 2.2-6.6), while OS was 6.6 months (CI95%: 1.1-12.1). At the end of the follow-up, 9.4% (n=3) of patients' disease did not progress, and 12.5% (n=4) were still alive. AE were present in 53.1% of patients (n=17), being asthenia the most frequent (15.6%), followed by anemia, hyperthyroidism, hepatitis, nephritis, pruritus and constipation (9.4% each; n=3). Of these, grade 3/4 AE was recorded in 9.4% (n=3) of patients with nephritis, 6.3% (n=2) of patients with hyperthyroidism, and in 3.1% (n=1) of patients with whether hepatitis, pruritus, or nephritis.

Conclusion/Recommendations:

- In our real-world study, atezolizumab showed as an effective second-line treatment for advanced bladder cancer, although these data should be considered with caution until multicentric study with further follow-up is available.
- Adverse effects were as expected with atezolizumab treatment.

030

Effectiveness and safety of adjuvant pembrolizumab and nivolumab in high-risk resected melanoma patients

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Objective/Purpose: High-risk resected melanoma have at high-risk of recurrence although regional or distant metastases may be surgically resected. In the adjuvant context, pembrolizumab and nivolumab have demonstrated efficacy and safety in mitigating this risk. The aim of this study was to analyze the effectiveness and safety of nivolumab and pembrolizumab in adjuvant treatment in patients with high-risk resected melanoma in real live.

Study Design/Methods: Descriptive, observational and retrospective study of all patients with high-risk resected melanoma melanoma treated with nivolumab and pembrolizumab, under follow-up from the oncology and pharmacy department of a tertiary hospital from April 2019 to September 2022. Variables collected: demographic (sex and age), clinical (disease stage, Eastern Cooperative Oncology Group (ECOG) and BRAF biomarker mutation), pharmacological (treatment with nivolumab or pembrolizumab) and median treatment time. The endpoints were the percentage of patients alive at the end of the study, and the effectiveness by relapse-free survival (RFS). The safety was studied by recording adverse effects (AE).

Results/Key Findings: Twenty-two patients were included with a mean age of 67,6 ± 12,6 years, of whom 31,8% (n=7) were male. Of the patients, 9% (n=2) had stage IIIA, 27,3% (n=6) stage IIIB, 45,5% (n=10) stage IIIC and 18,2% (n=4) stage IV disease (all of them in treatment with nivolumab). 59% (n=13) had ECOG 0 before starting therapy and 41% (n=9) ECOG 1. The BRAF mutation was present in 45,5% (n=10) of the patients and was unknown in 4,5% (n=1). Of all patients, 54,5% (n=12) were treated with nivolumab and the rest with pembrolizumab. The median treatment duration was 9,63 months (0,5-12) and 86,4% (n=19) of patients remained alive after the end of the study. 54% (n=12) of patients completed 12 months of adjuvant treatment and the rest had to discontinue due to loss to follow-up 4,5% (n=1), unacceptable toxicity 9% (n=2), progression 23,7% (n=6) or death 4,5% (n=1). The median RFS was not reached. 50% of patients who completed treatment showed no signs of progression at 6 months and the other 50% (n=6) have so far also shown no signs of progression although they have recently finished adjuvant treatment with nivolumab or pembrolizumab (1-3 months) and their effectiveness at 6 months could not yet be assessed. Regarding the safety profile, 72,7% (n=16) had some type of AE and these were mainly: skin rash in 45,5% (n=10); asthenia in 31,8% (n=7); arthralgia, nausea and vomiting in 18,2% (n=4); diarrhoea and headache in 13,6% (n=3) and hair loss, renal failure, hypothyroidism, ataxia, dyspnoea, flu-like syndrome and paraesthesia in 4,5% (n=1) of patients.

Conclusion/Recommendations: Our study population includes patients with a higher median age, higher percentage of women and higher ECOG than the population of the pivotal clinical trials (Checkmate 238 and Keynote-054). None the less, the effectiveness, the percentage of patients completing treatment as well as the main adverse reactions are very similar to these pivotal clinical trials. However, further long-term clinical follow-up is needed to evaluate the RFS in patients who have recently completed one year of adjuvant treatment.

031

Everolimus therapeutic drug monitoring in cancer renal patient when drug-drug interaction is suspected: from precision to individualized treatment

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Objective/Purpose: Several new oral targeted therapies have become available in oncology over the past two decades. Mostly, drug label establishes a standard fixed dose, that may result in higher variability in pharmacokinetic profile, lower efficacy or higher toxicity of the treatment. Therapeutic Drug Monitoring (TDM) can be used to select the appropriate dose for each individual patient. In this case report we exposed how individualized everolimus TDM can help to achieve optimal steady state concentration (Css)

Study Design/Methods: Two interaction databases are used to detect major or moderate potential drug-drug interaction (Drugs® /Lexicomp). We describe a case report of TDM due to a potential everolimus-carbamazepine-phenytoin interaction in cancer renal patient. The administration schedule of everolimus was in a fasting state and whole blood samples were obtained just before taking everolimus after minimum of 14 days after start everolimus treatment and each dose adjustment until achieve optimal Css. A metanalysis reported that a two-fold increase in everolimus Css could lead to reduction in tumour growth and that Css >10ng/ml could be used as cut-off as therapeutic drug level. Ultra-high-performance liquid chromatography coupled to tandem mass spectrometey was used

Results/Key Findings: A 72-year-old woman with smoking and epilepsy history was diagnosed from a stage pT3a renal carcinoma in December 2015. Radical nephrectomy was performed on February 2016 and on September 2018, a pulmonary segmentectomy was practiced due to lung adenocarcinoma. on February 2021 disease progressed (adrenal right massive bleeding and hilar adenopathy). She received first line treatment with nivolumab from May to November 2021, cabozantinib as second line treatment at 60 mg daily, from December 2021 to March 2022 and finally third line treatment with everolimus was started in March 2022 at a standard dose of 10 mg OD (fasting condition, before breakfast). Her chronic medication plan was reviewed by the pharmacist and included Carbamazepine, Phenytoin, Acetaminophen and Tramadol. An interaction within Carbamazepine and Phenytoin was detected since both are strong CYP3A4 inducers and could lead to a decreased blood concentration (Css) and a diminished everolimus efficacy. A TDM was planned after fourteen days of treatment and a Css of 3,7ng/ml was found. Adherence to treatment was reinforced to patient and, since patient didn't have any relevant toxicities, according to patient's oncologist, we suggested an everolimus dose increase to 15 mg (10 mg before breakfast -5 mg before dinner). A second TDM was made two weeks later and showed that Css had increased to 6,4 ng/ml, without relevant toxicities. A new dose adjustment was made up to 10mg BID before meals, and reaching two Css were determined: 10,6ng/ml and 8,7ng/ml and stable disease. Finally, patient died on July 2022 due to lung progression, pleural effusion and respiratory insufficiency.

Conclusion/Recommendations: In this case report the interaction within strong CYP3A4 inducers altered everolimus hepatic metabolism leading to under therapeutic Css. After TDM, everolimus blood concentration rise up from 3.7ng/ml to 10.6ng/ml. Potential drug-drug interactions detection by Clinical Hospital Pharmacist and TDM could be useful to achieve optimal Css and eventually clinical response to treatment in our clinical daily practice

Funding: Therapeutic Drug Monitoring of Everolimus in Oncology: Evidences and Perspectives.

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Pharmacist's role in the management of drug-drug interactions caused by nirmatrelvir/ritonavir in COVID-19 oncohematology patients

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Objective/Purpose: The antiviral drug nirmatrelvir/ritonavir (NMV/r) has been licensed to treat patients with COVID-19 at high risk of progression to severe disease, such as oncohematology patients. The NMV/r is a CYP3A inhibitor and can increase plasma concentrations of drugs primarily metabolized by CYP3A. They are also substrates of CYP3A. Oncohaematology patients are at high risk of drug-drug interactions (DDIs). The main objective was to assess the severity and pharmacist detection of clinically relevant potential DDIs OF NMV/r and concomitant medications in oncohematology patients with confirmed SARS-CoV-2 infection.

Study Design/Methods: A prospective, observational,6-month study was conducted in a tertiary hospital, including all oncohematology patients undergoing treatment with NMV/r. A Board Certified Oncology Pharmacist (BCOP) attended the study population and checked the treatment. Potential DDIs with a high degree of probability of clinical relevance will be reported to the prescribing physician describing the severity of the DDIs with recommendations. The severity of DDIs was evaluated using three different databases (Lexi-Interact®, Micromedex® and Liverpool's website). The DDIs were classified as C, D, or X according to their Lexi-Interact rating (C=monitor therapy, D=consider therapy modification, X=avoid combination). All identified potential DDIs with a moderate or higher severity rating were recorded. Data on antineoplastic drugs and home treatment were obtained from the electronic prescribing program. The data were analyzed using Statistical Package for Social Sciences v.25.0.

Results/Key Findings: During the study period, a total of 28 oncohematology patients were included, 19 patients with hematological cancers and the rest with solid tumors. Their mean age was 61.4±17.9 years (17–81) and 50% were male. All patients were prescribed NMV/r 300/100 mg every12h for 5 days, with the exception of 4 patients who were prescribed 150 mg/100 mg every12h for 5 days due to renal insufficiency. The mean number of drugs prescribed in total was 6.1±3.9 with a range of 0-14 drugs. Clinically relevant potential DDIs were detected in 17 patients, and the prevalence was therefore 60.7%. The average number of DDIs per patient was 1. The number of DDIs was 29 involving 19 different drug interaction pairs. The drugs most commonly involved in DDIs were: amlodipine, atorvastatin, dexamethasone, fentanyl, imatinib, metamizole and tramadol. The type of DDIs most frequent was category C (58.6%), followed by D (17.2%) and X (10.3%). In all detected DDIs, the pharmacist prevented them from reaching the patient. Suggestions for avoiding the occurrence of types C, D and X included close patient monitoring, consideration of dose reduction (edoxaban and dexamethasone) and discontinuation of the drug (atorvastatin, domperidone and simvastatin) and were accepted in 100 % of cases. Five patients were discontinued due to the following overlapping cycles with COVID-19 and 4 patients had DDIs detected with chemotherapy and NMV/r: 3 had their dose decreased (imatinib and ibrutinib) and 1 had his drug stopped (imatinib).

Conclusion/Recommendations: The prevalence of DDIs with NMV/r and concomitant medications in oncohematology patients is high. The pharmacist can contribute significantly by checking the treatment prescribed and detecting interactions, to reduce medication-related problems and optimize drug therapy for these patients.

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Toxicity events associated to inadequate premedication in patients treated with Pemetrexed in Non-small Cell Lung Cancer (NSCLC)

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Objective/Purpose: The goal of this study is to assess whether non-compliance to the recommended premedication regimes prescribed with Pemetrexed has any impact on the overall toxicity events reported during the treatment of Non-small Cell Lung Cancer (NSCLC). Regimes containing Pemetrexed must include concomitant prescriptions with vitamin B12 and folic acid to reduce the risk of haematological toxicity, and dexamethasone to reduce the risk of cutaneous toxicity. Additionally, the other purpose of this study is also to identify any prescription errors affecting these drugs and to come up with solutions to improve clinical practice.

Study Design/Methods: This is a single-centre retrospective observational study. In it, 102 patients were screened with Pemetrexed prescribed for NSCLC between 01/01/20 and 30/06/21. Of these, 9 patients were excluded from the study as they did not meet inclusion criteria, which were: at least one dose of Pemetrexed administered and patients must have dispensing records available for review. E-prescribing tools / software and medical history were used to review these patients. Endpoints to confirm successful and complete premedication in line with manufacturer's recommendations for Pemetrexed included: prescription date, first dispensing date, dose and frequency, consecutive dispensing records (no 'gaps' during treatment), toxicity events reported and treatment modifications/delay due to toxicity events, amongst others. All of these were analysed for both folic acid and dexamethasone prescriptions. Prescriptions containing vitamin B12 were excluded from this study since its administration was not recorded consistently on the local e-prescribing software.

Results/Key Findings: Among the 93 patients included, 76 patients (81,72%) were inadequately premedicated with either folic acid, dexamethasone or both drugs, and only 17 patients (18,28%) were premedicated as per manufacturer's recommendations. 38 patients (40,86%) had toxicity events (any kind) reported, of these, 36 patients (94,74%) were inadequately premedicated and 2 patients (5,26%) were adequately premedicated.21 patients (55,26%) of the 38 patients who experienced toxicity events (any kind) were identified as having developed either haematological or cutaneous toxicity events likely related to being inadequately premedicated with folic acid or dexamethasone, respectively. Prescriptions and dispensing records also revealed the following: 64 patients (68,82%) of all patients did not take dexamethasone accordingly, of these, 36 patients (38,71%) did not have dexamethasone prescribed at all. These same results for folic acid were 35 patients (37,63%) and 3 patients (3,23%) respectively.

Conclusion/Recommendations: These results suggest that patients on inadequate premedication with folic acid and dexamethasone for Pemetrexed have a greater risk of developing toxicity events (47,37%) compared to those that take their premedication as per manufacturer's recommendations (11,76%). Furthermore, other outcomes from this study may be used to raise awareness and to reduce the risk of preventable toxicity events caused by prescription errors. A double approach is therefore encouraged, based on these results: First directed to prescribers, to ensure these drugs are prescribed correctly and timely; and secondly to oncologists and hospital pharmacists, so they highlight to patients the importance of taking both folic acid and dexamethasone and consequently improving patient adherence.

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Safety profile of cyclin-dependent kinase inhibitors in breast cancer patients

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Objective/Purpose: The introduction of cyclin-dependent kinase inhibitors (i-CDKs) in combination with endocrine therapy represents the most relevant advance in the management of hormone receptor positive (HR+), HER2-negative (HER2-) metastatic breast cancer over the last few years. The aim of our study is to determine the safety profile of treatment with i-CDKs in patients with HR+/HER2- metastatic breast cancer in real clinical practice. As well as to analyse which drug has the most favourable safety profile.

Study Design/Methods: Retrospective observational study including patients with HR+/HER2- metastatic breast cancer, who started treatment with palbociclib, ribociclib or abemaciclib between October 2020 and April 2022. Demographic variables were collected: age and sex; disease-related variables: menopausal status at diagnosis and metastatic disease at onset; pharmacotherapeutic variables: prescribed drug, concomitant hormonal therapy, presence of toxicity and type, dose reduction and/or delay, and treatment termination. The type of toxicity was collected by device and classified according to the Common Terminology Criteria for Adverse Events (CTCAE) v5.0. Data were obtained through the corporate ATHOS program and the DIRAYA clinical history. In the statistical analysis, the quantitative variables were described in tables of frequencies and measures of central tendency. The relationship between the appearance of adverse effects and the drug was studied with the chi-square test. The IBM SPSS 20.0 statistical program was used.

Results/Key Findings: 99 patients were included, with a median age of 59 years (RIQ: 51-69), 98% women. At diagnosis 83.8% were menopausal and 32.3% had metastatic disease. A total of 46.5% (46) of patients were being treated with palbociclib, 27.3% (27) with ribociclib and 26.3% (26) with abemaciclib. Regarding concomitant hormonal treatment, more than half of the patients were on treatment with letrozole (62.6%), followed by 31.3% with fulvestrant. A total of 91.9% of the patients presented some type of toxicity (with no significant differences between abemaciclib, ribociclib and palbociblib), highlighting 65.7% suffering haematological toxicity and 64.6% gastrointestinal toxicity. Greater gastrointestinal toxicity was associated with abemaciclib, 92.3%, versus palbociclib, 56.5%, and ribociclib, 53.8%, (p=0.003) and greater hematologic toxicity with palbociclib, 76.1%, versus ribociclib, 66.7%, and abemaciclib, 46.2% (p=0.037).54.5% of patients delayed dosing due to toxicity (63% of patients with palbociclib, 62.9% with ribociclib and 30.7% with abemaciclib; p=0.018), and 33.3% required dose reduction (no significant differences were found). At the end of the study period, 53.5% of the patients were still on treatment, 30.3% had dropped out due to disease progression, and 16.2% had dropped out due to toxicity.

Conclusion/Recommendations: A priori there are no differences in the presence of toxicity among the three drugs. In our study, abemaciclib and palbociclib have a more unfavourable digestive and hematologic toxicity profile, respectively. Further studies are needed to confirm this trend.

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N-Acetylcistein for thrombotic thrombocytopenic purpura

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Objective/Purpose: Acquired thrombotic thrombocytopenic purpura (TTP) is an acute microangiopathic thrombotic disease affecting many organs and characterized by the presence of haemolytic anaemia, severe thrombocytopenia, neurologic abnormalities and organ failure. The pathogenesis is a deficiency in the plasma metalloprotease ADAMTS 13 (a disintegrin and metalloprotease with thrombospondin type 1 motif, member 13, which cleaves the prothrombotic ultra-large von Willebrand factor (vWF) multimers) due to the appearance of anti-ADAMTS 13 autoantibodies. This deficiency leads to platelet consumption in von Willebrand factor–platelet aggregates and microvascular thrombosis. N-Acetylcistein, a potent antioxidative drug, decreases mucus viscosity by reducing disulphide bonds between mucin multimers. Due to strikingly structural similarities between mucin and vWF, this drug could have the ability of rapidly degrade ultra-large vWF multimers by disrupting the disulfide bonds in human plasma. The objective is to describe the effectiveness and tolerability of NAC used in patients with TTP.

Study Design/Methods: This retrospective, observational study, was performed from September 2018 to March 2022. The patients included in the study were age over 18 years with newly diagnosis of TTP who were treated with NAC. NAC was added the first day of admission at the Haematology ward. The induction dose of NAC was 150 mg/kg/day i.v. in 1 hour followed by 150 mg/Kg/d administered in 17 hours for ten consecutive days. The dose of NAC and the length of therapy was firstly stablished by Li and colleagues, based on recommendations for acetaminophen toxicity. The maintenance dose to prevent relapses was 600 mg/d, orally, and was started on the eleventh day of treatment. The following variables were collected: age, sex, haemoglobin, platelets, LDH and adverse effects reported (CTCAE v5.0). A complete response was considered when the platelet count reach al least 100.000 per cubic millimeter. Ethical approval for this study was obtained from the Institutional Review Board. Written informed consent was obtained from all participants.

Results/Key Findings: Seven consecutive patients with newly diagnosed acquired TTP were treated. The median age was 46 years (range 25-57), 3 men and 4 women. The median of haemoglobin and LDH before the treatment was 8,8 g/dL and 1.130 U/L respectively. All patients were treated with high dose NAC with plasma exchanges and steroids; and 5 patients received rituximab as well. A complete response was observed in all 7 patients. Moreover, a quick complete response, in less than 10 days, was observed in 5 patients (71,4%). This response was not related with the front-line addition of rituximab in some patients. All patients were discharged with oral NAC, but only 5 continued the treatment (2 withdrawals were unjustified). The median duration of follow-up was 8 months and no relapses have been detected to date. Regarding tolerance, no side effects were observed during the 10 days of high-dose NAC infusion. Oral NAC was also well tolerated.

Conclusion/Recommendations: NAC may be a useful supplementary therapy along with plasma exchange and immunosuppressive therapy for TTP patients due to its wide availability, low cost, and safety profile and it could be used before more aggressive agents.

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Clinical benefit analysis from supporting evidence for the use of medicines in special situations in oncology in a comprehensive cancer centre

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Objective/Purpose: The legal framework for the use of medications in special situations (MSS) is the Regulation 726/2004 of the European Parliament and the Spanish RD 1015/2009. It includes any use of a licensed drug other than its marketing authorization (off-label) and an investigational use through a compassionate/expanded access provided by the pharmaceutical company. Drug-indications pending price/reimbursement (P&R) conditions in Spain are also considered as MSS in our institution. We aim to describe the procedure of evaluation of MSS in a comprehensive cancer centre and to focus on the quality of the supporting evidence for solid tumours requests

Study Design/Methods: MSS evaluation depends on the Pharmacy and Therapeutics Committee, a multicentric group composed by oncologists, haematologists, pharmacists, and medical directors. Requesting physicians submit an MSS application form that includes clinical justification and evidence supported by either the ESMO Magnitude of Clinical Benefit Scale Score (ESMO-MCBS) (for randomized phase II-III trials in advanced disease (1-5) and adjuvant setting (A-C)) or the overall response rate (ORR) (if only non-randomized phase I-II trials are available). Ultra-orphan pathology (≤1/50,000) requests are also accepted. For patients ≥75 years the submission must include a favourable geriatric evaluation. Efficacy, safety, and cost are discussed individually by committee in biweekly scheduled meetings, based on the clinical evidence and considering the available alternatives (including clinical trials available at the centre). For approved treatments, efficacy results are collected subsequently. A descriptive analysis of the requests discussed in 2021 is presented (number of requests and patients, department, type of MSS). For oncology requests, alignment to previously described evidence criteria is analysed.

Results/Key Findings: In 2021 there were 550 requests for 495 patients, mean age of 63 (17-89) years and 17.8% ≥ 75 years. This represents a 3.5% of all treated patients (n=14,138) and a 27.3% increase vs 2020. Haematology requests were 50.2% (276), oncology 47.8% (263) and palliative care 2.0% (11). Most frequent solid tumours requested were breast, lung, melanoma, ovarian and prostate (38.9%). For the global study sample and within oncology, requests were classified as unlicensed drug-indications (61.1% [336]; 21.5% [118]), compassionate/expanded access drugs (11.6% [64]; 9.6% [53]) and drugs pending P&R (27.3% [150]; 16.7% [92]). Requests denials were 8.0% (21). Within oncology approved MSS requests (242), supporting evidence was classified as ESMO-MCBS-3 in 30.6% (74), ESMO-MCBS-4 in 12.4% (30), ESMO-MCBS-5 in 2.5% (6) and ESMO-MCBS-A for all the requests in the adjuvant setting (19.4%; 47). The remaining 35.1% were approved with more degree of uncertainty: 5.4% (13) with ESMO-MCBS 1-2, 27.2% (66) from phase I-II non-randomized clinical trials (95.5% with ORR≥30%) and 2.5% (6) were ultra-orphan situations. Although limited evidence of benefit, all these requests were approved by consensus by the committee considering the individual characteristics and clinical context of the patients.

Conclusion/Recommendations: The number and complexity of MSS in oncology is increasing, with different degrees of uncertainty. Discussing MSS through a defined method by a multidisciplinary team is considered helpful for the institution and allows to provide treatment equity. Procedure review along with treatment results evaluation is necessary to identify areas for improvement.

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Pharmaceutical care: Lorlatinib selection in Non-Small-Cell Lung cancer with ROS1 rearrangement

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Objective/Purpose: Pharmaceutical care involves provision of drug information and patient counseling, but clinical pharmacist are also involved in therapy decisions for individual patients, in order to obtain the maximum clinical benefit and improve health outcome efficiently. The objective of the study is to describe an oncology pharmacist intervention in the selection of the best therapy for a patient with non-small-cell lung cancer (NSCLC) ROS1 positive, ALK negative.

Study Design/Methods: A 53-year-old woman was diagnosed in July 2017 with stage IV NSCLC. Molecular analysis revealed ROS1 rearrangement, confirmed by fluorescent in situ hybridization and immunohistochemistry. ALK molecular analysis was negative. ALK and ROS1 are usually approached together as lung cancer oncogenes. The first-in-class molecule crizotinib is a Tyrosine Kinase Inhibitor (TKI) indicated in ALK or ROS1 positive diseases. The patient started treatment with crizotinib 250 mg two times per day. After 27 months of treatment, in October 2019, computed tomography scan showed disease progression with central-nervous-system (CNS) metastases. Due to the treatment failure, a new line of treatment is required and oncology pharmacist, as part of the oncology team, was consulted about alectinib treatment as second line. Alectinib is a second-generation TKI against ALK positive but not retaining anti-ROS1 activity. The oncology pharmacist initiated a bibliographic research with the aim of find the best treatment in ROS1-positive lung cancer after first line therapy progression, and checked the availability of the different options at that moment.

Results/Key Findings: As well as crizotinib, several TKIs are active against ROS1: ceritinib, entrectinib and lorlatinib. In 2019, none of them was authorized by European Medicines Agency (EMA) in ROS1 positive NSCLC. Lorlatinib is a brain-penetrant third generation TKI of ALK and ROS1 and there were studies that showed activity *in vitro* on several crizotinib-resistant ROS1 mutations and a phase I study in which 7 patients with ROS1 positive NSCLC that had previously received crizotinib obtained a median progression-free survival (PFS) of 7 months. We obtained Compassionate Use of lorlatinib by the Spanish Medicine Agency and the patient started treatment with lorlatinib 100 mg daily as an expanded access program to investigational drugs. Currently, in 2022, after 37 months of treatment the patient continues with lorlatinib treatment. She presented some treatment-related adverse events, hypercholesterolaemia and hypertriglyceridaemia, which are consistent with previously published data. The patient presents a performance status 0-1 and the treatment continues as part of expanded access without cost for our hospital, a general publish hospital.

Conclusion/Recommendations: In this case, lorlatinib has proven to be an efficient treatment as second line therapy in NSCLC ROS1 positive with CNS metastases. Oncology pharmacists play an important role in cancer patient care. Pharmacist interventions improve accessibility to cancer treatments and contribute to both clinical and social health outcomes.

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Use of monodose syringes of plerixafor for WHIM syndrome

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Objective/Purpose: WHIM syndrome is a primary immunodeficiency caused by autosomal dominant mutations in chemoquine receptor CXCR4 that leads to pancytopenia, hipogammaglubilemia, infections and warts. Patients are usually treated with granulocyte colony-stimulating factor (G-CSF). Recently, a case series of 3 patients have shown promising results using plerixafor, an inducer of mobilization of hematopoietic stem cells (McDermott et al., 2019). Plerixafor is generally used for bone marrow transplantation and has a high economic impact. Here, we present the case of a patient affected by WHIM syndrome who has been treated with plerixafor for 4 months. Here, we present a 36 years old woman who has the first manifestation (warts) at the age of 12, squamous cell carcinoma diagnosed at 20 and recurrent infections. She has been recently diagnosed with WHIM syndrome, an immunodeficiency caused by a mutation in RAC2 that causes a gain of function.

Study Design/Methods: Endovenous pembrolizumab treatment (200 mg every 21 days) was started in February 2022 to treat metastatic squamous cell carcinoma. After multidisciplinary revision and case discussion, plerixafor treatment was approved and initiated. Initial dose was 0.01mg/kg/12h administered subcutaneously (0.57mg in 0.03ml per dose), and it was sequentially increased to 0.02 (1,14mg in 0,06ml), 0.04 (2,28mg in 0,11ml), 0.06 (3,06mg in 0,15ml) and 0.08 (4,20mg in 0,21ml) mg/kg/12h every three weeks. Monodose syringes without dead-volume (1ml, Braun®) were prepared in a vertical membrane flux cell using aseptic technique according to Good Pharmacy Practice using vials of Mozobil® 20 mg/ml solution for injection. According to the risk matrix described in the Spanish Good Pharmacy Practice in Hospital Pharmacy, syringes were considered stable for 9 days protected from light in the fridge (2-8°C). A hospital pharmacist trained the patient to ensure a proper conservation and administration; the patient had her regular medical appointments with Oncology, Haematology, Infectious Diseases, Dermatology and Wound Care Nurse.

Results/Key Findings: During the 4 months follow-up the patient has only one infection caused by *Candida spp*. that required treatment with fluconazol 200mg every 12 hours. Skin lesions including warts have remarkably improved and it has been an important tumoral response. An increase in all blood cell count was observed over the 4 months of treatment: lymphocytes (0.3 to 0.8*10E9/L), hemoglobin (8.3 to 11.2g/dL) and stable platelet (333 to 296*10E9/L). No allergic reactions have been reported, the onset of flatulence 3 months after treatment initiation could be related to plerixafor, it did not require treatment discontinuation and was managed with probiotics and activated carbon.

Conclusion/Recommendations: Monodose plerixafor syringes for subcutaneous administration have been successfully prepared and self administered. Treatment has been well tolerated by our patient with WHIM syndrome, the only adverse event attributable to the treatment was mild flatulence (due to other comorbidities, it would have been difficult to detect other toxicities such as fatigue or arthralgia). Plerixafor might be an interesting option for patients with WHIM syndrome; however, more data should be gathered in order to confirm its effectiveness.

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Risk factors of cetuximab-related hypomagnesemia in squamous cell carcinoma of head and neck

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Objective/Purpose: Hypomagnesemia is an adverse event associated with cetuximab (Ctx) treatment. However, only a few observational studies have investigated the incidence and risk factors of developing hypomagnesemia or the influence of concomitant drugs. The aim of this study is to identify the incidence of hypomagnesemia and the risk factors associated with Ctx-related hypomagnesemia in patients with squamous cell carcinoma of head and neck (SCCHN).

Study Design/Methods: This is an observational retrospective study including all the patients with SCCHN who were treated with Ctx containing therapy between January 2019 and December 2021 in our center. Sociodemographic and clinical data were collected from clinical records: age, gender, treatment duration, baseline analytical levels (magnesium, calcium, phosphate and proteins), the presence of hypomagnesemia during Ctx therapy, platinum-based chemotherapy history, the use of concomitant omeprazole and other adverse events related to Ctx. Bivariable analysis was performed. Numerical variables were compared using the Student's t-test or the Mann-Whitney test and categorical variables using the $\chi 2$ or Fisher's exact test. Variables with a p-value <0.2 in binary logistic regression were included in a multivariable logistic regression model to assess the factors independently associated with hypomagnesemia occurrence(p-value<0.05).

Results/Key Findings: 74 patients who met eligibility criteria were included. Mean age was 66.0±7.8 and 85% were men. The 71.6% (53) had recurrent or metastatic and 28.4% (21) locally advanced SCCHN. The incidence of hypomagnesemia was 63.5% (47), of which 36.2% (17) was > grade 2. Median baseline serum Mg level was 1.99±0.22 mg/dl. The patients with hypomagnesemia showed significantly higher concomitant use of omeprazole (OR 3.36, 95%CI: 1.050-10.100, p<0.043) and higher Ctx-related skin rash (OR 3.54, 95%CI: 1.260-9.960, p<0.014). Multivariate regression analyses showed the concomitant use of omeprazole (OR 3.860, 95%CI: 1.004-14.840, p<0.001) as independent risk factor. The use of platinum-based chemotherapy, duration of treatment or patients' background data and laboratory values before starting cetuximab therapy did not affect the development of hypomagnesemia.

Conclusion/Recommendations: In our experience, more than half of the SCCHN patients treated with cetuximab developed hypomagnesemia. This study found cetuximab-related hypomagnesemia independently associated with omeprazole concomitant use. Further investigation with a larger sample size is warranted to support the potential association between omeprazole and cetuximab-related hypomagnesemia. In addition, studying the effect of other concomitant drugs or knowing the baseline nutritional status of the patient would provide further evidence.

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Effectiveness and safety of atezolizumab in stage IV small cell lung cancer

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Objective/Purpose: Due to the lack of information about this therapy in real life, this study is designed to be an early analysis of the effectiveness and safety of the combination of atezolizumab with chemotherapy in stage IV small cell lung cancer (SCLC) in clinical practice comparing with pivotal trial.

Study Design/Methods: Retrospective, observational, single center (350-bed university hospital) study of patients diagnosed with **SCLC** in stage IV, that start therapy with atezolizumab as first line treatment, during the period of time: 08/10/2021-01/10/2022. Criteria to receive atezolizumab was: histologic diagnosis of SCLC, no previous treatment, Eastern Cooperative Oncology Group (ECOG) 0-1 and adequate hematological and organic function. Outcomes were collected from medical records and antineoplasic prescription program: Gender, age, diagnosis, stage, initial and final ECOG, smoke habit, cycles and posology received, disease progression, deaths and adverse events (AEs). To evaluate the effectiveness, Progression-free survival (PFS) and Overall survival (OS) were determined by SPSS estadistic application. To evaluate safety, number and type of AEs, delays and reductions were recorded. Results were compared with clinical trial IMpower110.

Results/Key Findings: There were 10 patients (70% male). Population presented a mean age of 64,5 years (50-82). All the patients were diagnosed with SCLC in stage IV. Initial ECOG: 0 (N=4),1 (N=6). Final ECOG: 0 (N=1), 1 (N=7), 2 (N=2). Smoke habit (100%). Mean number of cycles received was 7 (1-16), all the patients received the four first cycles of atezolizumab (1.200mg) combined with carboplatin plus etoposide every 21 days, followed by monotherapy of atezolizumab (1.200mg) every 21 days. At the time of analysis 6 patients (60%) continue treatment, 4 patients (40%) presented disease progression while 3 deaths (30%) were registered. The median PFS, although is not reached yet, appears to be longer than 12 months vs 8,1 months of the clinical trial. The median OS, although is not reached yet, appears to be longer than 12 months vs 13,4 months of the clinical trial. AEs grade I-II were observed in 80% of patients compared with 90% of the clinical trial. Nausea (N=4), asthenia (N=4), diarrhea (N=2), musculoskeletal pain (N=2). No AEs grade III-IV were observed vs 30,1% of the clinical trial. Nausea and asthenia were the most registered AEs while nausea and alopecia were the most observed AEs in the clinical trial. No delays related to treatment were registered in our population, reductions neither.

Conclusion/Recommendations: Our results have a high grade of uncertainty due to the limitation of the small size population. Despite this limitation, PFS observed was longer than in the reference clinical trial, whereas OS was shorter than in the clinical trial. Related to safety, atezolizumab shows a better adverse events profile than in the clinical trial, with a shorter percentage of grade I-II AEs and without grade III-IV AEs.

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Vulvar and vaginal cancer in a third-level hospital

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Objective/Purpose: Vulvar and vaginal cancer are the gynecological cancers with the lowest incidence, so the scientific evidence regarding their management is limited. Treatment, in both localized and metastatic disease, has been extrapolated from the results obtained in cervical cancer clinical trials: surgery in early stages, chemoradiotherapy with cisplatin in locally advanced and chemotherapy with platinum and bevacizumab as initial treatment of metastatic disease. Risk factors involved in vaginal and vulvar cancer have been described, such as human papillomavirus(HPV) infection, toxic habits such as smoking, and age. The objective of this study is to describe the characteristics of patients with vulvar and vaginal cancer and the survival obtained in a third-level hospital.

Study Design/Methods: Retrospective observational study of patients with vulvar and vaginal cancer who were treated with chemotherapy from January 2018 to September 2022. Data were obtained from the electronic medical record and the Farmis-Oncofarm® program. The variables collected were: age, type of cancer (vulvar or vaginal), HPV infection, toxic habits, histology and stage of the tumor at diagnosis, patients treated with adjuvant chemoradiotherapy and in advanced disease as well as the chemotherapy regimens used. There were included those patients with more than 1 chemotherapy cycle. Progression-free survival(PFS) of the disease was measured after early-stage radical treatment and after advanced-stage chemotherapy with paclitaxel-carboplatin +/- bevacizumab. Overall survival(OS) was studied in early and advanced stages of the disease.

Results/Key Findings: 14 patients were diagnosed with vaginal or vulvar cancer with a median age of 72 years(65-78), 11(78.6%) had vulvar cancer and 3(21.4%) vaginal cancer.4(28.6%) patients had HPV infection. No patients smoked. The majority histology was squamous, only 1(7.1%) was adenosquamous. 11(78.6%) patients were diagnosed in early stages.5(45.5%) were treated with surgery and cisplatin-based chemoradiotherapy a median of 5 cycles(5-6), and 6(54.5%) patients with surgery. The median PFS from localized treatment was 12 months(7-21). 9 patients who had received treatment for localized disease and 3 newly diagnosed metastatic patients received treatment for advanced disease.5(41.7%) patients were treated with at least two lines and 2(16.7%) with three lines of therapy. 9(75%) patients were treated with paclitaxel-carboplatin a median of 5 cycles(4-6) achieving a median PFS of 5 months(3.5-9.5), which was the most frequent regimen. 2 patients also received maintenance with bevacizumab(22.2%). A patient was treated with paclitaxel-carboplatin in 1st and 2nd line, in 2nd line combined with cetuximab used off-label achieving PFS of 18 months. Other treatment regimens in advanced disease were: cisplatin-taxol, cisplatin-vinorelbine; cisplatin, taxol, vinorelbine and pembrolizumab(off-label) as monotherapy. The median OS of patients with vaginal and vulvar cancer who received localized treatment was 17 months(11.5-38) versus the OS of treatment in advanced disease that was 15 months(12.5-31.3).

Conclusion/Recommendations: Chemoradiotherapy with cisplatin(+/-initial surgery) continues to be the standard of treatment in high-risk localized stages. In stages IV, the most frequent regimen was paclitaxel-carboplatin +/- bevacizumab. The PFS and OS reached in our study were comparable to that observed in the literature although it was limited by the small sample size. More studies focused on vulvar and vaginal cancer are needed to optimize the therapeutic options of these patients.

042

Safety evaluation of atezolizumab in urinary tract transitional cell carcinoma

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Objective/Purpose: To evaluate the safety in routine clinical practice of atezolizumab in patients with locally advanced or metastatic urinary tract transitional cell carcinoma (including renal pelvis, ureters, bladder and urethra).

Study Design/Methods: Retrospective observational study carried out in a third level general hospital. All patients with urothelial cancer under treatment with atezolizumab between January 2017 and August 2022 were included. The following variables were collected: demographic (sex, age), anatomopathological (type of urothelial cancer), clinical (ECOG, smoking habits and autoimmune diseases) and toxicity (cardiac, cutaneous, endocrine, gastrointestinal, haematological, neurological, ocular, pulmonary, renal and musculoskeletal). The data collected were extracted from the OrionClinic12®, Abucasis® y Oncofarm® computer programs.

Results/Key Findings: Nineteen patients were analyzed, 14 males and 5 females with a mean age of 69±8 years and 61±5 years, respectively. 18 patients were diagnosed with bladder cancer and 1 with ureter cancer. ECOG at baseline: 18 patients ECOG 0-1 and 1 patient ECOG 2. Smoking habits: 10 patients ex-smokers, 7 patients smokers and 2 patients non-smokers. Presence of autoimmune diseases in 3 patients: ulcerative colitis, rheumatoid arthritis and dermatomyositis. Toxicity: cutaneous (pruritus: 1 patient), endocrine (hypothyroidism: 2 patients, hyperthyroidism: 1 patient), gastrointestinal (diarrhoea, nausea and/or constipation: 11 patients, colitis: 1 patient), haematological (lymphopenia and/or anaemia: 16 patients), neurological (meningoencephalitis: 2 patients), pulmonary (pneumonitis: 1 patient), musculoskeletal (asthenia and/or myalgias: 9 patients). It should be noted that the 2 patients non-smokers did not present cutaneous, neurological, pulmonary or musculoskeletal toxicity. No patients had cardiac, ocular and/or renal toxicity. Reason for discontinuation of treatment: exitus 31.58%, disease progression 31.58%, meningoencephalitis 10.53%, pneumonitis 5.26%, colitis 5.26%, immuno-related hepatitis 5.26% and 10.53% continue in treatment.

Conclusion/Recommendations: The safety profile of atezolizumab conforms to that described in the drug's authorisation clinical trials, with no adverse reactions found that have not been previously described.

043

Pharmaceutical care activity at clinical trials unit, focusing in phase 1 trials. experience from two hospitals of a comprehensive cancer institution

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Objective/Purpose: To perform a descriptive analysis of the activities developed by pharmacists in clinical trials (CT) area from two centers from a cancer institution with shared pharmaceutical care procedures, focusing on patients included in phase I CT (PICT).

Study Design/Methods: The portfolio of pharmaceutical care (PhC) tasks in PICT patients agreed within centers to provide equity to patients and is described as follows:1- Pharmaceutical support to researchers, study coordinators, nurses and economic management staff.2- Building CT treatment schemes in the institution's chemotherapy software, used as a support tool throughout the treatment process (prescription, validation, preparation, dispensing and administration). This involves reviewing and calculating of doses, stability, and resolution of aspects related to CT drug compounding and administration.3- Validation of medical prescriptions according to protocol requirements.4- Providing health education to outpatients whenever a new treatment is prescribed or drug dose is changed.5- Evaluation of patient therapeutic compliance (by counting returned medication) and follow-up visit with the pharmacist to reinforce adherence to treatment, if inadequate compliance is detected.6- Patients concomitant medication reviewing and interaction checking during the CT screening process, to detect possible interactions or exclusion criteria related to medication.7- Participation in PICT team meetings. For the analysis, active CTs during 2021 were reviewed, both in active recruitment period and after closing recruitment period. Data from CT involving either oral drug dispensing or parenteral drug compounding was collected classified according to the pathology and the CT study phase. Within PICT, the number of patients attended for the first time, number of preparations, treatment validations, dispensations, screening drug reviews, adherence evaluations and follow-up visits made by the pharmacist were recorded.

Results/Key Findings: As of 31/Dec/2021, there were 777 open CTs in both centers (1,2): (center 1:446, center 2: 331)., . PICT were 15.2% (118) of them (1:14.8%, 2:15.7%), 52.5% (62) corresponding to Hematology CT (1:36%, 2:73%). Pharmacists created 553 protocols (252 and 301) in chemotherapy software, regarding to PICTs initiated in 2021 or previous protocols requiring treatment changes due to CT protocol or pharmacy manual amendments. During 2021, there were 270 PICT patients (157 and 113). Pharmacists treatment validations were 1,842 (1,086 and 756), 3,130 treatments were prepared at a vertical laminar flow hood (2,034 and 1,096) and 1,283 treatments were dispensed (449 and 834). Concomitant medication was reviewed for 214 (149 and 65) screened patients and 78 (48 and 30) health education visits were carried out. Compliance to treatment was reviewed for 1,042 drugs (346 and 696) and pharmaceutical intervention due to inadequate compliance was performed in 76 (41 and 35) cases.

Conclusion/Recommendations: Pharmacist role in CT is wide and carries a significant workload. It offers relevant benefits to patient care, eventually contributing to treatment efficacy. In PICT, where treatment schemes are specially complex, pharmacist role allows preventing medication problems and enhancing adherence to treatment. Collaboration within centers with shared procedures promotes equity in pharmaceutical care for patients treated at the institution.

044

Analysis of the messages sent by breast cancer patients to the oncology pharmacist through an eHealth platform

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Objective/Purpose: To analyze the messages from breast cancer patients received by the oncology pharmacists through an eHealth platform.

Study Design/Methods: Descriptive, retrospective analysis developed in a tertiary level hospital. A web page for healthcare professionals and a mobile application for patients (EMMASalud) was designed and implemented in a new eHealth multidisciplinary healthcare model in the breast cancer outpatient clinic. Patients using the eHealth tool were able to register their symptoms and other variables (psychological, clinical, nutritional and treatment adherence), as well as send messages to a specific healthcare professional, including the oncology pharmacist. Each healthcare professional of the oncology multidisciplinary team could either proactively send messages or respond to messages received. Messages about clinical issues addressed to the oncology pharmacist from September 2020 to September 2022 were analyzed. The variables collected were the number of messages received per patient, the age of the patients and the subject of the consultation classified into 5 categories: compatibility/interactions with other drugs, integrative therapies, symptoms/adverse effects management, other queries about drugs, other queries not related to treatments.

Results/Key Findings: There were 78 patients included in the eHealth platform (98.7% women). Fifty nine patients (75.6%) used the functionality to send messages to any member of the oncology multidisciplinary team, with a total of 636 messages received. The oncology pharmacist received a total of 83 messages on any matter from 19 patients. The total number of messages sent to the oncology pharmacist regarding clinical issues was 60, coming from 18 patients (23% of the patients included in the study). The mean age of these patients was 52 years (range 34-67). The mean number of messages per patient was 3.3 (range 1-13). The percentage of messages for each subject was: 43.3% (n=26) integrative therapies; 33.3% (n=20) symptoms/adverse effects management; 13.3% (n=8) compatibility/interactions with other drugs; 6.7% (n=4) other queries about drugs; 3.3% (n=2) other queries not related to treatments.

Conclusion/Recommendations: The eHealth tool was useful providing pharmaceutical care to breast cancer patients on a sustainable basis in clinical practice. We helped the patient and the team to deal with non-urgent consultations, by facilitating communication and identifying areas of greatest concern, that in our case were integrative therapies and symptoms/adverse effects management.

Funding: Hospital de la Santa Creu I Sant Pau has participated in the EITHealth Oncommun project as an external partner.

045

Effectiveness and safety of pembrolizumab plus chemotherapy in metastatic non-small-cell lung cancer

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Objective/Purpose: To assess the effectiveness and safety of the combination of pemetrexed and cisplatin/ carboplatin plus pembrolizumab as a first line therapy for patients with previously untreated metastatic nonsquamous non–small-cell lung cancer without EGFR or ALK mutations.

Study Design/Methods: This is a retrospective observational study conducted in a 400-bed secondary care hospital serving a population of 250,000 in Spain. We included all the patients that initiated treatment with the therapy combination cited between December/2019 and May/2022. Data were recorded until September/2022. A Microsoft-Excel® database was designed to record and process the following variables: demographics, smoking history, brain metastases at baseline, PD-L1 status, Eastern Cooperative Oncology Group (ECOG) at the beginning of the therapy, duration of the therapy and number of cycles received. The patient response was assessed according to the Response Evaluation Criteria in Solid Tumors (RECIST version 1.1). For toxicity we used the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4. Data were recorded from the electronic prescription program (HPHCISv.3.8 and Farmis-Oncofarm v4.0.11.118). The SPSSv.25 Software was used to conduct the statistical analysis.

Results/Key Findings: Forty-two patients (64.3% men) were included in the study. The median age was 64.5±9.1 years and 92.9% were current or former smokers. Brain metastases at baseline were confirmed in 16.7% of patients. Regarding the PD-L1 expression: PD-L1 1-49% in 21.4% of patients; <1% in 66.7%; could not be determined: 11.9%. The ECOG performance-status was ≤1 in 85.7% of patients, the rest presented an ECOG 2. Cisplatin was chosen as the platinum-based chemotherapy in 52.4% of patients (two of them changed to carboplatin due to cisplatin toxicity). The median duration of treatment was 5.0 months (range, 0.2 to 26.4) and the median number of treatment cycles was 8.0 (1-37). Overall, 9.5% achieved complete response, 50% partial response, and 14.3% had stable disease. For the rest (20.2%): 8 patients died, 3 showed progressions and 2 stopped treatment because of unacceptable toxicity, during the induction (first four cycles). The median Progression-free survival (PFS) was 6.5 months (IC 95%, 3.8 to 9.3). Beyond progression, 18 patients received a second line therapy and 5 patients a third line. The median Overall Survival (OS) was 10.6 months (IC95%, 5.1 to 16.0). At the time of the analysis, 31 patients had died and 8 were still on treatment. Treatment-related adverse events occurred in 78.6% of the patients, most of them grade≤2 (69.7%). The most common treatment-related adverse events were: asthenia (54.8%), nausea and vomiting (28.6%) and cutaneous toxicity (23.8%). Grade 3 more frequent toxicity was diarrhea. Discontinuation of treatment because of treatment-related adverse events occurred in 14.3% of the patients (colitis and pneumonitis mostly).

Conclusion/Recommendations: The effectiveness results obtained in our population were inferior to those observed in the pivotal study KEYNOTE-189. These could be explained, by the presence of patients who started therapy with ECOG2 (not represented in KEYNOTE-189), of whom 50.0% died during the induction. These could represent a less fit population. Finally, the percentage of adverse events was similar to the pivotal study.

046

Prostate-specific antigen decline with apalutamide in advanced prostate cancer treatment

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Objective/Purpose: Apalutamide is indicated for the treatment of nonmetastatic castration-resistant prostate cancer (nmCRPC) with high risk of developing metastases and metastatic castration-sensitive prostate cancer (mCSPC) in combination with androgen deprivation therapy (ADT). The objective was to evaluate the effectiveness of apalutamide in the treatment of prostate cancer for the two indications mentioned above.

Study Design/Methods: A retrospective observational study was developed. Patients diagnosed with prostate cancer who had started treatment with apalutamide from June 2018 to July 2022 were included. Collected data were age, type of prostate cancer (nmCRPC or mCSPC), start and end date of treatment, reason of treatment discontinuation, prostate-specific antigen (PSA) (at baseline, at 1, 3, 6, and 12 months), date of progression and date of death. Effectiveness was evaluated by three variables: the percentage of patients with a PSA decline greater than 50% and 90% from baseline, the percentage of patients with PSA ≤ 0.2 ng/ml (at 1, 3, 6 and 12 months) and the progression-free survival (PFS).

Results/Key Findings: Nineteen patients were included, with a mean age of 78.4 (9.9) years, 63.2% (12 patients) with diagnosis of mCSPC and 36.8% (7 patients) with nmCRPC. The median baseline PSA was 6.5 (IQR 2.5-51.0) ng/ml. At 1 month, 72.2% (13/18 patients) had PSA decrease by more than 50% and 27.8% (5/18 patients) by more than 90%; at 3 months 100% (17/17 patients) had PSA decline by more than 50% and 82.4% (14/17 patients) by more than 90%; at 6 months 91.7% (11/12 patients) had PSA decline by more than 50% and 83.3% (10/12 patients) by more than 90%; and at 1 year 100% (5/5 patients) had PSA decline by more than 50 % and 80.0% (4/5 patients) by more than 90%. In addition, at 1 month 11.1% (2/18 patients) has had a PSA ≤ 0.2 ng/ml, at 3 months 52.9% (9/17 patients), at 6 months 50.0% (6/12 patients) and at 1 year 60.0% (3/5 patients). In 7 (36.8%) patients' treatment was discontinued, 4 due to side effects, 2 due to progression and 1 due to death. The median estimated PFS was 47.1 (95%CI 0.0-95.3) months with a median follow-up of 8.0 (IQR 5.3-14.4) months.

Conclusion/Recommendations: Apalutamide was effective in the treatment of non-metastatic castration-resistant and metastatic hormone-sensitive prostate cancer, achieving high percentages of PSA reduction during first year of treatment. Further clinical practice studies with longer follow-up are needed to determine whether there is a correlation with higher median PFS and overall survival, as shown by post hoc analyses of the TITAN and SPARTAN clinical trials.

047

Health-related quality-of-life in patients with advanced prostate cancer orally treated in a tertiary hospital in Spain. A cross-sectional study

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Objective/Purpose: Prostate cancer accounts for approximately 10% of cancer deaths in men worldwide. Clinical trials for advanced prostate cancer (PCa) have established survival benefit with the use of abiraterone, enzalutamide, and apalutamide. Despite their wide utilization, little is known about health-related quality-of-life (HRQOL) outcomes for these agents. Our aim is to measure HRQOL through Patient Reported Outcomes (PROs) in patients with PCa treated with oral hormone therapy in a tertiary hospital in Spain.

Study Design/Methods: Cross-sectional study. For this population-based study, a survey was administered, which contained validated measures to assess functional outcomes (urinary incontinence, urinary irritation and obstruction, bowel, sexual, and vitality and hormonal function), measured with the Expanded Prostate Cancer Index Composite short form (EPIC-26: 26 items and 5 domains) as it is recommended by the International Consortium for Health Outcomes Measurement (ICHOM). Response options for each EPIC item form a Likert scale, and multi-item scale scores are transformed linearly to a 0-100 scale, with higher scores representing better HRQOL. Using the item groupings listed for each HRQOL Domain Score, average the standardized values for all items within a group to create the summary or subscale score. (If >20% of the items that comprise a domain summary score or subscale score are missing a response, the corresponding domain summary or subscale score can not be calculated)

Results/Key Findings: Forty-two patients accepted and signed the informed consent. The EPIC-26 survey was returned by 34 patients. 28 answered 100% of items, 5 answered 80% of items or more and one of them did not answer any item. The mean and standard deviation of the EPIC-26 domains were: urinary incontinence = 68 ± 34.3, urinary irritation and obstruction = 82±15.6, bowel = 87±16.0, sexual = 11±7.0, and vitality and hormonal function = 64±23.2.

Conclusion/Recommendations: Mean EPIC-26 domain scores were high, indicating good function, except for sexual function, for which scores were much lower. Service improvements around sexual rehabilitation and measures to reduce the effects of androgen deprivation therapy are required. The implementation of PROs systems is beginning to take an increasingly important place in medicine and research patient-focus.

048

Histiocytic Sarcoma successfully treated with anti PD-1 inmunotherapy and radiotherapy: a case report

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Objective/Purpose: Histiocytic sarcoma (HS) is an extremely rare non-Langerhans histiocyte disorder of unknown cause, affecting lymph nodes and extranodal sites, which may be clonally related to a haematological malignancy. Combination of Checkpoint Inhibitors (ICI) and radiotherapy led to promising outcomes in some refractory to chemotherapy-haematological tumours. The biological justification for a potential synergy between them lies in the fact that radiotherapy used for anti-tumour properties increases the expression of PD-1 and PD-L1 in the tumour cells, which may promote the effectiveness of ICI. We aimed to present the case of a patient diagnosed of histiocytic sarcoma stage IV treated with pembrolizumab (anti PD-1) and radiotherapy and to report the effectiveness and safety of treatment.

Study Design/Methods: Case: 32-year-old male diagnosed in November/2021 of HS with a damage in the gluteal region, affecting sacrum and coxal bone, accompanied by extensive supra and infradiaphragmatic lymph node involvement and evening fever. The patient was treated with DHAP, but after two cycles he suffered hearing loss. He refused to continue receiving treatment, requiring a cycle of CHOP therapy. Audiometry did not show significant hearing loss, so treatment with DHAP was continued (with oxaliplatin). The gluteal injury, which previously had decreased, progressed after the 4th cycle, so EPOCH treatment was started. After 2 cycles, the patient has stable disease in the intermediate control but the gluteal injury quickly worsened. The expression of PD-1 was determined in 95% of tumour cells. In this context, based on previous case reports in other pathology, it was proposed combined treatment with pembrolizumab and radiotherapy for this patient. Subsequently, a follow-up of the clinical evolution was conducted during successive visits (June-October 2022) to evaluate the effectiveness and safety of the treatment.

Results/Key Findings: Once literature was review and due to the exceptional nature of the pathology and to the limited availability of therapeutic options, combination of pembrolizumab and radiotherapy was agreed for this case. After 4 months from the start of treatment, our patient had received a total of 6 cycles of Pembrolizumab 200 mg (every 21 days) and 20 Gy of radiotherapy in 5 sessions. At the end of radiotherapy and 3 cycles of pembrolizumab, he experienced a rapid clinical response with no palpable lymphadenopathies, masses or megalia. In the PET-CT performed after the 6th cycle of Pembrolizumab it was observe a marked reduction in the gluteal injury, with some hyper-uptake remnants persisting (partial response) but with a disappearance of supraclavicular hypermetabolic adenopathy and a decreased metabolism of the splenic parenchyma and bone marrow. Regarding the safety, no serious adverse reactions/notable toxicities associated with the treatment were detected. Only skin rash, which responded to topical treatment, and grade 1 asthenia were observed.

Conclusion/Recommendations: In this clinical case, despite the limited evidence available, treatment with pembrolizumab and radiotherapy resulted effective and well tolerate. In our knowledge, this is the first case treated with pembrolizumab and radiotherapy looking for an abscopal effect. A longer follow-up period of the patient will be required to figure out the duration of the response, survival and other events.

049

Real word experience with atezolizumab plus carboplatin and etoposide in extensive-stage small-cell lung cancer

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Objective/Purpose: Atezolizumab combined with carboplatin and etoposide has been recently authorized in extensive-stage small cell lung cancer (ES-SCLC) based on the overall survival (OS) benefit obtained in the IMPOWER133 clinical trial. In our institution, this therapy has been funded in patients who met similar selection criteria to pivotal clinical trial. The objective of this study was to analyze the effectiveness of atezolizumab combined with chemotherapy in real-world patients with ES-SLCL and to compare it with the outcomes obtained in the pivotal clinical trial.

Study Design/Methods: In this single-center retrospective observational study, we included all patients with ES-SCLC who received as first-line treatment atezolizumab plus carboplatin and etoposide between September 2021 to April 2022. The following variables were collected: age, sex, history of smoking, baseline Eastern Cooperative Oncology Group Stage Performance Status (ECOG PS), metastasis site, comorbidities, date of progression disease and death. To evaluate effectiveness, we analyze the rate of response according to Recist criteria v1.1, OS and progression free survival (PFS). Kaplan-meier method was applied to perform survival analysis. All data were obtained from digital clinical records and oncology pharmacy database. Statistical analysis was performed with the software SPSS 24.0.

Results/Key Findings: 16 patients were included in the study, of which 56.3% were men, the mean age was 65 years (±5.03) and 50% (n=8) were older than 65 years. All patients were current/former smokers and had ECOG PS 0-1. Liver was the most frequent site of metastasis (50.0% of patients) followed by bone (37.5%) Only one patient had asymptomatic brain metastasis. Fifty percent of patients had some comorbidity. Hypertension (50.0%) and diabetes mellitus (50.0%) were the most frequent ,followed by chronic obstructive pulmonary disease (18.0%) and dyslipidemia (12.0%). Regarding to rate of response, 43.8% (n=7) had partial response, 12.5 % (n=2) stable disease and 25% (n=4) progression disease and non evaluated in the rest. At the date cut-off (September 30, 2022), 87.5% and 62.5% of patients had progressed and dead, respectively. One patient was ongoing with the treatment. There were no discontinuations due to toxicity. Median OS and PFS were 10.4 months (95% CI, 6.4-14.4) and 4.2 months (95% CI, 3.7-4.7), respectively.

Conclusion/Recommendations: Despite the fact that our study population was similar to that included in the pivotal clinical trial IMPOWER133, clinical outcomes of atezolizumab plus chemotherapy in ES-SCLC in real-world clinical practice have been lower in terms of OS, PFS, and rate of response. Further studies with higher sample size are necessary in order to identify identifying which profile of patients could best benefit from this therapy.

050

Olaparib safety in ovarian cancer: single centre experience and review of the real-world literature

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Objective/Purpose: Different real-world studies in the literature have demonstrated toxicities low grade and manageable with olaparib for the treatment of ovarian cancer. The aim of this study is to describe the characteristics of our population treated with olaparib and to analyse olaparib safety with respect other real world date studies

Study Design/Methods: An observational, retrospective and descriptive study was conducted. We included patients treated with olaparib from December 2016-September 2022. Following variables were collected: age, basal Eastern Cooperative Oncology Group(ECOG) performance status, basal International Federation of Gynecology and Obstetrics(FIGO) staging system, BRCA1/2 mutation, type of ovarian cancer and treatment indication, platinum-free interval(PFI) and response to first-line platinum-based chemotherapy, duration of treatment, and adverse events(AE) according CTCAE ”Common Terminology Criteria for Adverse Events v.5”, as well as dose reductions/interruptions and discontinuations and their causes. We obtained data from electronic clinical records, and processed with SPSS Statistics v.21. In parallel, a bibliographic search was carried out in Pubmed® database: “olaparib safety AND ovarian cancer AND real world data”. Articles that provide real-world data (RWD) on the safety of olaparib in ovarian cancer were selected. The following variables were collected: indication, simple size(n°), median duration of treatment, interruption, dose adjustment or discontinuation due to toxicity, most frequently reported AEs, and percentage of reported G3-G4 AEs. These results were compared with those obtained in our study.

Results/Key Findings: Thirty-two patients were included, mean age 57.9 years (range:39-78). Most of the patients had a baseline ECOG 0(50%) or 1(44%). More than 60% had an initial FIGO stage IIIC(41%) or higher. Almost 97% presented BRCA mutation. High-grade serous ovarian adenocarcinoma(81.3%) was the predominant histology. 58% received olaparib as maintenance after completing a first line of platinum-based chemotherapy and 42% as maintenance therapy with platinum-sensitive relapsed (PFI> 12 months:34.4%). 59.4% patients had a complete response to first-line platinum-based chemotherapy, 37.5% had partial response. The median duration of treatment was 17 months (IQR:6-26.7). Most frequents AEs were: asthenia (75%(G3:3.12%)), nausea (68.8%(G3:0%)), anemia (46.2%(G3:6.3%)), vomiting (9.4%(G3:0%)) and headache (3.1%(G3:0%)). 11 patients experienced dose reduction, 12 interruptions and 3 discontinuations due to AEs. In the literature search, 9 RWD studies reported about safety data with olaparib in ovarian cancer, which included a mean of 100 patients (range: 40-251). The median duration of treatment was 11.6 months(IQR:8.6-15.5). Only 4 studies provided data on suspension due to toxicity. The mean rate of discontinuation due to toxicity was reported in 6 studies, 7.5%(range:3-15.8%), as well as the dose adjustment 19.7%(range:5-25.9%). The most frequent AEs were reported by 6 studies: anemia in 5 of 6 with a mean of 47%(range:14.3-65), nausea and asthenia in 5 of 6 with a mean of 28.5%(range:4.4-35.7%) and 35.7%(range:10-70%), respectively. Only 2 of 6 reported vomiting and none reported headache. The percentage of G3-G4 AEs was reported by 8 studies, with a mean of 19.4%(range:9.6-52.5%).

Conclusion/Recommendations: In our patients, olaparib has shown to be safe and recorded adverse events are in line with those reported in the studies found in literature, despite our smaller sample size.

051

Safety and efficacy of Niraparib in maintenance after relapse in ovarian cancer. Real World Data

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Objective/Purpose: Niraparib was approved for maintenance therapy in patients with platinum-sensitive relapsed ovarian cancer regardless of BRCA mutation, in patients who are in response (complete or partial) after completing a second line of platinum-based chemotherapy. Several studies in the literature demonstrated efficacy and toxicities manageable with niraparib in ovarian cancer. Real world population studies are needed to confirm those results. The aim of this study is to describe the characteristics of our population treated with niraparib in maintenance after completing a second line of platinum-based chemotherapy, after relapse of ovarian cancer, as well as its efficacy and safety.

Study Design/Methods: An observational, retrospective and descriptive study was conducted. We included patients treated with niraparib from August 2017 to September 2022. Following variables were recorded: age, body-mass index (BMI), basal Eastern Cooperative Oncology Group (ECOG) performance status, basal International Federation of Gynecology and Obstetrics (FIGO) staging system, BRCA mutation (somatic and germline), histology, platinum-free interval (PFI) and response to first-line platinum-based chemotherapy, Progression Free Survival (PFS), Overall survival (OS) and adverse events (AE) according CTCAE ”Common Terminology Criteria for Adverse Events v.5”, recorded during the first year of treatment as well as dose reductions/interruptions and discontinuations and their causes. We obtained data from electronic clinical records, and processed with SPSS Statistics v.21.

Results/Key Findings: Thirty-two patients were included, mean age 62.4 years (SD 10.4, range 37-77), with mean BMI 26.3 (SD 4.9). More than 50% of woman presented overweight or obesity. Patients had an initial ECOG 0 (46.9%), 1 (53.1%). More than 80% had an initial FIGO stage of III (59.4%) or higher (IV 25%). Thirty-seven-point five percent presented BRCA wild type (both germinal as somatic line), 43.8% presented BRCA germinal wild type-BRCA somatic not determined. Three patients presented BRCA mutation (9.4%), 2 in germinal line and 1 in somatic line. Regarding the histological type: high-grade serous ovarian adenocarcinoma (78.1%), ovarian papillary serous carcinoma(9.3%), primary peritoneal ovarian carcinomatosis(6.3%), clear cell carcinoma of the ovary (6.3%). Platinum-sensitive relapsed ovarian cancer after first-line, PFI>12 months:75%,PFI>6<12 months: 25%. Response to first-line platinum-based chemotherapy was complete in 71.9% patients and 28.1% was a partial response. Median PFS and OS were 8 months (95% CI, 3.1-12.9) and 30 months (95% CI, 0-63.2), respectively. Regarding safety, 93.8% of patients had some AE during the first year of treatment. Most frequents were: asthenia (68.8% (G3:3.1%)), nausea (34.4% (G3:0%)), anemia (43.8% (G3: 9.4%)), thrombocytopenia (40.6% (G3:9.4%), hypertension (25% (G3:3.1%) and abdominal pain (21.9% (G3:0%)). 16 patients experienced dose reduction, 17 interruptions and 6 discontinuations due to AEs. 4 patients needed blood transfusion and 2 patients platelets.

Conclusion/Recommendations: In our patients, PFS was similar to BRCA germinal wild type cohort of NOVA trial. Niraparib had a high incidence but manageable adverse events recorded. In the NOVA trial, AEs were similar to those in our population, but G3-4 AEs were recorded more frequently. It would be interesting to incorporate patient outcome reporting (PRO) tools to register. AEs and improve the characterized safety profile and quality of life adjusted benefit.

052

Osimertinib and rifampicin: a case study

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Objective/Purpose: To describe the pharmaceutical intervention regarding management of interactions between rifampicin and the treatment of a patient with metastatic non-small-cell lung cancer treated with osimertinib.

Study Design/Methods: Seventy-one-year-old male with dyslipidaemia, with no other known previous medical history or toxic habits. Usual medication: tramadol/paracetamol 37.5/325mg/8h, metamizole 575mg/8h, diazepam 5mg/24h, lorazepam 1mg/8h, pregabalin 75mg/24h, simvastatin 10mg/24h, duloxetine 60mg/24h. Due to cervicobrachial pain treated with analgesics, he was diagnosed in December 2021 with pulmonary neoplasm, cT3cN1cM1c, with bone dissemination and spinal cord compression, exon 19 mutation and EGFR amplification, PDL1 <1%. He underwent surgery with vertical spinal cord decompression and posterolateral cervical arthrodesis. Analgesic treatment was intensified. In January 2022 he started osimertinib 80mg/24h. In April he presented a partial response with radiological improvement and correct treatment tolerance. In May 2022, he underwent another operation with expansion of the arthrodesis due to mechanical loosening. Ten days later he was admitted due to infection of the surgical wound. *E. Faecalis* was detected in the blood culture and, in the wound, *S.epiderdimis.* Ampicillin and ceftriaxone were started, the wound was debrided, and vancomycin was added. Other foci were ruled out, concluding that the bacteraemia was caused by the wound. After three weeks, antibiotic treatment was changed from intravenous to oral. *S.epiderdimis* was resistant to quinolones, exclusively sensitive to linezolid and rifampicin. Due to linezolid-duloxetine contraindication, tedizolid 200mg/24h and rifampicin 600mg/24h were started for eight weeks post-debridement. Relevant interaction between rifampicin-osimertinib was detected.

Results/Key Findings: Rifampicin is a strong inducer of CYP450, the main route for osimertinib's metabolism. A literature search on osimertinib dose adjustment was performed to avoid potential underdosing caused by the interaction. Different databases were reviewed: UpToDate®, Liverpool Cancer Drug Interactions and Medscape®, as well as osimertinib's summary of product characteristics (European Medicines Agency). In all of them, the concomitant use is discouraged and no management recommendations were found. Only the FDA data sheet recommends doubling the dose of osimertinib to 160mg/24h when co-administered with a cytochrome strong inducer and maintaining this dosage for up to three weeks after discontinuation. The patient started this dose in June 2022, showing acceptable tolerance with grade 2 asthenia. On the other hand, he reported insomnia. Considering the possible interactions with rifampicin, lorazepam dose was increased to 5mg/24h without being effective, so the dose was reduced. Mirtazapine 30mg/24h was added, which was discontinued due to poor tolerance. Trazodone was started, which was effective. In August 2022 (after completion of double-dose treatment) the treatment with osimertinib 80mg/24h was recovered. One month later, PET-CT reported bone progression with stable lung disease. It was decided to terminate osimertinib and assess the next therapeutic approach.

Conclusion/Recommendations: Managing drug interactions remains a challenge. Increasing osimertinib's dose presented acceptable tolerance, although at the end of treatment with rifampicin, disease progression was confirmed. More studies are needed to guarantee the efficacy of oncological drugs in case of drug interactions. It would be important, in cases like this one, to count on pharmacokinetic techniques to help decision-making.

053

Challenge with bevacizumab after temozolomide induced durable aplastic anemia: a case report

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Objective/Purpose: Standard first-line treatment of high-grade gliomas consists of radiotherapy with concomitant temozolomide (RT+TMZ) followed by adjuvant temozolomide (Stupp protocol). Though temozolomide induced myelosuppression is considered reversible, rarely idiosyncratic drug reactions (IDR) resulting in durable aplastic anemia (AA) have also been reported. These occur predominantly in females, during radiotherapy concomitance, after a median latency of 30 days. On diagnosis, immediate discontinuation of causative agents is imperative. On disease progression, bevacizumab should be considered as second-line treatment. Because of VEGF's key role in vascular function and angiogenesis, bevacizumab can produce serious adverse vascular events, including bleeding, thromboembolic events, and neutropenia. Therefore, use experience is very limited in AA context. Aim was to report a 38-year-old female's clinical case who, after developing durable idiosyncratic AA secondary to RT+TMZ, received bevacizumab at disease progression, despite presenting high hemorrhagic risk due to G4 thrombocytopenia.

Study Design/Methods: She was diagnosed grade III anaplastic astrocytoma in Apr-2020, after a clinical debut with seizures. Following subtotal excision with persistence of a frontal tumoral nodule, RT+TMZ was started on 18-Jan-2021. After 25/33 radiotherapy sessions, petechiae were observed and blood tests revealed severe myelosuppression (Hemoglobin 9,5 g/dL; Platelets 0/mm3; Neutrophils 90/mm3). Then, temozolomide was permanently discontinued and platelet transfusion support and prophylactic antibiotic therapy were started. Also, seizure prophylaxis with levetiracetam was switched to lacosamide. Bone marrow biopsy was performed.

Results/Key Findings: Despite temozolomide discontinuation, myelosuppression did not improve. Bone marrow hypocellularity (<20%), together with peripheral blood cytopenias, confirmed the diagnosis of severe AA. The early onset and low cumulative dose of temozolomide supported the IDR diagnosis, which was reported to the autonomic pharmacovigilance center. With no active treatment since temozolomide discontinuation, cranial MRI scan performed on 26-Apr-2021 showed tumor progression. However, due to persistent G4 thrombocytopenia, risk-benefit balance to start bevacizumab was considered unfavorable. Then, she started with eltrombopag on 10-Jun-2021 to aid in count recovery. Despite megakaryopoiesis stimulation, G4 thrombocytopenia, G4 neutropenia and G1 anemia persisted for months, so she did not start on bevacizumab. A follow-up MRI confirmed progression on 6-Aug-2021. Neurologically asymptomatic until then, on 20-Sep-2021 she presented facial hemiparalysis. At that point, she was admitted to hospital, dexamethasone dosing was increased and after receiving a platelet pool (previously 11000/mm3), she started on bevacizumab with close monitoring. After 11 cycles, cranial MRI scan performed on 12-May-2022 showed tumor progression. However, lomustine was ruled out due to persistent thrombocytopenia, despite ongoing eltrombopag. She followed up to 16 cycles with bevacizumab with no signs of bleeding. Finally, disease progression led to her death, 29 months after diagnosis.

Conclusion/Recommendations: Usually temozolomide has an acceptable safety profile; however, very rarely, profound myelosuppression and aplastic anemia after a limited exposure to temozolomide have been reported in a few reviews. Experience with bevacizumab is limited and very valuable in this context since it is the second preferred line and bleeding is a frequent complication. Indeed, intracranial hemorrhages have been associated with bevacizumab in patients with high-grade glioma. In this case, treatment was safe despite persistent thrombocytopenia. Progression free survival was 7,8 months and overall survival 11,7 months.

054

Comparison of oxaliplatin and mitomycin based Hyperthermic Intraperitoneal Chemotherapy after two years of early experience

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Objective/Purpose: To compare clinical features of two cohort of patients diagnosed of peritoneal carcinomatosis who undergone cytoreductive surgery (CRS) plus hyperthermic intraperitoneal chemotherapy (HIPEC) using a protocol based on oxaliplatin or mitomycin. Secondary objective, to assessed mortality between groups.

Study Design/Methods: Retrospective study performed in a tertiary hospital between May 2019 and January 2022. We included all patients who undergone CRS+HIPEC. Demographic, clinical, treatment variables and mortality were collected. Chemotherapy used for HIPEC was chosen by the responsible surgeon. Arm A: intraperitoneal oxaliplatin administered for 30 minutes and intravenous 5-fluorouracil and folinic acid. Arm B: mitomycin administered for 60 minutes in monotherapy or combined (doxorubicin or cisplatin). Quantitative variables expressed as frequency (%) and qualitative variables expressed as median (IQR).

Results/Key Findings: We included 36 patients, female 18 (50%), 64.0 (29-77) years and BMI 26.9 (17.1- 38.8) kg/m^2. Charlson-Comorbidity-Index was 10 (6-15) and the number of concomitant drugs 4 (0-8). In all cases the primary tumour was digestive. Extraperitoneal-metastases: liver 8(22.2%), gut 2(5.6%) and suprarenal 1(2.8%). Arm A versus Arm B: female 6(37.5%) vs 12(60.0%) (p=0.180); 62.0(29-77) vs 64.5(37-76) years (p= 0.741); BMI 25.9(21.8-31.1) kg/m^2 vs 27.0(17.1-38.7) kg/m^2 (p= 0.789); BSA 1.85(1.5-2.3) m^2 vs 1.80(1.4-2.1) m^2 (p= 0.694); Charlson-Comorbidity-Index 9.5(7-15) vs 10.0(6-12) (p= 0.694); Number of concomitant drugs 2.5(0-8) vs 3.0(0-6) (p= 0.912). Chemotherapy previous to HIPEC 3(18.75%) vs 4(20.0%) (p=0.925). A 30-day-mortality-rate of 8.3% (3/36) was observed. Arm A versus Arm B: 0(0.0%) patients vs 3(15.0%) (p=0.106). A 365-mortality-rate was 16.7% (6/36). Arm A versus Arm B: 2(5.5%) patients vs 4(11.1%) (p=0.549). No predictors of mortality found.

Conclusion/Recommendations: No significant differences in demographic, clinical or treatment variables were observed between intraperitoneal oxaliplatin or mitomycin. No better outcomes with mitomycin were observed in contrast of preclinical data. Further studies are needed to evaluate the role of oxaliplatin and mitomycin in HIPEC for the treatment of peritoneal carcinomatosis.

055

Real-world effectiveness and safety of ibrutinib in chronic lymphocytic leukemia

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Objective/Purpose: To evaluate the effectiveness and safety of ibrutinib in patients with chronic lymphocytic leukemia (CLL) both in first and subsequent lines.

Study Design/Methods: A retrospective observational, multidisciplinary single center was conducted. All patients who received ibrutinib from 1 July 2015 to 30 September 2021 were included (follow-up end date: 11/10/2022). Data collected were: sex, age, Eastern Cooperative Oncology Group (ECOG), beta-2 microglobulin level and presence of deletion 17p/TP53 or IGHV gene rearrangement. To assess the effectiveness, the kind of response (partial/complete) at 6 months, progression-free disease (PFS), and overall survival (OS). The safety variable recorded was the presence of adverse effects (AE) according to Common Terminology Criteria for Adverse Events (CTCAE v. 5.0). Quantitative variables were described with measures of central tendency and the qualitative ones in frequency tables. PFS and OS were analyzed according to the Kaplan-Meier method, considering progression/death as an event. The statistical (IBM SPSS 20.0).

Results/Key Findings: 27 patients were included, 51.9% were men with a median age of 71 (Range: 55-87). 92.6% had ECOG 0-1 (two patients ECOG-2) and 76.2% patients with a beta-2 microglobulin level ≥3.5 mg/L. Eight patients were treated in first line (29.6%), 9 in second (33.0%) and the remaining 37.4% had 3 or more previous lines. All first-line patients had deletion 17p/TP53 or IGHV gene rearrangement. Six patients presented deletion 17p/TP53 and 6 mutation IGHV gene rearrangement, within the subsequent lines of treatment which confers an unfavorable prognosis. The median follow-up time was 32.2 months (IQR: 15-52.5). In first line patients, 3 died, one was suspended due to toxicity and 4 were still in treatment. The overall response was 100.0%. Best response was complete response in one patients and partial response in the remaining seven. Median PFS was 34.2 (IC95%: 27.9-40.5) and OS has not yet been reached. In the subsequent line's patients, 9 patients died, three discontinued treatment and seven were still in treatment. The overall response was 78.9%. Four patients achieved complete response, 11 partial response and 4 did not respond to treatment. Median PFS was 15.0 (IC95%: 0.0-30.8) and OS has not yet been reached. AE were registered in 70.4 % of patients (n=19), being cramps, arthralgias (25.9%) and minor bleeding (25.9%) followed by hematological toxicity (22.2%) and gastrointestinal disorders (22.2). Grade 3-4 AE were registered in 25.9% of patients (n=7). Neutropenia and respiratory infections were the most frequent AEs, reducing the dose in 6 patients for this reason.

Conclusion/Recommendations: Ibrutinib achieves a good overall response rate both in first and later lines. Longer follow-up is needed to draw conclusions on PFS and OS, since a significant number of patients are still alive. The AE observed were those expected and coincide with those described in clinical trials.

056

Real-world study of eltrombopag in the treatment of primary immune thrombocytopenia

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Objective/Purpose: To evaluate the effectiveness and safety of eltrombopag in patients with primary immune thrombocytopenia (ITP).

Study Design/Methods: Observational, retrospective study, in a speciality hospital of patients diagnosed with ITP treated with eltrombopag between January-2014/June-2022 (end of follow-up: 10-October-2022). The following variables were collected: sex, age, baseline platelet count ≤15.000/µL, bleeding symptoms, number of previous treatments (glucocorticoids, human immunoglobulins, splenectomy, romiplostim), concomitant treatment, duration of treatment with eltrombopag and reason for discontinuation of treatment. The effectiveness variables recorded were platelet count >50.000/µL at 6 weeks, number of weeks with platelet count >50.000/µL, achieve a durable platelet response (defined as a weekly platelet count ≥50.000/µL 6 or more times during the last 8 weeks of study in the absence of rescue therapy) and achieve a transient platelet response (defined as a weekly platelet count ≥50.000/µL 4 or more times during the study weeks but no durable platelet response). The safety variable recorded was percentage of patients with adverse reactions (ARs). Data source: outpatient dispensing software (Farmatools®) and electronic medical records (Diraya®). Data processing: SPSS®v.25.0 statistical software.

Results/Key Findings: 32 patients with a diagnosis of ITP who were treated with eltrombopag were included, 19 women (59.4%), median age 63,5 years (IQR:4-87) at baseline. Baseline platelet count was ≤15.000/µL in 59.4% (n=19). Prior to treatment, bleeding symptoms of any grade were found in 50.0% (n=16), being clinically significant (grades 2-4) in 9 (28.1%). Regarding treatment prior to eltrombopag: 30 patients (93.8%) received corticosteroids, 7 (21.9%) received human immunoglobulin treatment (34.4%), 4 patients (12.5%) resorted to splenectomy and 9.4% (n=3) received romiplostim. Only 1 patient (3.1%) used eltrombopag as first line. Two patients (6.3%) received concomitant treatment with corticosteroids and 1 with rituximab (3.1%). The median duration of eltrombopag treatment was 32,4 weeks (IQR:1-373,7). At the end of the study 11 patients (34.4%) were still on eltrombopag and 21 (65.6%) were discontinued. The reasons for treatment discontinuation were remission (n=8, 38.1%), non-response (n=6, 28.6%), hepatotoxicity (n=2, 9.5%), clinical deterioration (n=2, 9.5%) and 2 patients were lost to follow-up. Platelet count at 6 weeks was >50.000/µL in 19 patients (59.4%). Patients had >50.000/µL for a median of 28,65 weeks (IQR=0-368,7). A durable platelet response occurred in 68.8% (n=22), 12.5% (n=4) showed transient platelet response and 6 patients did not respond to treatment (18.8%). As for ARs, they occurred in 25.0% of patients (n=8) with liver toxicity being the most frequent AR (n=4, 12.5%). The remaining four patients experienced: headaches (3.1%), cytopenia (3.1%), cholelithiasis (3.1%) and one of them experienced both paraesthesia and cough (3.1%).

Conclusion/Recommendations: Eltrombopag has demonstrated effectiveness in our real-world study with a high percentage of patients who have achieved response, most of them sustained. In addition, the incidence of ARs is low, with the most frequent ARs coinciding with those described in its product information.

057

Drug-drug interactions of pharmacokinetic mechanism during conditioning for hematopoietic stem cells transplantation

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Objective/Purpose: To determine the prevalence and analyze the profile of potential pharmacokinetic-type drug-drug interactions (DDI-PKs) in hematopoietic stem cell transplantation (HSCT) conditioning regimens, using two databases.

Study Design/Methods: Observational, retrospective and descriptive study, including all adult patients conditioned for HSCT, in a university hospital, during three years. The variables collected were: sex, age, diagnosis, conditioning scheme, prescribed drugs and detected DDI-PKs. Treatments were analyzed from conditioning start day to the day of stem cell infusion. For the study of DDI-PKs, the international databases Lexicomp® were used, collecting the DDI-PKs with risk rating D and X, and Micromedex®, compiling the DDI-PKs classified as major and contraindicated. The detection of potential DDI-PKs was retrospective, with the aim of detecting areas for improvement. Possible interventions performed were not recorded.

Results/Key Findings: A total of 141 treatments were analyzed, adding up 3,231 prescribed drugs (211 different drugs) and with a median of 23 drugs per patient (15-36). In 78 cases patients were men (55.3%) and the mean age was 55.95±11.68 years. The predominant diagnoses were: multiple myeloma and other monoclonal gammopathies (65), mature B-cells neoplasms (34), acute myeloid leukemia (11), Hodgkin's lymphoma (11), solid tumors (6) and T-cell neoplasms (5). Conditioning regimens had a mean duration of 4.4±2.1 days and 26 patients received triple intrathecal therapy. The most prescribed drugs were: ursodeoxycholic acid and ondansetron in all patients, acyclovir and potassium chloride (139 patients), furosemide (138), omeprazole (135), enoxaparin (134), allopurinol (131), cotrimoxazole (130). The most used antineoplastic drugs were: melphalan (103), fludarabine (36), etoposide (33), cyclophosphamide (32), and carmustine (31). The overall prevalence of DDI-PKs was 40.4% for Lexicomp® and 54.6% for Micromedex®. At Lexicomp® all the DDI-PKs detected were risk D, while the prevalence in Micromedex® for major DDI-PKs was 51.1% and 14.9% for those contraindicated. With Lexicomp®, 85 DDI-PKs were obtained grouped in 33 pairs and with Micromedex, 207 DDI-PKs in 57 pairs (186 majors; 21 contraindicated). The mean DDI-PKs per patient was 0.6±0.9 for Lexicomp® and 1.4±1.6 for Micromedex®. The most frequent level D DDI-PKs (Lexicomp®) were: fentanyl/fluconazole(16), furosemide/methotrexate(14), tacrolimus/fluconazole(6), tacrolimus/omeprazole(5), clopidogrel/omeprazole(4), diazepam/fluconazole(3), escitalopram/omeprazole(3), dexamethasone/calcium (carbonate)(3) and clopidogrel/fluconazole(3). The DDI-PKs in which fluconazole and omeprazole intervene produce the inhibition of CYP3A4 or CYP2C19, increasing the serum concentrations of their substrates. More frequent major DDI-PKs (Micromedex®): methotrexate/omeprazole(23) and methotrexate/cotrimoxazole(22), which may decrease renal excretion of methotrexate; dexamethasone/fentanyl(16) and fentanyl/fluconazole(16), by induction and inhibition, respectively, of fentanyl metabolism (CYP3A4); metoclopramide/tacrolimus(7), omeprazole/tacrolimus(7), with risk of tacrolimus toxicity due to inhibition of its metabolism (CYP3A4) (omeprazole) or by favoring its absorption (metoclopramide). The most frequent contraindicated DDI-PKs were: fluconazole/tacrolimus(6) and fluconazole/mirtazapine(6), also related to greater exposure to tacrolimus; escitalopram/fluconazole(5) (CYP3A4 and CYP2C19 inhibition).

Conclusion/Recommendations: The prevalence of potential DDI-PKs during HSCT conditioning is high, with a higher overall prevalence and severity observed with Micromedex®. The drugs most frequently involved in DDI-PKs were fluconazole, omeprazole and tacrolimus in both databases, and also methotrexate in Micromedex®, giving rise to major DDI-PKs. The most common mechanism in DDI-PKs was the modification of drugs metabolism through the inhibition or induction of CYP3A4 or CYP2C19.

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Follow up of obese patients with conditioning chemotherapy dose adjustment in hematopoietic stem cell transplantation

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Objective/Purpose: Obesity is a factor contributing to a greater risk of inferior health, but it has not been conclusively proven to be a risk factor in the setting of hematopoietic stem cell transplantation (HSCT). Despite the insufficient scientific evidence about dose adjustment in conditioning therapy before HSCT in obese patients, the American Society for Blood and Marrow Transplantation consider it in some drugs used in the conditioning chemotherapy to reduce toxicities. Since 2021 we are following these recommendations and the objective of this study is to describe the dose drug adjustment and review the effectiveness and safety during hospital admission and follow-up after HSCT.

Study Design/Methods: Prospective observational study of obese patients receiving HSCT from January 2021 to July 2022. We reviewed clinical history of HSCT candidates who were going to receive chemotherapy as part of conditioning therapy with drugs that required weight dose adjustment:busulfan,etoposide,cyclophosphamide and thiotepa dosed by mg/kg, carmustine. Patients categorized by body mass index(BMI):normal(<25kg/m2),overweight(25-29.9kg/m2),obese(30-39.9kg/m2) or severely obese(BMI>40kg/m2). Dose adjustment was made when real weight>120% of ideal weight and BMI≥27kg/m2. Pharmaceutical interventions were carried out for a correct drug dosage.

Results/Key Findings: 103 adult patients received HSCT in the study period (57 autologous,46 allogeneic) for hematological diseases. In 73 patients had been prescribed a chemotherapy drug that required weight dose adjustment, 41 men, mean aged 52±14 years and 56%(41) were allogeneic HSCT (58% unrelated donor) . 24(33%) patients were overweight or obese, so they needed a prescription pharmaceutical review. Median IMC of these patients were 31 kg/m^2(28-32) and the median of percentage real weight higher than ideal weight was 137%(132-146) . 17 medical prescriptions were reviewed and 23 drug doses were modified after pharmaceutical intervention to get an appropriate dose in obese (10 busulfan, 6 thiotepa,5 carmustine, 2 cyclophosphamide). Among patients with a reduced dosage drugs in conditioning therapy because of obesity (17) the median time to engraftment was 14 (10-17) days to neutrophil count≥0.5×109/L, and 13(12-17) to platelet count≥20×109/L for at least 3 days with 2 patients not reaching it. During hospital admission the median days of G-CSF administered was 6 (5-11), median platelet transfusions units were 6 (3-13) and red blood cells transfusions were 3 (0-6). Cytomegalovirus reactivated after HSCT in 5 patients and graft versus host disease (GvHD) appeared in 6 patients (3 acute-GvHD y 3 chronic-GvHD). Gastrointestinal toxicities grade II-IV were registered in 4/5 patients and hematologic toxicities grade IV in 53% (9) of patients. Median days of hospital admissions 27 (22-43). 5 patients died after HSCT, 3 after +100 days post-HSCT.

Conclusion/Recommendations: Selecting the optimal dose of conditioning chemotherapy in obese patients is complicated and had to be a common objective between pharmacy and hematology medical services because contributes to avoid side effects like gastrointestinal or hematological toxicities that could prolong the days of hospital admissions. Further research is necessary to optimize dosing of chemotherapy in obese patients and realize real benefits.

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059

Efficacy and safety of Tepotinib in advanced Non-Small-Cell Lung Cancer with a confirmed MET exon 14 skipping mutation: a case report

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Objective/Purpose: A splice-site mutation that results in a loss of transcription of exon 14 in the oncogenic driver MET (METex14) only occurs in 3 to 4% of patients with Non-Small-Cell Lung Cancer (NSCLC). The MET proto-oncogene encodes a receptor tyrosine kinase, and binding to its ligand (hepatocyte growth factor [HGF]) induces downstream signaling through the RAS-RAF and phosphoinositide 3-kinase (PI3K) pathways. Tepotinib is a once-daily, highly selective oral METex14 inhibitor. Recently, based on the Phase II VISION clinical trial results, it has been approved by the European Medicines Agency (EMA) for patients with metastatic NSCLC harboring METex14 skipping mutations who progressed following immunotherapy or/and platinum-based chemotherapy. The aim of this study is to describe the efficacy and safety of tepotinib in a patient with advanced NSCLC with a confirmed METex14 alteration.

Study Design/Methods: We describe the case of a patient with metastatic NSCLC with the presence of a METex14 skipping mutation detected on tissue biopsy. Treatment response was evaluated according to the RECIST criteria v1.1 for complete response (CR), partial response (PR), stable disease (SD) and progressive disease (PD). Toxicities were categorized according to the CTCAE v5.0.

Results/Key Findings: The patient was a 58-year-old woman with a 15-pack year smoking history who presented a BRCA2 gene mutation. She was diagnosed in April 2019 with a lung adenocarcinoma T4N3M0 (negative ALK/ROS-1/EGFR mutations and PD-L1 ≥ 50%). She received platinum-based chemoradiation therapy with PR followed by Durvalumab until brain PD in November 2019. Then she received whole brain radiotherapy followed by many sessions of local radiosurgery. In the meanwhile, in October 2021 she was diagnosed with a colon adenocarcinoma. Finally, for brain extended metastases, ECOG 2, and the scarce therapeutic options, from March 2022, she started receiving uninterruptedly daily oral 500 mg of tepotinib. After 2 cycles of 28 days, RECIST response both in brain Nuclear Magnetic Resonance imaging and Computed Tomography showed PR. To date, after 7 completed cycles she showed SD. Subjectively, the patient reported neurological improvement (less drowsiness, dizziness, headache, and insomnia) and movement improvement (walking autonomy). The only adverse event reported was peripheral edema G2 (controlled with furosemide).

Conclusion/Recommendations: In our patient with metastatic NSCLC with a confirmed METex14 skipping mutation, the use of tepotinib has been an effective treatment and has led to a significant improvement in this patient quality of life. Tepotinib also has been well-tolerated, being peripheral edema the main toxic effect, showing a similar safety profile compared with the VISION trial. Further follow-up of our patient is needed to demonstrate that tepotinib has durable antitumor and clinical activity.

060

Real-life analysis of treatment results with durvalumab in patients with non-small-cell lung cancer

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Objective/Purpose: Durvalumab is the treatment of choice in adults for locally advanced non-small cell lung cancer (NSCLC) and whose disease has not progressed after platinum-based chemoradiotherapy. To analyse the effectiveness and safety of durvalumab treatment in these patients.

Study Design/Methods: Observational retrospective study of patients diagnosed with NSCLC in the period from January 2017 to December 2020. Clinical variables registered were sex, age, genetic mutations and PDL-1 expression, quality of life (measured by the ECOG scale), comorbidities, previous chemotherapy treatment, duration and type of response (complete, partial). To determine effectiveness we recorded duration and type of response (stable disease, tumour progression or death) of Durvalumab treatment. Adverse reactions were collected to determine safety. The recommended dosage of durvalumab was 10 mg/kg administered every 2 weeks, until disease progression or unacceptable toxicity, or up to a maximum of 12 months. Data was obtained from oncology electronic prescription with the application Oncopharm® and electronic health records with Diraya®.

Results/Key Findings: The 20 patients involved in the study were 85% male with a median age of 67 years (IQR 61-73.5). 3 patients had genetic mutations (KRAS, ALK and EGFR genes). 4 patients had PDL-1 higher or equal to 80%, 8 patients below 50%, 1 PDL-1 negative and the remaining had PDL-1 between 50 and 79%. ECOG was 0 in 12 patients and ECOG 1 in 7 patients. Comorbidities included arterial hypertension (8 patients), diabetes mellitus (6patients), dyslipidemia (6 patients) and chronic obstructive pulmonary disease (6 patients). 4 patients smoked and 3 patients were consuming alcohol at the time of diagnosis and 9patients were non-smokers. 11 patients had a first line of treatment based on cisplatin and vinorelbine and 9patients with carboplatin and paclitaxel. There was 13 parcial response (PR) to platinum-based treatment, 5 almost complete responses, 1 tumour progression and 1 discontinuation due to toxicity. 2 patients required second-line of treatment based on cisplatin with almost complete responses. The median of durvalumab treatment was 12 months. 12 patients maintained stable disease, 4patients had a PR and 4patients had tumour progression during treatment. After finishing treatment, of the 16 patients who had maintained response or improved, 5 patients lost response and progressed (median 3 months after end of treatment IQR 1-6). After progression with durvalumab, 5 patients received other immunotherapy (pembrolizumab 3 patients, atezolizumab 1 patient and nivolumab 1patient). 3 patients died. The most frequent adverse effects associated with durvalumab treatment were dyspnea (7 patients), mild asthenia (6patients), cough (5 patients), arthromyalgia (4 patients) and skin toxicity (3patients). 11 patients needed corticosteroid treatment for dyspnea, cough or arthromyalgia. 3 patients had no adverse effects.

Conclusion/Recommendations: Durvalumab is an effective treatment in most patients, although primary failure or loss of response after the end of treatment is observed in a small number of patients. Frequent but mild and easily manageable adverse effects, which do not reduce the patient’s quality of life.

061

Analysis of the use of paxlovid and prophylactic remdesivir in oncological patients

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Objective/Purpose: To describe the results of the analysis of the effectiveness of treatment with paxlovid and remdesivir prophylactic and the pharmacist's role in the adjustment of therapy prescribed.

Study Design/Methods: Observational prospective study of oncology patients with paxlovid or remdesivir prophylactic from January 2022 to August 2022 in a 1000-bed university hospital. Clinical variables were obtained using medical records (Diraya®) applications. We registered sex, age, vaccination status and number of doses, previous pathologies, needs of hospitalisation for covid, contraindications, potential interactions, need for treatment with covid treatment (baricitinib or corticoids). Interventions performed by the pharmacist are classified into 5 types (dosage adjustment (1), notification of undetected contraindication (2), undetected potential interaction (3), non-compliance with prescription criteria (4) or incorrect length of treatment (5).

Results/Key Findings: There were 31 patients involved in the study. 24 with paxlovid (median age 62 years, IQR 48-76, 69.2% female) and 7 with remdesivir (median age 68, IQR 38-73, 60% male). All of them were receiving chemotherapy treatment at the time of prescription. The most frequent tumours were: non-small cell lung (9), breast cancer (5), colon carcinoma (5) and sarcoma (3). As for previous pathologies, 9 patients had respiratory pathologies, 8 hypertension, 6 autoimmune diseases, 5 liver disorders, 3 diabetes mellitus and none of the patients had kidney disorders. All of the patients except one were vaccinated for COVID (22 with 3 doses and 9 with 2 doses) and 25% of them required subsequent hospitalisation due to the illness (5 patients were treated with remdesivir and 3 with paxlovid) and none of them died. Only 3 patients required corticosteroid treatment during hospital admission with no further specific treatment for SARS-CoV2 infection. Only 2 patients experienced adverse effects to paxlovid treatment such as fever and constipation. The pharmacist intervened in 20 out of 31 prescriptions, and carried out 36 interventions of which 15 were type 1, 3 type 2, 8 type 3, 2 type 4 and 8 type 5. A total of 10 potential interactions were detected, including 6 with statins (simvastatin, rosuvastatin and atorvastatin), benzodiazepines, amlodipine and modafinil, as well as 5 contraindications, in which statins again stood out. Out of the 31 prescriptions that were endorsed by the pharmacist,1 patient did not pick up the medicine.

Conclusion/Recommendations: The risk of disease progression in treated patients is very low. The recent addition of paxlovid and remdesivir to the COVID-19 prophylactic therapeutic algorithm and the intervention of the hospital pharmacist is beneficial for prescribing. It is important to encourage multidisciplinary work with prescribers to reduce potential dosing errors, adverse reactions and increase patient safety.

062

Study of empirical antibiotic therapy in bacteraemia in onco-haematological patients

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Objective/Purpose: To analyse the appropriateness of the empirical treatment of bacteraemia in patients with onco-haematological pathologies and the clinical outcomes.

Study Design/Methods: Observational retrospective study from January 2021 to December 2021 in a 1000-bed university hospital. Clinical variables registered were sex, age, Charlson Comorbidity Index, days of hospitalization, responsible medical department, antibiotic prescription, duration of the treatment and dose, in vitro activity of the antibiotic, microorganism, COVID infection, source of the infection, risk factors for multi-resistant bacteria (MDR) and clinical evolution. Data was gathered from electronic prescription (Prisma®) and medical records (Diraya®) applications. Adequate empirical treatment is considered to be that which is prescribed and administered within 48 hours of blood culture collection, has in vitro activity against the micro-organism and is administered at the correct dose.

Results/Key Findings: In total 98 onco- haematological patients with bacteraemia were included. 59.2% were men. Median age was 65 years (IQR: 59-73), Charlson index 5 (4-7). 52.0% of patients had oncological pathology and 48.0% haematological neoplasia. In addition to the onco haematological pathology, 7 patients had neutropenia, 6 obstructive biliary pathology and 1 repeated urinary tract infections. The risk factors for multi-resistant bacteria more frequently were contact with the social and health care system (81%), hospital admission in the last month (25), antibiotics treatment 30 days previous (28) and MDR colonisation in previous 12 months(5). Length of hospital stays was 24 days (IQR 11-47). 73 patients were admitted to the medical department, 12 critical care, 10 surgeries and 3 emergencies. 28.5% of patients were in sepsis and/ or septic shock at the time of blood culture extraction. The microorganisms implicated in bacteraemia were E. coli (31.0%), E. faecalis (10.2%), K. pneumoniae (8.1%), P. aeruginosa (8.1%), E. faecium (7.1%), S. aureus (6.1%), S. marcescens (3.0%), S. maltophilia (2.0%) and C. albicans (2.0%). 86.7% of these bacteremia were monobacterial and 68.3% were nosocomial infections. The most commonly used antibiotics for empirical treatment were meropenem (45), piperacillin/tazobactam (32), daptomycin (24), linezolid (19), ceftazidime (7), aminoglycosides (7), ciprofloxacin (6) and amoxicillin/clavulanic acid (5). 95% of empirical treatments were monotherapy.28.5% empirical treatment was not appropriate. 76.5% of patients started empirical treatment on the day of blood culture collection. The principal factors were inadequate dosage (12.2%), inadequate method of administration (11.2%) or the antibiotic had no in vitro activity against the microorganism (10.2%). Finally, the in-hospital mortality was 48.9%.

Conclusion/Recommendations: The data show a high rate of empirical treatment error, which is associated with high mortality. Therefore, risk factors and early and appropriate empirical treatment are vital in frail patients such as oncohematological patients.

063

Discontinuation of lenalidomide treatment in patients with myelodysplastic syndrome with 5q deletion: clinical and economic impact

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Objective/Purpose: To evaluate clinical benefit and economic impact of using risk stratification to apply targeted therapy and discontinue or reduce the dose of Lenalidomide in patients with 5q-MDS.

Study Design/Methods: Retrospective observational study conducted over four years. 30 patients diagnosed with MDS (5q) were analyzed. 19 MDS associated with (5q): 14 MDS (5q) as isolated anomalies, 3 novo MDS (5q) associated with (20q) and 2 novo MDS (5q) associated with trisomy 8, with the rest of the patients being AREB-1 and AREB-2 myelodysplastic syndrome with 5q deletion. An analysis of the mutational profile was performed by Next-generation sequencing (NGS) to determine cases with high-risk mutational profiles mainly associated with the TP53 variant. Response to treatment can be predicted knowing that it is not recommended to use lenalidomide in patients with MDS (5q) and with the presence of a TP53 mutation because this could favor clonal evolution, expansion of the tumor clone and progression to acute myeloid leukemia. Discontinuation of treatment due to adverse reactions or intolerance was studied measuring: duration of treatment, mean dose, dose variations, start of discontinuation, adverse reactions, follow-up time since discontinuation, evaluation of the response and cost savings. For statistical analysis SPSS software and the Chi-square test were used.

Results/Key Findings: 75 cases of MDS by NGS. 63% men and 37% women. Median age was 74 years. 19 patients with MDS (5q) (25.3%), of which 43.7% were TP53 positive. High-risk mutational profile in 7.8% of cases, 30.4% low-risk, 26.1% intermediate risk, 11.4% very high risk, and 24.6% very low risk. Hypomethylating drugs (5 azacitidine or decitabine) were used, since in high-risk MDS they are election therapy. Regarding mutational profile, 43.7% TP53 mutation was detected, 15.8% RUNX1 and 40,5% the DNMT3A, ASXL1 and TET2. 66.6% of patients with MDS associated with (5q) were treated with Lenalidomide, of which 58.3% discontinued due to adverse effects and 25% reduced dose due to intolerance. Patients who discontinued due to adverse effects maintained a complete hematologic and cytogenetic response. The adverse reactions for which lenalidomide treatment had to be discontinued were: neutropenia, rhabdomyolysis, erythematous and pruritic reactions, hemolytic crises and ischemic peripheral arterial disease. Savings from discontinuation amounted to 43,000 euros per patient discontinued per year.

Conclusion/Recommendations: Discontinuation of treatment with Lenalidomide in patients with MDS associated with 5q deletion due to adverse reactions or intolerance to treatment is recommended and they maintain a complete hematological response after discontinuation of treatment. The high percentage of discontinuation could be attributed to the advanced age of the patients, which may increase intolerance to this drug.

064

Study of pharmaceutical interventions during the dispensation of medication in the oncohematological consultation

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Objective/Purpose: To quantify and describe pharmaceutical interventions in oncohematology consultations, detect the most frequent prescription errors, interactions and adverse effects in oncohematology patients.

Study Design/Methods: Prospective observational study of oncohematology patients in a tertiary hospital for January 2021 to September 2022. The demographic variables collected were age, sex, medical service responsible, pathology and oncohematological medication. A database was created using an Excell® spreadsheet to record and categorize the type of intervention. Once identified, it was entered as an episode in the patients medical record in the Diraya Clinica® programme so that the clinician could consult it in the patients evolution. In the case of urgent or dubious interventions, the doctor is also contacted by telephone. Finally, errors, interactions, avoided adverse reactions and the type of intervention were recorded.

Results/Key Findings: A total of 45 oncohematology patients underwent pharmaceutical interventions. 55% men and 45% women. The median age was 64 years (IQR: 58-72). The patients belonged to two clinical services, 40.8% to Hematology and 59.2% to Oncology. The oncohematological pathologies where most interventions were performed were: Prostate Cancer (35%), Colon Cancer (22%), Chronic Lymphatic Leukemia (18%), Multiple Myeloma (10%), Ovarian Cancer (7%), Brain Tumors (5%), Lung Cancer (1%), Breast Cancer (1%). 55% of the pharmaceutical interventions performed were incorrect doses of antineoplastic drugs, 20% relevant drug interactions, 18% omission of the drug, 5% incorrect frequency of administration and 2% detected adverse reactions. The most frequent dose errors were poor adjustment for renal function (50%), failure to write the dose in the patient's clinical course (25%), failure to adjust for liver failure (20%), poor adjustment for body surface area (5%). All errors were detected in the pharmaceutical validation process during the dispensing of oral and subcutaneous cytostatics. 100% of the pharmaceutical interventions were entered in the patients clinical history as a clinical report. 15% of the interventions were contacted by telephone with the medical specialist in responsible care with the aim of resolving the discrepancies as soon as possible. 95% were accepted and prevented 95% of medication errors in patients.

Conclusion/Recommendations: Pharmaceutical interventions have proven to be an effective tool to contribute to the achievement of the patients therapeutic goals, safety and to improve adherence to treatment.

065

Safety and tolerance analysis of Nab-paclitaxel in patients with breast cancer

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Objective/Purpose: Intravenous (IV) taxanes for breast cancer (BC) are associated with toxicities such as chemotherapy-induced peripheral neuropathy (CIPN)that can negatively affect treatment outcomes and patients' quality of life. Nab-Paclitaxel (nab-P) is used as an alternative to IV taxanes in patients who have experienced adverse reactions(AR) or are candidates such as diabetic patients. The aim of this study is to analyse the safety and tolerance of nab-P treatment in these patients.

Study Design/Methods: Observational retrospective study was conducted of patients diagnosed with BC from January 2017 to April 2022. The age of the patients and the type of treatment (neoadjuvant or metastatic) were recorded. We registered patients who used nab-P because of a reaction to IV taxanes or because they were diabetic patients. The adverse reactions to IV taxanes that prompted the switch to nab-P were recorded. Treatment tolerance was reviewed (Neoadjuvant patients were considered tolerant to nab-P treatment if they completed 12 cycles of treatment and metastatic patients if they did not finish treatment due to nab-P toxicity) The adverse reactions presented with nab-P were recorded according to common terminology criteria of adverse events (CTCAE). Data was obtained from oncology electronic prescription with Oncopharm® application and electronic health records Diraya®.

Results/Key Findings: 51 patients with a mean age of 58 years (33-82 years) were included. 37 patients used nab-P in neoadjuvant treatment and 14 patients in metastatic treatment. 34 patients switched from IV taxanes to nab-P because of an adverse reaction and 17 patients started on nab-P because they were diabetic. The adverse reactions to IV taxanes recorded were severe infusion reaction with malaise, tachycardia, dyspnoea and generalized erythema in 26 patients (2 patients required hospital admission), intense joint pain in 4 patients, poorly controlled blood glucose in 2 patients and gastrointestinal discomfort in 2 patients. 27 patients out of 37 patients on neoadjuvant treatment tolerated nab-P treatment and completed all 12 treatment cycles. Only 2 patients out of 14 patients on metastatic treatment dropped out of treatment due to toxicity. The adverse reactions presented with nab-P were mainly grade I: asthenia (22 patients),neurotoxicity (17 patients),dermal toxicity and diarrhea (14 patients),other digestive toxicity (11 patients). Neurotoxicity grade II in 8 patients and neurotoxicity grade III in 3 patients.

Conclusion/Recommendations: Nab-P treatment was mainly used for severe infusional reactions to intravenous taxanes. Nab-P treatment was well tolerated both in neoadjuvant treatment where most patients complete their treatment and in metastatic patients. Adverse reactions were varied and frequent, but most of them were grade I. Although neurotoxicity reactions with Nab-P still occur, these were grade III in a few patients. Nab-P treatment is mostly a well tolerated treatment which allows patients to complete their treatments when it would otherwise not have been possible.

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066

Survival analysis and profile of multiple myeloma patients treated with daratumumab after 6 years of experience

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Objective/Purpose: Daratumumab was originally approved in combination with lenalidomide and dexamethasone (DRd), or bortezomib/carfilzomib and dexamethasone (DVd/DKd), for the treatment of adults with multiple myeloma (MM) who have received at least one prior treatment and in monotherapy for MM in progression and refractory to treatment. The authorisation of two new indications of daratumumab in first-line therapy took a major step in MM treatment. The first one in combination with lenalidomide and dexamethasone (DRd) or with bortezomib, melphalan and prednisone (DVMp) for patients not candidates for autologous stem-cell transplantation (ASCT). The second one in combination with bortezomib, thalidomide and dexamethasone (DVTd) for candidates. The objective is to describe the use of daratumumab in clinical practice after more than 6 years of experience and the profile of treatment patients.

Study Design/Methods: A single-centre, retrospective, and observational study was conducted on MM patients treated with daratumumab from May 2016 until September 2022. Variables: age at diagnosis, age at initiation of treatment, type of MM, type of light chain, presence of unfavourable prognosis mutations, line of therapy, used regimen treatment and ASCT. The median progression-free survival (PFS) and the overall survival (OS) were calculated by the Kaplan-Meier estimator.

Results/Key Findings: Forty-nine treated patients were identified, of which 57.1% (28) were male. When diagnosed, the patients' median age was 71.6 (36.2 - 87.6) years. Among the patients the type of MM was: 44.9% (22) IgG, 28.6% (14) IgA, 12.2% (6) Bence-Jones, 10.2% (5) oligosecretory and 4.1% (2) IgD. The predominant light chain was kappa present in 63.3% (31) of the MM. Twenty-seven patients (55. 1%) had at least one unfavourable prognostic mutation, consisting of: seven gain 1q, 6 complex cytogenetic, 4 deletion 17, 2 deletion 13, 1 deletion TP53, 1 deletion 17p and t(4;14), 1 gain 1q and deletion 17p, 1 t(11;14), 2 t(14;16), 1 t(4;14), 1 t(4;14) and t(11;14). The patients' median age at initiation of the treatment was 75.4 (38.9 - 88.8) years and the median line was 3 (1-9). The used treatment regimens were: 21 DVd, 13 monotherapy, 9 DVMp, 5 DRd and 1 DKd. Eifteen patients (30.6%) received ASCT, of which 12 patients (24.5%) got the transplant prior to daratumumab and 3 patients (6.1%) after the treatment. Thirty-five patients (71.4%) progressed during treatment and the median PFS was 6.5 months (95% CI; 1.1 - 11.9), while other real-world studies with similar characteristics obtained 12 months of PFS[1,2]. Twenty-eight patients (57.1%) died and the median OS was 17.9 months (95%CI; 0.1 – 35.8). Thirteen patients had OS greater than 2 years.

Conclusion/Recommendations: The baseline characteristics of our study were similar to those of clinical trials. This study has shown that MM is a very heterogeneous pathology for which the prognosis depends on the patient's genetic profile and response to treatment. The differences in survival compared to other studies may be due to its use in very late lines of treatment in our centre, whereas its benefit has been demonstrated in earlier lines.

067

Effectiveness and safety of apalutamide in a tertiary hospital

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Objective/Purpose: Apalutamide is a selective androgen receptor inhibitor that has been approved for the treatment of high-risk metastatic hormone-sensitive (mHSPC) and castration-resistant non-metastatic (nmCRPC) prostate cancer in combination with androgen deprivation therapy (ADT). The aim of this study is to evaluate the effectiveness and safety of apalutamide treatment at our centre.

Study Design/Methods: A retrospective and observational study was conducted from January 2019 to August 2022. Patients with prostate cancer (PC) on treatment with apalutamide and the following demographic and clinical variables were included: age, type of PC, Gleason score at diagnosis, follow-up time with apalutamide, having received previous surgery and/or radiotherapy, presence of metastases and type, and type of concomitant APT. Effectiveness was calculated by the reduction of prostate-specific antigen (PSA) in blood at one month after apalutamide treatment, and at third and sixth month. To assess safety, adverse events (AEs) were collected according to the Common Terminology Criteria for Adverse Events (CTCAE) v5.0, discontinuation or treatment delay.

Results/Key Findings: Eighteen patients with a median age of 73 (63 - 85) years were included. Fourteen patients (77.78%) had mHSPC and 4 (22.22%) had nmCRPC. The median Gleason score at diagnosis was 7.5 (6 - 10). The median follow-up time was 5.77 (1.70 - 14.92) months. Eight patients had received previous surgery: three prostactectomy, 2 lymphadenectomy, 2 both and 1 transurethral resection of the prostate. Eleven patients had undergone previous radiotherapy. Fourteen patients had bone (4), lymph node (5), both (3), lymph node, bone and muscle (1) and liver and bone (1) metastases. All patients were on luteinising hormone-releasing hormone (LHRH) agonists (13 leuprorelin and 5 triptorelin) and 6 patients were also on first generation anti-androgens (all of them bicalutamide). All patients continue under treatment with apalutamide. The median baseline PSA was 0.90 (0.02 - 142) ng/ml. After one month of treatment PSA was reduced by ≥50% in 70.59% of patients. By the third month in 88.67% of 15 patients and by the sixth month in 88.89% of 9 patients. Our results can be compared with other real-world studies that measured PSA to evaluate response to treatment in the third and sixth month as well. Eleven patients (61.11%) experienced AEs with the following frequency: sweating and/or hot flushes (36.36%), asthenia (27.27%), diarrhoea (27.27%), alopecia (18.18%), erythema (18.18%), loss of appetite (9.09%), muscle spasms (9.09%), and elevated cholesterol and triglycerides (9.09%). Two patients had to stop treatment temporarily due to grade 3 diarrhoea. These results agree with other studies which found similar common AEs.

Conclusion/Recommendations: Apalutamide has proven to be, in our centre, an effective treatment in the control of mHSPC and nmCRPC disease with a reduction of PSA in a considerably short time. However, more follow-up time is needed to assess whether it influences progression-free and overall survival of patients, as assessed in pivotal trials. Apalutamide has been well tolerated although more than half of the patients experienced some type of AE and two of them required discontinuation of the drug.

068

A case series on pain accompanying photoimmunotherapy for head and neck cancer

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Objective/Purpose: Photoimmunotherapy (PIT) is a treatment in which cancer cells are selectively destroyed by injection of cetuximab sarotalocan sodium (a conjugate of the epidermal growth factor receptor antibody cetuximab, and a light-activated dye (IRDye700DX: IR700)), followed by non-thermal red light (690 nm) illumination of the tumor site using a frontal or cylindrical diffuser 20–28 hours later. In light of the results of phase I trials in Japan and phase I/II trials in the United States of America, PIT was conditionally approved in Japan in January 2021 for the treatment of unresectable locally advanced or locally recurrent head and neck cancer that cannot be treated with chemoradiotherapy (CRT) or other standard therapies. One of the most severe side effects of PIT is pain. Unfortunately, the number of patients who receive PIT is low because of PIT's highly specific indication, namely, unresectable, locally advanced or recurrent head and neck cancer that was previously treated with CRT. As there are presently no detailed reports on pain and pain management in PIT, we conducted a retrospective case series study on these aspects.

Study Design/Methods: We conducted a retrospective study of five of the six HNSCC patients who had received PIT at the National Cancer Center Hospital East between January 2021 and June 2022 using medical chart data. One patient was excluded from the study because she was advanced in age and cognitively impaired, which made it difficult to assess his pain correctly. Additionally, of the five participants, one received PIT at another hospital, and one received PIT as part of a clinical trial; these two participants were therefore excluded from the initial data analysis.

Results/Key Findings: All patients experienced pain after PIT evidenced by increased numerical rating scale (NRS) regardless of the illumination method. The daily change in mean NRS rating shows that pain was highest on the day of PIT, with ratings of 6.8 and 7.8 for the frontal and cylindrical diffuser methods, respectively; it dropped quickly on the following day. Four of the five patients received fentanyl injections for postoperative pain management beginning on postoperative day 0. All patients who underwent therapy using a cylindrical diffuser required postoperative pain management with opioid drugs, but in one of the two patients who underwent therapy using a frontal diffuser, opioid pain management was deemed unnecessary and was thus not performed.

Conclusion/Recommendations: To our knowledge, this is the first case series study on pain and pain management after PIT. All patients experienced pain after PIT, which is consistent with the results of the phase I clinical trial in Japan. Even though this study is a case series, the data obtained clearly described characteristics of pain caused by PIT in daily clinical practice. Pain after PIT tended to be most intense immediately after or one hour after illumination and declined the following day, suggesting the need to have a pain relief plan in place beforehand. This study also revealed that, although the pain accompanying PIT varies according to the method used, it develops early and can be controlled primarily using opioid analgesics.

069

Analysis of immune checkpoint inhibitors-adverse effects in advanced or metastatic non-small cell lung cancer: a review in real-world

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Objective/Purpose: Immunotherapy has become a standard of care in non-small cell lung cancer (NSCLC) treatment in recent years. Immune checkpoint inhibitors (ICIs) are increasingly used, which has led to an increase in reports of immune-related adverse events (irAEs), and adverse events (AEs) of any kind, providing increased safety knowledge beyond clinical trials. The aim is to evaluate the safety of ICIs used as monotherapy in advanced or metastatic NSCLC patients.

Study Design/Methods: Retrospective, descriptive study of patients with advanced or metastatic NSCLC treated with pembrolizumab, nivolumab, atezolizumab and durvalumab monotherapy in the last two years (between 2020 and 2021). Data collected: demographics, basal Eastern Cooperative Oncology Group (ECOG), AEs were recorded according to CTCEA v4.3 criteria, irAEs, grade, management and appearance time of toxicity, treatment interruptions and suspensions.

Results/Key Findings: A total of 136 patients were included, 44,8% pembrolizumab, 29,4% nivolumab, 17,6% atezolizumab and 8,1% durvalumab. Median age was 63.2±11,6 years old. 73.5% were men and 67.6% ECOG-1.77% of patients suffered from some AE to pembrolizumab, 82.5% to nivolumab, 79.2% to atezolizumab and 100% to durvalumab. No grade 4 AE was recorded. Grade 3 events were: two patients with diarrhea and one immune-related nephrotoxicity with pembrolizumab, one immune-related ocular toxicity and one pneumonitis with nivolumab, two pneumonitis and one immune-related cutaneous AE with durvalumab, no grade 3 AE with atezolizumab. These toxicities forced suspensions of treatment, in addition to a progressive neurological dysfunction in one patient that forced stopping treatment with atezolizumab. The remaining AE were grade 1-2. AE occurring in at least 5% were: Asthenia (42.6% pembrolizumab, 52.5% nivolumab, 45.8% atezolizumab and 63.6% durvalumab), skin rash (8.2% pembrolizumab, 22.5% nivolumab, and 27.3% durvalumab), pruritus (8.2% pembrolizumab, 20% nivolumab, 8.3% atezolizumab and 18.2% durvalumab), myalgia (12.5% nivolumab, and 9.1% durvalumab), arthralgia (11.5% pembrolizumab, 10% nivolumab, 16.6% atezolizumab and 9.1% durvalumab), dyspnea (10% nivolumab, 12.5% atezolizumab and 27.2% durvalumab), anorexia (8.2% pembrolizumab, 10% nivolumab, and 16.6% atezolizumab), vomiting (11.5% pembrolizumab, 2.5% nivolumab, 4.1% atezolizumab and 9.1% durvalumab), renal toxicity (11.5% pembrolizumab), diarrhoea (8.2% pembrolizumab, 7.5% nivolumab, 8.3% atezolizumab and 18.2% durvalumab), constipation (4.9% pembrolizumab, and 12.5% atezolizumab), cough (27.3% durvalumab), pneumonitis (4.9% pembrolizumab, 5% nivolumab, 12.5% atezolizumab and 36.4% durvalumab), endocrinopathies involving the thyroid (11.5% pembrolizumab, 10% nivolumab, and 27.2% durvalumab), and colitis (5% nivolumab). Asthenia was the AE that occurred most frequently and was common to all four drugs. The most serious reactions were irAEs. Nivolumab and durvalumab were characterized by cutaneous toxicity. Renal toxicity appeared only with pembrolizumab. Endocrine toxicity and pneumonitis were notable with durvalumab.80% of immune-related cutaneous AEs, 33.3% of endocrine iAEs, and 100% of pneumonitis occurred before 6 months of treatment. Grade 3 iAEs resolved with intravenous corticosteroids. No relationship was found between the iAEs and the mechanism of action.

Conclusion/Recommendations: Understanding and management organ-specific toxicities are critical goals for not only oncologists, but for many other specialists who encounter these patients throughout their treatment course. In addition, although AEs are not usually severe, their frequency is high, so early identification and supportive medication can prevent suspensions of ICIs treatment.

070

A retrospective review of the incidence of hypersensitivity and infusion reactions in patients treated with sSacituzumab Govitecan without H2-antagonist pre-medication

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Objective/Purpose: Sacituzumab Govitecan is a targeted biological therapy which is licensed for the treatment of unresectable locally advanced or metastatic triple-negative breast cancer in adults, after 2 or more prior systemic therapies. In the ASCENT trial, hypersensitivity reactions occurred in 37% of patients within 24 hours of Sacituzumab Govitecan infusion, with 2% of these having G3-G4 reactions (1). Furthermore, In IMMU-32-05, hypersensitivity reactions within 24 hours of dosing occurred in 34.1% of patients in the Sacituzumab arm compared to 20.5% in the TPC arm (2) Consequently, pre-medications have been recommended to prevent infusion related hypersensitivity reactions, which include a H2 antagonist. Ranitidine is a popular H2 antagonist which was given within our pre-medication regime for patients receiving this drug, but unfortunately this is no longer available. Additionally, there is a lack of evidence surrounding the use of H2 antagonists for hypersensitivity reactions, as demonstrated by Foreman et al in a study which concluded that H2 antagonists can be safely removed from standard pre-medication regimes for paclitaxel (3,4,5). Due to this, and an array of similar research confirming the lack of advantage served by H2 antagonists in this setting, at the Royal Marsden we took the decision to omit H2 antagonists from the standard pre-medication regimen for Sacituzumab Govitecan. The purpose of this review was to assess if the omission of H2 antagonist prior to treatment with Sacituzumab Govitecan affected the frequency of hypersensitivity reactions. This information will be valuable to other centres which will begin using Sacituzumab Govitecan following local approval.

Study Design/Methods: A retrospective review was conducted to analyse the records of all patients who had been treated with Sacituzumab Govitecan over the last year at The Royal Marsden. The review tool collected data on; the length of treatment, the use of a H2 antagonist before or during treatment and the incidence of hypersensitivity reactions (as defined by the ASCENT trial). Data was collected by systematic analysis of patient drug records and case notes during the treatment period. Limitations of this method were namely the sample size and variation in documentation between different medical practitioners.

Results/Key Findings: A total of 30 patients have received treatment with Sacituzumab Govitecan in the past year and were included in the analysis. None of these had received a H2 antagonist prior to or at any point during their treatment. There were no documented hypersensitivity reactions in any patients (n=0, 0%). The median number of cycles received was 3, ranging from 1 to 14.

Conclusion/Recommendations: The data shows that omitting the H2 antagonist from the pre-medication regimen did not increase the chance of infusion related hyposensitivity reactions in our patients. We can conclude that chlorphenamine, paracetamol and dexamethasone were sufficient in preventing hypersensitivity reactions related to Sacituzumab Govitecan. At The Royal Marsden NHS Foundation Trust, we will not be including an H2 antagonist as part of a standardised pre-medication regime.

Funding: The Royal Marsden NHS Foundation Trust

071

What is the concordance in the prognostic value of haematological biomarkers in immunotherapy treatments?

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Objective/Purpose: To compare the cut-off points of the neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) described in the scientific literature with those obtained in a cohort of patients from our center.

Study Design/Methods: Observational and retrospective study in a tertiary level hospital. We used the results obtained in previous studies of our working group on the prognostic value of NLR and PLR; obtained from a population of patients with non-small-cell lung carcinoma (NSCLC) treated with pembrolizumab. A bibliographic query was made in the published studies in order to obtain different cut-off points for comparison, the search path was: “Lymphocytes”[Mesh])AND “Neutrophils”[Mesh])AND “Immunotherapy”[Mesh]); filters: since 2017 and type study “meta-analysis”.

Results/Key Findings: Literature search for NLR and PLR cut-off points: 4 meta-analyses were obtained: doi:10.18632/aging.203256; doi:10.3390/medicina58081069; doi:10.1080/07357907.2019.1639057; doi:10.1007/s00262-018-2126-z. In order to compare NLR and PLR values, studies containing patients diagnosed with NSCLC and treated with pembrolizumab were chosen. 1. *Suh et al.* (2017), cut-off NLR=5 and PLR=169, n=54. 2. *Pavan et al.* (2019), cut-off=NLR 3 and PLR=180, n=184. 3. *Prelaj et al.* (2020), cut-off NLR=4 n=154. 4. *Takada et al.* (2020), cut-off NLR=6,05 and PLR=245, n=226. 5. *Ksienski et al*. (2021), cut-off NLR=6,4 and PLR=441,8, n=220. In our previous study the cut-off points were NLR=5 and PLR=200, n=74.

Conclusion/Recommendations: The results obtained in our previous works for NLR and PLR cut-off differ with the results obtained by different authors. These differences may be due to the methodology for calculating progression times or overall survival. Gender and age do not seem to influence the differences between the results. NLR is the most studied compared to PLR. Our work shows that the role of hematological ratios in the prognosis of immunotherapy therapies is still quite controversial despite the amount of work that exists, so it is necessary to carry out specifically designed studies that allow us to find out their real value, and define the most appropriate cut-off points for each type of population, taking into account factors such as histology, stage or previous treatments. It would also be interesting to include time since diagnosis as a variable to be considered, a variable that is not specified in the studies consulted. Currently, our research team continues to analyze more data in more patients and incorporate more variables to analyze how these biomarkers affect prognosis with immunotherapy-based therapies.

072

Adverse drug reactions due to haematology/oncology medicines as recorded in Kenya

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Objective/Purpose: The objective of the study was to assess the adverse drug reactions related to heamatology/oncology medicines as reported in the PVERSE system on the prevalence, types, severity and outcomes.

Study Design/Methods: This was a cross sectional study. The pharmacy and poisons board is the medicines regulatory agency in Kenya. They developed an online web based system (referred to as PVERSE) for online reporting of adverse drug reactions (ADRs) in 2013. In 2021, the system was revamped and publicised. Health care professionals in Kenya are required to report all ADRs through PVERSE. We downloaded the data on ADRs related to haematology/oncology medicines reported in the PVERSE since May 2021 to May 2022 into a Microsoft Excel document and analysed it.

Results/Key Findings: A total of 64 events were recorded in this period of review. The medicines that were reported to have caused the ADRs on were Imatinib (33.85%), hydroxyurea (12.3%), volexotor (9.23%), docetaxel (7.69%), ifosfamide (6.15%), oxaliplatin (4.62%), paclitaxel (4.62%), etoposide (4.62%), cisplatin (3.08%), rituximab (3.08%), fluorouracil (1.54%), vincristine (1.54%), methotrexate (1.54%), bortezomib (1.54%), lenalidomide (1.54%), gemcitabine (1.54%) and capecitabine (1.54%). The ADRs reported were hypersensitivity reactions ((35.94%), death (17.19%), dyspnoea (10.94), diarrhoea (6.25%), palpitations (4.69%), neuropathy (4.69%), encephalopathy (4.69%), muscle spasticity (3.13%), angioedema (1.56%), pseudocellulities (1.56%), skin discolourations (1.56%), sleep disorders (1.56%), chronic myeloid leukemia transformation to acute myeloid leukemia (1.56%), flu-like symptoms (1.56%) and arthralgia (1.56%). Of these 64 ADRs reported, 11 resulted in death as is shown, 20 resulted in hospitalization and 5 resulted in disability. The remaining 28 did not cause death, hospitalization or disability. Imatinib was the most reported medicine accounting for 33.85% of all the reports. The ADRs associated with the imatinib were death, skin discolouration, transformation of chronic myeloid leukemia to acute myeloid leukemia, sleep disorders, muscle spasticityand flu-like symptoms. Volexotor was associated with hypersensitivity reactions and dyspnoea. Where death occurred, it was not possible to tell from the data retrieved if the death was due to the medicine or due to disease progression or any other factor. According to data from the Ministry of Health in Kenya, there were more that 25000 sessions of chemotherapy administered in the country in the year 2021. Comparing this data to the number of reported ADRs shows that a very low number of ADRs were reported. It is very likely that more ADRs occurred but were not reported. Imatinib is dispensed through a sponsored program in a few select hospitals in the country. Volexotor was being used in a clinical trial. This could explain why many reports of ADRs were related to the two medicines.

Conclusion/Recommendations: The Pharmacy and Poisons Board of Kenya and the pharmaceutical industry should develop a robust mobile phone application that can be used to report the ADRs in real time. They should also develop strong campaigns to encourage reporting of the data. The system should also allow for estimation of causality of a medicines likelihood to have caused the ADR.

Process Improvement / Pharmacoeconomics (PR)

073

Satisfaction degree of the professionals in the safety of the oncohematological compounding circuit prior to the implementation of a safety device in the pharmacy service

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Objective/Purpose: To find out the degree of satisfaction and perception of safety for the different professional categories (pharmacists, nurses and assistants/technicians) involved in the preparation of oncohaematological mixtures prior to the implementation of a safety device in the preparation and the convenience of adding a control system in the preparation.

Study Design/Methods: An anonymous online survey was conducted for professionals involved in the oncohaematological mixtures circuit, with 21 questions, 14 compulsory and 7 optional, the former multiple-choice and the latter free-choice, to gather comments from those professionals who wished to be more explicit in their answers. The first section of the survey sought to describe the characteristics of the worker: professional category and work experience in the oncohaematological compounding circuit; the second section were specific questions on the effectiveness of the five control points. The third and fourth sections asked about the suitability of the addition of a safety device on the efficiency of the process and about the perception of safety with the current circuit, respectively; and the last section, about satisfaction and comments. A descriptive analysis of the qualitative variables was carried out and the results are expressed in absolute values and percentages.

Results/Key Findings: The survey obtained a response rate of 41.5% (9/9 pharmacists, 19/31 nurses and 6/42 TCAEs/pharmacy technicians). 58.8% of professionals had more than 6 years of work experience in the processing area. Most of them (79.4%) agreed on the effectiveness of the current checkpoints. All current control points were considered to be effective. 55.9% considered that risk points still existed, in particular 25% mentioned the lack of means of validation in cabin processing. The majority of professionals (57.6%) answered that the addition of a safety system would have a considerable impact on the delay of treatments, however, 73.5% considered the addition of a safety device to be appropriate and necessary, as the estimated incidence of errors for 22 workers should be between 0-5% and between 5-10% for 5 other workers. It was felt that the quality of the preparations would increase with the addition of a safety system in processing by 85.3% of the respondents. The overall level of satisfaction with the way of working was found to be adequate by 75.8%, as well as the preference to work with a safety system by 85.3%, the latter question being answered by 100% of the respondents. Among the most positive aspects, the safety of the patient and the safety of the processor were highlighted. Suggested improvements included the need for continuous training and compensating for delays by increasing the number of staff.

Conclusion/Recommendations: The perception of the Pharmacy Department employees regarding safety in the preparation of intravenous mixtures is satisfactory, although they consider that the addition of a safety device could improve the quality of the preparations and would improve stages in which there is a greater risk of error. In general, professionals prefer the addition of a safety device in the preparation. The main drawback is the delay in processing.

074

Antineoplastic drugs requiring filtration for their preparation and/or administration at the outpatient unit in a tertiary care hospital

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Objective/Purpose: More parenteral drugs used in hospitals require filters for their preparation and/or administration. These drugs represent a medium risk according to the Spanish Good Practices Guidelines on the Preparation of Medicines, and the Pharmacy Department must guarantee their adequate management for safe use. Our aims were:

- Identify the parenteral antineoplastic drugs that require filtration and the steps at which this is needed.
- Define improvement actions to reduce the risk of the medicine reaching the patient without prior filtration.

Study Design/Methods: We screened parenteral antineoplastic drugs consumed by the outpatient unit of our hospital during the second semester of 2021. We reviewed the literature and the summary of product characteristic (SPCs), as well as the protocols that included them. Based on the information obtained, a database was developed defining active ingredient, stage at which filtration is required (preparation or administration), filter pore size and specifications included in our software.

Results/Key Findings: Out of 63 parenteral antineoplastics reviewed, 29 were found to require filtration. According to the SPCs, 3 of them during preparation and 26 of them during administration. Of those requiring filtration during preparation, all 3 are prepared in the Pharmacy Department and both the need for filtration and the pore size are specified to the compounder in the information system used. The specific information for filtered administration was available in the protocols for the 26 drugs that require filtration during administration. These drugs are sent from the Pharmacy Department with the suitable infusion system and filter. It was found that 3 of them did not specify the pore size. We noticed that, although the filter requirement at each step is specified, the pore size is only specified in the computerised protocols. The following improvement actions were proposed: 1. Review and update of protocols, if appropriate, in the prescription and compounding programme paying particular attention to reference to the filter to be used for reconstitution and the filter to be included for delivery. 2. Update the information available to the outpatient unit nursing team concerning the filter delivered from pharmacy.

Conclusion/Recommendations: Information on the material and pore size of the filter to be used is limited or unspecified in the SPCs for some medicinal products. Review and improvement actions are suitable for any hospital with or without a computerised prescribing system. Every hospital should keep the management of antineoplastic medicines requiring filtration up to date and should be reviewed with the inclusion of every new drug. Integration of filter information increases patient safety, as there is a double check by the nursing team of the outpatient unit.

075

Evaluation of a measure for dealing with an increase demand of parenteral chemotherapy treatments

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Objective/Purpose: To evaluate the implementation of a recently adopted measure for dealing with an increase demand of parenteral chemotherapy treatments in a tertiary hospital.

Study Design/Methods: In 2020, the need for parenteral chemotherapy administration remarkably augmented. This situation created difficulties in the management of the patient care, caused delays in waiting rooms and decreased patient safety. In June 2020, our day hospital interdisciplinary team decided to implement a new measure in order to reduce the spontaneous demand of chemotherapy treatments and set up a better planification system. The measure consisted in administrating chemotherapy the day after the medical appointment instead of the same day. The main exceptions to this measure were: patients transferred from another hospital in the Osakidetza (Basque Country Health Service) network; totally, severely or moderately dependent patients according to the Barthel scale (0-61); those who are fragile/vulnerable or need an ambulance for any transfer to get to the hospital; patients who need a complete rest or are likely to be admitted to the hospital at the time of medical appointment due to some symptoms: dyspnea, extreme fatigue, nausea and vomiting; patient in lawful or institutional custody. The main variable measured was the number of treatments prescribed. The data about date of the prescription, date of the preparation and the medical speciality which prescribed it were obtained from chemotherapy electronical prescription software. The team established four different times to get data information before and after the implementation of the measure.

Results/Key Findings: In September 2019, the year before the implementation, 38% (361 of 959 chemotherapy prescriptions) were not administered on the same day of the medical appointment. This rate was higher in the hematology service 65% (156 of 240 treatments) than in the oncology service 29% (205 of 719 treatments). In 2020, after the measure implementation, this percentage improved up to 70% (712 of 1011), 91% in hematology and 64% in oncology. In 2021, the improvement was slightly higher 74% (836/1132), 94% in hematology and 66% in oncology service. In 2022, the results were a little lower the 70% (794 of 1140), 90% in hematology and 62% in oncology but nearly doubled the results of 2019, before measure implementation. The best results in hematology can be explained, in part, because their chemotherapy protocols are based on administrations on consecutive days but prescribed on the first day of the cycle.

Conclusion/Recommendations: The percentage of patients whose chemotherapy treatment was administered the day after medical consult improved after the new protocol was implemented. The new protocol increased the time to organize the workload. It would be interesting to probe if these measures suppose an improvement in oncohematological patient care and security as well as in patient and professional satisfaction.

076

Planning and design consultation of ambulatory oncological pharmaceutical care

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Objective/Purpose: Pharmaceutical care to the oncohematological patient implies an improvement in the care and results of oncohematological treatment. Documents of the Spanish Society of Hospital Pharmacy, Spanish Society of Medical Oncology and the Ministry of Health recommend the incorporation of the hospital pharmaceutical specialized in oncohematology into the multidisciplinary team of oncological patient care from the consultations of the day hospital, providing a global approach to the global approach of the Oncohematological treatment. The objective of this work is to describe the planning, design and its adaptation to the care circuit of a pharmaceutical care consultation to the oncohematological patient in the dependencies of the day hospital and analyze the expected activity of said consultation in an oncological reference hospital.

Study Design/Methods: In the design and planning phase an analysis of the current situation and the context in which the consultation would be implemented by means of a SWOT analysis tool was carried out. The objective of the consultation was established, a model of care was designed and agreed according to the hospital care structure. For the analysis of the activity, the data of the number of preparations and drugs used for intravenous antineoplastic mixtures and number of oral drug dispensations of the records of the oncological pharmacy and pharmacy and pharmacy service applications during the year 2021.

Results/Key Findings: The hospital serves a population of 650,000 inhabitants and is reference in the province for oncological treatment. In the starting situation, intravenous treatments are validated by a pharmacist specializing in oncohematology located in the pharmacy service and oral treatments are by a hospital pharmacist in the consultation of general external patients. In the SWOT analysis, the existence of two different applications for the validation of intravenous and oral oncological prescriptions was found as more significant weakness, as a threat the volume of care activity for oncohematological patients, as strength the existence of a pharmacist specializing in Oncohematology and as opportunity the reality of the incorporation of the pharmacist into the multidisciplinary team through different tumor committees. In the design of the consultation, the validation activities of all electronic prescriptions of intravenous mixtures and the comprehensive care of lung cancer in treatment with oral directed therapies were incorporated. The activity planned from the consultation includes the validation of intravenous treatments of 1,873 patients with a total of 28,187 mixtures (112 mixtures/day), of which 271 (14%) patients with 3,168 (11%) would be for cancer patients of cancer lung. As for oral drugs, 92 patients with a total of 52 pharmaceutical care consultations per month would be served.

Conclusion/Recommendations: The planning and design of the consultation with a standardized methodology has allowed to adjust the activity of this to the care needs and detect structural and material gaps that must be solved, always improving the care of the oncological patient.

077

Real world data of durvalumab in locally advanced non-small cell lung cancer

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Objective/Purpose: Durvalumab (DMab) is indicated in adults for the treatment of lung cancer, unresectable, locally advanced small cell disease (nSCLC), whose tumors express PD-L1≥1% and whose disease has not progressed after chemoradiotherapy platinum based. The effectiveness and cost of the treatment can be affected in real clinical practice, so it is important to know if the health outcomes obtained reach the efficacy data of the pivotal trial. To evaluate the effectiveness and cost-effectiveness of Dmab in nSCLC, real world data.

Study Design/Methods: We designed an observational study in an oncology referral hospital serving an area of 650,000 inhabitants. We include all patients (pts) treated with Dmab for nSCLC since January 2018 to September 2022 in a hospital in the south of Spain. The main variable was overall survival (OS) and treatment cost (TC) according to the reference price of Dmab for the National Health System. Other outcome variables were progression-free survival (PFS) and treatment duration (TD). We also collected age, sex, smoker, performance status (ECOG), number of doses administered, total cumulative dose of Dmab. A Kaplan-Meier analysis is performed for PFS, TD and OS and frequency analysis, or with measures of central tendency and dispersion for the rest. We calculate the cost-effectiveness by the following formula: $\Sigma OS\ benefit\ (m)\ /\ \Sigma TC$ (€). OS benefit (months=m) for each patient was calculated: OS(m)-[OS(m)*hr (PACIFIC trial)].

Results/Key Findings: Twenty-five pts (92 % male) were included. The mean was 64.9 years old (σ=9.3). Twenty-four pts were smokers at diagnosis, mean 60 paks/year. The histology was squamous in 16 pts (64%), no squamous 8 pts (32%) and NOS 1 pts (4%). The median follow-up was 20.5 m. TD median was 6.5 months (95% CI: 2.2-10.2), 10.5 doses administered [. Seven pts completed 12 months of therapy, 2 continue in treatment, 7 pts discontinued treatment due to progression disease, 8 by adverse events and one patient due to death, only 2 pts continue in treatment at date cute-off. Nine patients received another line of treatment after Dmab. The median PFS was 18.7 months (95% CI: 4.4-33.0). The median of OS could not be calculated as it did not reach the number of events after the follow-up time, the mean assuming normal distribution was 33.9 months (95% CI: 26.4-41.3). At cute-off date the ∑OS benefit at population was 149 months (12,4 years), the total cost of Dmab was 519,912€ and the mean TC 20,796€ (σ= 15,953). The cost per year of life gained was 41,779€ (95% CI: 28,177€-100,967€).

Conclusion/Recommendations: Real world data show similar PFS and OS to those obtained for the pacific trial, however there is uncertainty regarding the analysis cost- effectiveness. The cost per year life gained has a very wide range that includes values that are below and values that exceed the willingness-to-pay in our country.

078

Let's communicate cancer: developing an e-learning package for the whole community pharmacy team

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Objective/Purpose: Community pharmacies are a free and widely accessible health resource. In the UK, most people live closer to a pharmacy than their family doctor, making them well placed to deliver cancer care particularly in areas of high social deprivation.[1] However, previous research cites lack of cancer knowledge amongst community pharmacy teams, highlighting a barrier to developing cancer services.[2] Let's Communicate Cancer (LCC) is an e-learning package developed by the British Oncology Pharmacy Association to support community pharmacy teams. The objective was to deliver a package which:

Covers the whole cancer pathway

- Is easy to access and use
- Improves user's confidence in communicating about cancer.

This survey aimed to investigate the impact of LCC on participants confidence and identify improvements for further development.

1. Todd A, Copeland A, Husband A, Kasim A, Bambra C. Access all areas? An area-level analysis of accessibility to general practice and community pharmacy services in England by urbanity and social deprivation. BMJ Open. 2015, May; 8(5). DOI: 10.1136/bmjopen-2014-007328
2. Lindsey L, Husband A, Nazar H, Todd A. Promoting the early detection of cancer: a systematic review of community pharmacy-based education and screening interventions. Cancer Epidemiology. 2015, October; 39(5). DOI: 10.1016/j.canep.2015.07.011

Study Design/Methods: A 24 question feedback questionnaire was developed using SurveyMonkey (Momentive, California). The survey was piloted and updated before inclusion in the LCC website; LCC participants who completed the whole course were invited to participate in the survey. Survey data was exported to Excel for analysis.

Results/Key Findings: At June 2022, 3851 distinct user ID's has accessed LCC; 87 users had completed LCC with 82 submitting a feedback survey (response rate 94%). Following completion:

- 84% of participants reported improved confidence discussing cancer with members of the public
- 76% agreed the whole pathway was covered
- 79% reported the course was easy to access and navigate
- 84% felt modules were the right duration
- 75% of participants were pharmacists/trainees, 9% technicians, 6% dispensers, 2% counter assistants – demonstrating a bias towards highly educated users

Conclusion/Recommendations: These results provide evidence to demonstrate the impact of LCC on community pharmacy staff. They illustrate a significant improvement in self-reported confidence in discussing cancer with patients, recognising the signs and symptoms of potential cancers and referring patients into appropriate pathways. While these results limited by a small sample size and high number of pharmacists, BOPA have collaborated with Health Education England on an in-depth qualitative to provide greater clarity. Module 1 of LCC is now a requirement for all patient-facing pharmacy staff in NHS England and further funding has been secured to for improvements and additional material. LCC is accredited by the Royal Society of Public Health (UK) and available free at https://www.bopa.org.uk/

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079

Impact of a mobile app on the control of treatment adherence and on patient-hospital pharmacist communication: results in its first year of implementation

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Objective/Purpose: Mobile applications (apps) can connect and improve pharmacotherapeutic follow-up, communication with healthcare providers, medication adherence, and management of treatments' side effects. The primary end point of this pilot study is to measure medication adherence to tyrosine kinase Inhibitors (TKIs) in chronic myeloid leukemia (CML) patients by computer dispensing records during the first 6 and 12 months of using the app compared to 6 months prior to inclusion in the study. The secondary aims were to (1) to determinate medication adherence with the *Spanish-version Adherence to Refills and Medications Scale* (ARMS-e) (2) measure patient satisfaction with the app and its usability and (3) explore the impact of the app on patient-pharmacist communication.

Study Design/Methods: Observational study consisting of a control phase (CP) (follow-up prior to inclusion in the study) and an intervention phase (IP) (app). Participants must have received TKI for at least 6 months. Measure of medication adherence was performed by two methods: using dispensing records and with the ARMS-e (validated questionnaire) Patient satisfaction with the app and its perceived usability (using the *System Usability Scale*) were assessed 6 and 12 months after registration in the app.

Results/Key Findings: In total, 32 evaluable patients were included. D**emographic and clinical characteristics:** Mean age 53 years (29-76), men 69%, ECOG (0): 100%. Prognostic factors: Sokal (high-intermediate-low) 11%-11%-78%. Optimal response according to ELN criteria: 100%. Number of previous treatments: 1 ITK 13 (41%), 2 ITKS 15 (47%), ≥3 ITKs (12%). ITK at the time of study entry: Imatinib (12), dasatinib (7), nilotinib (13). Mean time from diagnosis: 7.8 years (2-25). Median duration of TKI therapy: 60 months (3-204). Comorbidity (>2 concurrent diseases): 25%, polypharmacy (>6 medications): 14%. M**easure of ITK adherence by using dispensing records (CP, IP 6 and 12 months)**: 96.2% (SD=14.7) and 98.8% (SD=2.9) and 99.0% (SD=9.5) respectively. R**esults of the questionnaires (ARMS-e, SUS and VAS) IP 12 months**: Completion rate was 43.8% (14 patients). The mean score for ARMS-e was 14 (SD=2.09; score range 12-48 best-worst adherence), usability 76.6 (SD=15.6; score range 0-100). Overall satisfaction with App was 8 (SD 1.7; score range 0-10) Up to 56.3% of users sent messages to pharmacists through the app (mostly about interactions and toxicities)

Conclusion/Recommendations: The results of this pilot study in its first year of implementation have shown an improvement in the treatment adherence. The reason for the low completion rate of the questionnaires was the study population, as they are patients with an average time with the ITK of 5 years. With these results, the platform could be offered to patients at the start of treatment, with a greater need for pharmaceutical support. This digital health project is applicable to other pharmacy services willing to incorporate telepharmacy to complement and improve specialized pharmaceutical care, offering alternatives, promoting the humanization of care, and providing the opportunity for patients and their caregivers to be accompanied during follow-up of disease in the outpatient setting.

080

Development of a process to manage oncology drug shortages

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Objective/Purpose: BC Cancer is a provincial organization with the responsibility of providing a comprehensive cancer control program for the people of British Columbia. There are six regional cancer centres working in partnership with 48 community oncology network hospitals to provide care. Drug shortages are now a common occurrence and shortages of oncology drugs are particularly difficult to manage. Implications of drug shortages include concerns about safety and quality of cancer care, evidence to support therapeutic alternatives, risk of adverse effects and potential for medication errors. Often there is little notice of a shortage and the system is left to manage the situation in crisis mode. The objective was to establish a process for quickly identifying oncology drug shortages, determining remaining inventory levels and patients on treatment, prioritizing and sharing remaining drug supplies across all treating centres, identifying therapeutic alternatives and communicating relevant information to all those involved in cancer care in British Columbia.

Study Design/Methods: Oncology drug shortages (defined as drugs used in the active treatment of cancer, for which there is no alternate brand available) were tracked for calendar years 2011 to 2021. Input was solicited from a variety of stakeholders, including physicians, pharmacists, pharmacy technicians and nurses via meetings and email communication. Based on this input, a process was developed and refined over time.

Results/Key Findings: In 2011 and 2012, there were four oncology drug shortages each year. By 2015, this had risen to 17 oncology drug shortages and for the calendar years 2019-2021, there were an average of 20 shortages per year. Stakeholder input indicated that there was a need for timely communication about drug shortages, information on available supplies, identification of patients on treatment and recommendations for therapeutic alternatives. In addition, information for patients, planning for a response to media in the event of news coverage and participation in national initiatives were needed. Based on this input, a 3-step process was developed to coordinate and manage oncology drug shortages: Step 1: Inventory Management – inventory counts, collating patient lists, working cooperatively on sharing remaining drug supplies. Step 2: Developing Therapeutic Alternatives – working with the Tumour Groups, Pharmacy and Nursing to determine therapeutic alternatives – including existing protocols, developing new protocols, delaying treatment, dose modification, medication safety review. Step 3: Communication Plan – liaising with community partners, standardized briefing note for clinicians, patient information, working with communications team in the event of news media coverage, staff education

Conclusion/Recommendations: By developing a standardized approach to managing oncology drug shortages, it is possible to optimize management of a drug shortage by managing inventory, working with the tumour groups, ensuring communication and educating staff and patients.

081

Trends in oral anticancer medication prescribing at a large regional cancer centre in Toronto, Ontario, Canada

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Objective/Purpose: The number of oral anticancer medications (OACMs) available to treat malignancies is increasing. As there is a paucity of literature on the prevalence of OACM use across time, the objective of this study is to summarize and explore OACM prescribing trends at a large Regional Cancer Centre to better understand anticancer treatment paradigms.

Study Design/Methods: This retrospective study used OACM dispensing data from the Odette Cancer Centre Pharmacy located on the Sunnybrook Health Sciences Bayview Campus in Toronto, Ontario, Canada. Data for dispensing events between 01 January 2018 to 31 March 2022 were extracted from the pharmacy's Kroll database. Data elements included patient name and identifier, prescriber, prescription number, fill date, and drug DIN, name, and strength. Data was organized to identify new starts per fiscal quarter for each OACM, and linear regression analyses (significance level of <0.05) were performed to assess trends of new prescriptions for different groups and classes of OACMs.

Results/Key Findings: A total of 87 different OACMs were dispensed across the 51-month study period. The 20 most frequently prescribed agents included bicalutamide (n=1026), capecitabine (n=807), temozolomide (n=553), letrozole (n=372), tamoxifen (n=275), abiraterone (n=230), 82laparib82ib (n=224), exemestane (n=201), 82laparib82ib (n=194), trametinib (n=183), dabrafenib (n=172), cyclophosphamide (n=170), lomustine (n=169), lenalidomide (n=146), enzalutamide (n=139), anastrozole (n=126), venetoclax (n=118), ibrutinib (n=102), niraparib (n=100), and sunitinib (n=91). Bicalutamide showed a significant reduction in prescribing rate (-2.0 new starts/quarter, p=0.01), whereas an increasing trend was observed for androgen receptor-axis-targeted agents given on a continuous basis (abiraterone, apalutamide, darolutamide, enzalutamide; +0.8 new starts/quarter, p=0.02). Prescription of PARP inhibitors (82laparib, niraparib) increased over time (+1.5 new starts/quarter, p<0.001). Axitinib exhibited an increasing trend over time (+0.2 new starts/quarter, p=0.04), but no statistically significant trend was observed when all TKIs prescribed for renal cancer were analyzed collectively. Cytotoxic agents (capecitabine, temozolomide, etoposide, cyclophosphamide, lomustine), BCR-ABL TKIs (imatinib, dasatinib), and EGFR TKIs exhibited decreasing trends across the study period (-1.2 new starts/quarter, p=0.03; -0.4 new starts/quarter, p=0.01; and -0.7 new starts/quarter, p=0.01, respectively). No statistically significant change in quarterly prescribing rate was found for anti-estrogen medications (anastrozole, exemestane, letrozole, tamoxifen), BTKIs (ibrutinib, acalabrutinib), CDK 4/6 inhibitors (82laparib82ib, ribociclib), immumodulators (lenalidomide, pomalidomide), and BRAF and MEK inhibitors (dabrafenib, encorafenib, vemurafenib, binimetinib, cobimetinib, trametinib), or PARP inhibitors (82laparib, niraparib),

Conclusion/Recommendations: Our findings identified several important prescribing trends that may indicate changing treatment landscapes in oncology. The reduction in traditional cytotoxic agents may reflect improved access to medications with better tolerance or efficacy, whereas the increased use of PARP inhibitors, axitinib and androgen receptor-axis-targeted agents may reflect changes in public drug plan reimbursement criteria. Future research will explore reasons for the observed changes in greater detail and describe changes in clinical and technical pharmacy workload associated with these trends.

082

Workload requirements for exceptional access drug applications and impact on pharmacy

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Objective/Purpose: The Exceptional Access Program (EAP) facilitates patient access to high-cost drugs which are not funded under the provincial drug formulary. To obtain reimbursement for drugs listed under EAP, the prescriber must submit a drug- and disease-specific form providing patient details, including past therapies, current treatment plan, and relevant clinical, biochemical, and radiographic information to the Ontario Ministry of Health (MOH). This is a labourious process, which takes time away from prescribers' clinical duties. As such, medical oncologists at the Odette Cancer Centre (OCC) have requested Registered Pharmacists assume this task as medication experts. The objective of this project is to quantify the demand for EAP submissions and estimate the number of staffing hours required for pharmacists to completely take over EAP management for all eligible patients of the OCC Pharmacy.

Study Design/Methods: The Sunnybrook OCC is the second largest Regional Cancer Centre in Canada. OCC Pharmacy records were used to identify active EAP approvals and submissions pending review by the MOH. These cases were organized and described as frequency counts by drug and prescriber. To estimate the anticipated workload associated with the EAP cases identified, an initial application was assigned a workload of 1h to complete, renewals were assigned a workload of 0.25-0.5h to complete, and 2 EAP renewals were required per year (as this varies between drugs). Total projected workload for EAP submissions was reported as in terms of FTE equivalent.

Results/Key Findings: A total of 910 active/pending EAP cases were identified for 42 unique drugs and requested by 45 different prescribers. The five most commonly requested drugs were 83laparib83ib (n=99), enzalutamide (n=91), abiraterone (n=76), 83laparib83ib (n=74), and ibrutinib (n=53). Drugs with 25-49 EAP submissions included niraparib, ribociclib, 83laparib, dabrafenib/trametinib, voriconazole, apalutamide, darolutamide, and alectinib. Drugs with 10-24 EAP submissions included ruxolitinib, axitinib, sunitinib, erythropoietin, venetoclax, cabozantinib, imatinib, dasatinib, and tramexemic acid. One genitourinary (GU) oncologist was identified as an EAP superuser with a total of 117 active/pending EAP submissions–almost double the quantity of the second highest prescriber, also GU, at 68 submissions. The third and fourth highest EAP users were a lung oncologist with 61 submissions and a hematologist with 57 submissions. It would require 24.3 weeks of a full-time-equivalent (FTE) (37.5hrs/week) to prepare and submit 910 initial EAP applications. Submitting 910 renewals would require 12.1-24.3 weeks of FTE time. Using these estimations, 0.7-0.9 FTE would be required to meet the demands of the administrative workload. These analyses do not encompass the workload for submissions that have been declined or patients who proceeded with dispensing at their local pharmacy; therefore the workload is estimated to be in excess of our estimations.

Conclusion/Recommendations: This data demonstrates the time intensive nature of EAP applications and the need for dedicated pharmacist resources to off-load the administrative burden from physicians. The data summarised in this analysis can be used to justify the role of pharmacists for medication-related administrative tasks at other centres.

083

Chemotherapy e-prescribing implementation in hemato-oncology

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Objective/Purpose: E-prescribing is fundamental for the modernization and optimization of health systems, with a significant impact on patient safety. Regarding Hemato-Oncology, it is decisive to develop an integrated and robust circuit of Chemotherapy E-Prescription (CEP) that ensures intervention standardization, medication errors reduction and resources rationalization. We aim to describe the CEP implementation in Hemato-Oncology and to perform a preliminary assessment through SWOT analysis.

Study Design/Methods: The implementation process was developed through phases: (1) Preparatory meetings with Hematology and Bone Marrow Transplant Service; (2) Creation and Validation of Therapeutic Protocols at Glintt® software, with subsequent Validation by Medical Team (MT) and Nursing Team (NT); (3) Circuit design: Prescription/E-Validation by NT/ Pharmaceutical Validation/ Administration Register; (4) Meetings to evaluate needs and define an implementation strategy, including Informatics Service and Glintt® teams; (5) Hospital staff training; (6) Continuous process monitoring and periodic updates. A SWOT analysis was performed.

Results/Key Findings: The CEP was instituted on May 2022 in Hematology Day Hospital (~55 Protocols), concurrently with e-validation and administration register by NT. In 5 months, 908 CEP were performed by 14 prescribers (considering a total of 19). 633 CEP were e-validated by NT. During this period, along with occasional inconsistencies detected in specific patients, a potential incompatibility was noticed between clinical services. Informatics support was required to solve irregularities on protocols parameterization and prescription specificities. SWOT analysis:**S (Strengths)**- Multidisciplinary team, committed and dedicated- Prescription uniformization- Transcription suppression- Traceability **W (Weaknesses)**- Resistance culture- Time allocated- Obsolete computer resources **O (Opportunities)**- Multidisciplinary communication and cooperation improvement- Hospital informatics circuit optimization- Health policies focused on Patient Safety **T (Threats)**- Software inadequacy to the Hemato-Oncology specificities- Greater exposure to the software weaknesses (random and unexpected errors)- Restricted investment on computer and automated resources

Conclusion/Recommendations: Hemato-Oncology chemotherapy e-prescribing implementation is challenging due to the diversity and complexity of therapeutic protocols. It is crucial to Patient Safety, as it has the potential to reduce medication errors, mainly with High-Alert Medication used in oncology therapy. Regarding the pharmaceutical activity, CEP allows an optimized reallocation to an improved pharmacotherapeutic intervention. The investment on computer and automated resources is essential to effective CEP implementation and its impact.

084

Outcomes of the implementation of the 5-azacitidine home administration programme in patients with myelodysplastic syndrome

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Objective/Purpose: To analyse the health impact of facilitating the administration of 5-azacitidine at home and to assess adherence and safety.

Study Design/Methods: Prospective observational study between January 2019 and December 2021, which included 30 patients diagnosed with myelodysplastic syndrome (MDS). The medication was prepared in the Pharmacy Service, using the reconstitution method with refrigerated water for injectable preparations (2° and 8°C) and kept in the refrigerator (between 2° and 8°C), obtaining a chemical and physical stability of 22 hours. Once the patient's inclusion has been confirmed by the haematologist, the prescriber informs the pharmacy service of the treatment regimen and the dose and the nurse to organise the home administration regimen. The variables measured were: sex, age, start of treatment with 5-azacitidine at home, duration of treatment, degree of patient satisfaction, adherence to treatment and adverse effects detected.

Results/Key Findings: 30 MDS patients with a median age of 80 years (IQR 71-89), who had difficulty travelling to a day hospital for treatment with 5-azacitidine for 7 days, were analysed. 85% were men. They were treated with 5-azacitidine on a home-administered basis for a mean of 20 months of treatment. 70% of patients had difficulty in travelling to the day hospital because they needed a person to accompany them and 30% because they had no infrastructure to support them. 100% of patients were very satisfied with this service, adherence to treatment improved by 95% and 15% of adverse reactions such as neutropenia, anaemia and gastrointestinal reactions were detected.

Conclusion/Recommendations: By home administration of 5-azacitidine in elderly MDS patients, it has been possible to make it easier for elderly patients with little support infrastructure to attend the day hospital to receive their treatment, improve day hospital logistics by reducing the number of patients attending for treatment administration, and increase patient satisfaction and adherence to treatment, offering a higher quality of care.

085

Validation of the PRONTO instrument, checklist for reviewing chemotherapy prescriptions

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Objective/Purpose: Objectives: To validate the PRONTO instrument (Patient, Regimen, Organ Function, Numbers, Toxicity, Order Verification), a checklist created to help young people and/or non-specialist pharmacists review chemotherapy prescriptions.

Study Design/Methods: Study design/Methods: A randomized clinical trial was carried out with 30 pharmacists with at least 1 year of experience in Oncology. In the 1st phase of the study, the subjects were allocated into two groups, FREE ANALYSIS (FA) and CHECKLIST (CL), and performed analyzes of 10 prescriptions prepared by the author and containing 22 medication errors. In the 2nd phase, 22 of the 30 pharmacists participated and underwent online training on checking chemotherapy prescriptions to analyze 05 prescriptions prepared by the author containing 05 medication errors. Descriptive statistical analysis and chi-square tests or Fisher's exact test was performed to compare categorical data.

Results/Key Findings: Results: Females were the most prevalent (73.3%) and the mean age of participants was 34.4 years (SD ± 7.80) in the CL arm and 32.5 (SD ± 4.05) in the FA arm. In PHASE 1, in the comparative analysis, the CL group was superior in the detection of 09/22 errors (40.9%), while the FA group was superior in the detection of 13/22 medication errors (59.1%). In PHASE 2, the CL arm, in the comparative analysis, the CL group was superior in detecting 1/5 medication errors (20%), while the FA group was superior in detecting 4/5 medication errors (80%).

Conclusion/Recommendations: Conclusion/Recommendation: The PRONTO checklist was less effective in detecting medication errors when compared to the free analysis of chemotherapy prescriptions.

086

Analysis and budgetary impact of the use of bevacizumab biosimilar in oncology

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Objective/Purpose: European regulation ensures for the approval of biosimilar drugs that the products are highly similar to their original biologics in terms of quality, efficacy and safety. In addition, since the approval and entry into the market of biosimilars of monoclonal antibodies in oncology, there have been great cost savings, thus contributing to the efficiency of the healthcare system. The aim of this study was to describe the entry of biosimilar bevazizumab in a tertiary level hospital and its budgetary impact on the center, within a protocol of mandatory use at the beginning of treatment and the possibility of switching under medical criteria.

Study Design/Methods: Retrospective and observational study from October 2020 to October 2022. All patients on treatment with brand-name and biosimilar, since the inclusion of bevacizumab biosimilar in the hospital, were included. All data were obtained from the electronic assisted prescribing program. Changes in use from Brand-name to biosimilar drug were recorded. The number of cycles and vials consumed (taking into account vial optimisation) per patient and diagnosis were recorded. Costs per cycle were recorded (using acquisition prices invoiced to hospitals), and total treatment costs per patient were calculated.

Results/Key Findings: 97 patients have been treated with biosimilar bevacizumab, and have consumed an average of 13.4 vials of biosimilar per patient in the study period, 59.6% of consumption was in ovarian cancer, 16.4% colon cancer, 12.1% cervix cancer, 4.6% rectum, 2.7% breast, 2.3% central nervous system cancer and 2.2% hepatocarcinoma.27 patients have continued to be treated with brand-name, and have consumed a total of 9.8 brand-name vials per patient in the study period, 34.1% of consumption was in ovarian cancer, 13.8% colon cancer, 16.3% cancer 7.7% rectal cancer, 5.7% renal, and 22.4% central nervous system cancer.100% of the initiations received biosimilar as indicated in the protocol, and only 6.9% of patients switching to biosimilar. The treatment of the 97 patients treated with biosimilar has meant an average cost per patient/year of € 2,322, and the 27 patients who continued with brand-name have meant an average cost per patient of € 4,367. The switch to biosimilar has resulted in a saving of about € 2,045 per patient/year. And a total saving of € 198,365 /year.

Conclusion/Recommendations: Access to biosimilars in the healthcare system will increase as clinicians become more aware of this option, and increase their knowledge of the totality of evidence that justifies aspects such as extrapolation and the switch. Cost studies in the decision-making process is a key point that increases the acceptance of biosimilars in healthcare systems. In addition, the reduction of the budgetary impact of the introduction of biosimilars has an impact on the opportunity to finance more treatments or new drugs.

087

Turning gold to platinum

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Objective/Purpose: The Southampton Oncology Centre Pharmacy consists of a team of 30 individuals comprising of both professional and support staff. Together we deliver a comprehensive and high quality service to the Southampton Oncology Centre. This encompasses an unlicensed aseptic dispensing service, clinical service to both in and out-patients, a regional chemotherapy electronic prescribing system as well as being responsible for the delivery of national and Trust priorities in relation to cancer medicines and acting as an expert resource. This service improvement project focusses on the aseptic until that delivers over 120 individual SACT per day. In July 2021 the department moved into a purpose built modular unit, Platinum House. Platinum House was designed, built, validated and opened in ten months leaving little time to familiarise staff with the layout and implement new operating procedures. This exposed the frailty of the service. Delays in the delivery of treatments led to a poor patient experience, increase in complaints and incidents reported on the hospital system and increased staff stress noted in staff surveys. A service improvement programme was instigated to identify issues and implement solutions. Data was analysed to determine the success of each intervention.

Study Design/Methods: Focus groups were conducted with staff to identify areas for improvement and possible solutions. The results of the focus groups were used in a cause and effect analysis, undertaken using the “fish-bone” service improvement methodology. The causes were categorised into those affecting;- capacity- equipment- staff- procedures- clothing- facility- stock- misc. Each category was examined and solutions implemented using mini PDSA cycles. Data was gathered on SACT treatment delays and incidents reports to assess the impact of each intervention.

Results/Key Findings: In excess of 22 improvements to workflows were implemented over a 12 month period. These ranged from the simple re-organisation of the fridge and storeroom space to enable better stock control, to implementing virtual communication between the different areas of the pharmacy using “TEAMS”, to the design, build and implementation of a tracker module on the electronic production system, Medcura. The tracker displays real time data on the production process and can be accessed by all staff in the hospital. This allows pharmacy and nursing staff to predict the time a product will be delivered to the clinical area. It reduces phone calls and interruptions. The sum of all the improvements has led to a significant reduction in the length and frequency of delays.

Conclusion/Recommendations: Oncology Pharmacy has been through a period of rapid transformation following the move to a new purpose-built unit. This exposed the existing frailty of the service. A series of quality improvement initiatives over twelve months has resulted in significant improvements in service delivery. Reported incidents have dropped in number as has the frequency and length of delays. There are plans in place to continue this work to further improve the efficiency and robustness of the service.

Translational / Basic Science (TS)

088

A randomized, phase II study to evaluate histological and clinical effects of imipramine in the treatment of patients with cancer over-expressing Fascin1 (HITCLIF)

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Objective/Purpose: HITCLIF is an ongoing phase II non-commercial clinical trial to evaluate the effectiveness of the tricyclic antidepressant imipramine as anti-metastatic agent in the treatment of colorectal cancer and triple negative breast cancer (TNBC) patients with overexpression of fascin1 (FSCN1). P**rimary objective.** To assess the development of prognostic histopathological features as infiltrative growth and tumour budding in the surgical resection piece after the treatment. S**econdary objectives.** (1) Monitoring of minimal residual disease using circulating DNA. (2) Quantification of serum FSCN1 expression.

Study Design/Methods: Study Population. Patients aged ≥18 years old with colorectal cancer or TNBC who overexpress FSCN1 in the diagnostic biopsy tissue. M**ain Inclusion Criteria.** (1) Adenocarcinoma of the colon or rectum or TNBC histologically diagnosed. (2) Overexpression of FSCN1 in primary tumour with immunohistochemistry confirmed. (3) Candidate for tumor resection. (4) Candidates for neoadjuvant therapy (rectal cancer or TNBC). M**ain Exclusion Criteria.** (1) Metastatic disease at diagnosis. (2) Intestinal obstruction. (3) ECOG Performance Status ≥ 3. (4) Inadequate liver and renal functions. (5) History of cardiac disease. (6) Comedication with selective serotonin or norepinephrine reuptake inhibitors. (7) Depressive disorder, bipolar depression or psychosis. S**tudy design.** Multicenter, double-blind, placebo-controlled and randomized, phase II study conducted in 2 parallel groups. The intervention treatment consists in imipramine 65 mg initially and this be increased by 65mg every other day as tolerated to 185 mg. For colon cancer cases with inclusion criteria, imipramine will be given during 3-4 weeks between diagnostic biopsy and surgical intervention. For rectal and TNBC cases with inclusion criteria, imipramine will be given during the neoadjuvant treatment (4-6 months) until surgical resection. Tumour samples will be collected at diagnostic biopsy and at surgical resection intervention. Blood samples will be collected at baseline, at pre-surgery and at post-surgery. The study has an estimated total sample size of 180 patients and is being developed in 3 university hospitals (Virgen de la Arrixaca, Morales Meseguer and Santa Lucia).

Results/Key Findings: Study Status. Regulatory phase. Approval was obtained by August 2022 from the Spain Health Authority and from the local Ethics Committee. S**tudy timelines.** Start of recruitment in September 2022**.** Expected Completion of recruitment: September 2022**.** Primary endpoint analysis expected in February 2023. EudraCT n°: 2021-001328-17.

Conclusion/Recommendations: Although advances have been made in screening, early detection, and management of colorectal cancer and TNBC, therapeutic innovations have been scarce. This study aims to solve an important problem in oncology; provide useful and specific treatments to cancers, which have poor prognosis and lack molecular targeted therapies. On the other hand, the study focuses invasion and metastasis, the processes responsible for the vast majority of deaths caused by cancer. As anti-metastatic drugs are not usually tested in clinical trial this study provides an important novelty.

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089

A comparison of area under curve (AUC)-guided vs trough-guided therapeutic drug monitoring of vancomycin in oncological and hematological patients

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Objective/Purpose: A recent revised consensus guideline and review of therapeutic drug monitoring (TDM) of vancomycin points out that trough values may not be an optimal surrogate for Area under the curve (AUC) values in the case of Methicillin-resistant Staphylococcus aureus (MRSA) infections. Then, AUC over 24 hours to minimum inhibitory concentration ratio (AUC/MIC) ≥400 is now the optimal pharmacokinetics/pharmacodynamics (PK/PD) "efficacy" target. To assess if AUC/MIC guided TDM of vancomycin yields different dose recommendations than trough-based TDM in patients with non-MRSA infection admitted to the oncology or hematology wards.

Study Design/Methods: We performed a retrospective and descriptive study that included oncological and hematological patients admitted to a second-level hospital, starting treatment with vancomycin and dose adjustment guided by TDM at the Pharmacy service. Data collected were: demographic variables, Cockcroft-Gault creatinine clearance (CrCl), initial dosage, dose adjustments, the first trough level, duration of treatment, and reason for withdrawal. Renal impairment was defined as CrCl < 60 ml/min. Trough levels between 10 and 15 µg/ml were considered optimal for intermittent infusion schedules and microorganisms other than MRSA. The patients with MRSA infection were excluded due to the need for higher target doses of vancomycin (trough levels between 15-20 µg/ml). In our environment, the incidence of such infection is very low. Because of the impossibility of calculating AUC-guided dosing, we did not include hemodialysis patients. We used PKS® software and a web-based AUC Bayesian calculator to perform TDM.

Results/Key Findings: Vancomycin trough levels were available in 46 patients (35 hematological and 11 oncological). In 32 patients (69.6%), the vancomycin treatment was empirical and targeted in 14 (30.4%). The isolated microorganisms were Enterococcus faecium (n=7), Enterococcus faecalis (n=3), Lactococcus garvieae (n=1), Staphylococcus warnieri (n=1), Staphylococcus epidermidis (n=1), Corynebacterium spp (n=1). The initial daily mean vancomycin dosage was 1975±530,5mg. In 32/46 cases (69.6%), trough-based TDM resulted in dose modification because 26/32 had a subtherapeutic level and 6/32 a supratherapeutic level. However, applying the AUC/MIC-based method in the same cases, the dose should be modified in 39/46 (84.8%) because 33/39 had a subtherapeutic level and 6/39 had a supratherapeutic level ($p<0,001$ for McNemar's Test). In 32 patients, the dose needed changes regardless of the method used (trough-based or AUC/MIC-based). The means of the proposed daily doses for vancomycin were 3048.5±1383.9 mg and 3090.9±1248.2 mg using through-based TDM and AUC/MIC-based TDM, respectively. The difference was not statistically significant (T-test for paired values). The mean duration of antibiotic treatment was 7±4.2 days. The reasons for stopping the treatment were: clinical improvement (n=28), switch to a target treatment (n=9), clinical deterioration (n=8) and nephrotoxicity (n=1). Nine patients died during the treatment.

Conclusion/Recommendations: In our oncological and hematological patients, there is no difference in the daily mean dosage of vancomycin comparing the trough-based TDM method (trough target 10 – 15 µg/ml) with the AUC/MIC-based method. However, more patients need to have dose modification when AUC/MIC-based TDM is applied. More studies are needed to evaluate vancomycin's resulting efficacy and toxicity when using both TDM methods in patients with infections other than those provoked by MRSA.

Trainee (TR)

090

Prevalence and patterns of cannabis use in cancer patients receiving systemic anticancer treatment at Sunnybrook Odette Cancer Centre: a prospective survey study

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Objective/Purpose: Cannabis is commonly used by cancer patients for various medical and non-medical reasons. It is often perceived by patients to be a relatively safe substance, however it may interact with anticancer drugs and cause unwanted side effects. The objective of this study was to clarify prevalence and patterns of cannabis use among cancer patients. This will help highlight the importance of screening for medical cannabis use and provide a deeper understanding of patient perspectives on medical cannabis in an oncology setting.

Study Design/Methods: Participants were adults (≥18) able to speak, read and understand English, currently receiving systemic anticancer treatment (SAT) at the Odette Cancer Centre. The exclusion criteria were as follows: (1) conditions/concerns that would make a participant unable to complete the survey, (2) currently only receiving radiation therapy OR undergoing surgery OR receiving oral anticancer therapy to treat their cancer, (3) enrolled in/being considered for a clinical trial, (4) currently assigned to isolation rooms, (5) Patient Reported Functional Status (PRFS) score ≥3 within last 6 months, (6) ongoing and debilitating mental health concerns. There were 2 survey versions, one for patients who had used medical cannabis since their cancer diagnosis, and one for those who had not. Survey questions related to the following themes: demographics/clinical characteristics, attitudes, prevalence/dosage forms, reasons for use, efficacy, concerns/side effects, access/availability, support, and information. Additionally, a validated survey to measure attitudes towards medical and recreational cannabis was added approximately halfway through the study and was completed by all participants from that point onwards.

Results/Key Findings: Of 234 patients who completed the survey, 61% were female (n=142) and 39% were male (n=91). Mean age was 60.2 (SD+/-13.3; range 22 – 89). The rate of cannabis use was 19% (95%CI 14%-24%). Of patients who had not used cannabis (n=190), 35% (n=66) were interested in trying medical cannabis and 72% (n=137) would consider using medical cannabis if recommended by their oncologist or family doctor. Of patients who had used cannabis (n=44), only 18% (n=8) were being followed by a cannabis clinic or consult service. 80% (n=35) of patients who had used cannabis believed it should be more readily available to cancer patients compared to 60% (n=113) of patients who had not used. Age and sex were not statistically significant predictors of medical cannabis use by patients (p=0.81 and p=0.95, respectively). Patients treated for advanced/metastatic disease were significantly more likely to use medical cannabis than patients treated for early/non-metastatic disease (p=0.0007).

Conclusion/Recommendations: Of the patients who use medical cannabis, few are followed by a healthcare professional. Disease status (advanced/metastatic vs early/non-metastatic) may predict for a decision to use medical cannabis by the patient. Although cannabis is not a first line option to mitigate SAT side effects, most patients would trial cannabis if recommended by their physician. We emphasize the need for health care providers to engage patients and have open dialogue to ensure safe and effective use of cannabis for medical purposes.

Funding: Study funded by Sunnybrook Health Sciences Centre Department of Pharmacy.

091

Safety profile of ibrutinib used for the treatment of haematological malignancies

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Objective/Purpose: To describe the frequency of appearance of adverse drug reaction's (ADRs) related to the use of ibrutinib in hematology patients, as well as to characterize these ADRs and the impact on the patient's treatment.

Study Design/Methods: Retrospective observational study conducted in a six-year period (January 2016 – September 2022) in tertiary hospital. Data was collected from electronic medical records (Mambrino XXI®) and the Hospital Pharmacy Department database (Farmatools®) and included: medical record number, date of birth, diagnosis, start and end date of treatment with ibrutinib, dose, comorbidities, ADRs that the patient presented, dose modification or discontinuation of treatment after ADRs and date of death.

Results/Key Findings: 82 patients were included, 38% were women (n=31), with the following diagnoses: 84% (n=69) had chronic lymphoid leukemia B (CLL-B), 9% (n=7) mantle cell lymphoma, 2% (n=2) monoclonal gammopathy of uncertain significance and 5% (n=4) other diagnoses. At the end of the study period 79% of the patients treated had died (n=35) and 57% (n=47) of them had presented some type of ADRs. The most frequent comorbidities found were hypertension with 25% of the total found (n=45), 13% dyslipidemia (n=24), 13% diabetes (n=24) and 12% heart disease (n=20). In decreasing order of occurrence, the ADRs' percentage of occurrence were: 14% cardiac toxicity, followed by 12% mild hemorrhage, skin toxicity and pneumonia, 9% neutropenia, 8% thrombopenia, 7% anemia and other infections (excluding those listed below), 3% diarrhea and urinary tract infections, 4% edema and 3% severe bleeding, neurotoxicity and nephrotoxicity. There was a total of 42 treatment modifications due to ADRs, 20 of them were dose reductions and 22 treatment discontinuations. 5 patients could not complete the month of treatment due to the appearance of ADRs, 7 completed only the first month of treatment until the appearance of ADRs, while the rest of the patients were able to receive treatment for a longer period of time. The mean time until the appearance of the first ADR was 14 months. The maximum treatment time was 79 months, while the mean treatment duration was 23 months.

Conclusion/Recommendations: A high number of patients treated with ibrutinib for haematological malignancies presented some ADRs that led to dose reduction or treatment discontinuation. It is important to note that, given the immunosuppressed condition of these patients, appearance of infectious processes could be due to treatment with ibrutinib, to the patient's own condition, or to a combination of both factors. On the other hand, the same happens with cytopenias, generating doubt as to whether they are produced by the lymphoproliferative process or by ibrutinib.

092

Effectiveness and safety of Pembrolizumab in First Line Monotherapy Treatment of Non-Small Cell Lung Cancer

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Objective/Purpose: To analyse the effectiveness and safety of pembrolizumab as monotherapy for the first-line treatment of metastatic non-small-cell lung cancer (NSCLC) in adults whose tumour expresses PD-L1 ≥ 50% without positive EFGR or ALK mutations.

Study Design/Methods: Setting: third level hospital. Design: observational, retrospective study that included all patients diagnosed with NSCLC with PD-L1 ≥ 50% who started treatment with pembrolizumab monotherapy between 2018 and 2021. Demographic variables: sex, age and smoking status. Clinical variables: histology, functional status according to ECOG scale, start date and number of treatment cycles, date and reason for discontinuation of treatment (intolerable toxicity/disease progression), adverse effects (AE), date and cause of exitus. Effectiveness variables: complete response assessed by CT, progression-free survival (PFS) and overall survival (OS) by Kaplan Meier analysis. Common Terminology Criteria for Adverse Events (CTCAEv5.0) was used for safety assessment. Data were obtained from the digitised Mambrino XXI® medical record and the outpatient prescription module of the Farmatools® software. Results were analysed using SPSS Statistics®21 and compared with those obtained in the pivotal clinical trial KEYNOTE-024.

Results/Key Findings: Nineteen patients were included, 15.8% (n=3) female, with a median age of 68 years (54-80) years. Smokers: 42.1% (n=8), non-smokers: 10.5% (n=2) and ex-smokers: 47.4% (n=9). Histology: adenocarcinoma 63.1% (n=12) and squamous NSCLC 36.8% (n=7). A total of 68.4% (n=13) patients had an ECOG ≤ 1. The median number of cycles received was 6 (1-32). Three patients received a single cycle of pembrolizumab. By the end of the study 94.7% (n=18) of patients had discontinued treatment: disease progression 68.4% (n=13) and intolerable toxicity 26.3% (n=5). Two patients (10.5%) completed 24 months of treatment without progression. The frequency of AE occurrence was 52.6% (n=10). Immune-related AE: hypothyroidism 10.5% (n=2), pneumonitis 10.5% (n=2) and haemolytic anaemia 5.3% (n=1). Other AEs: neuropathy 5.3% (n=1), diarrhoea 5.3% (n=1), vomiting 5.3% (n=1) and asthenia 5.3% (n=1). All deaths were due to progression, with the exception of one death due to immune-mediated pneumonitis. Complete response: 8 patients (42.1%). Median PFS was 5.25 months (95%CI, 0.3-10.1) and median OS was 13.75 months (95%CI, 7.9-19.60).

Conclusion/Recommendations: Although median PFS and OS were lower than those described in the literature (KEYNOTE-024), a high percentage of patients (42.1%) showed primary complete response in the practice setting. However, 42.1% of patients showed rapid disease progression. The inferior effectiveness results of our study with respect to KEYNOTE-024 are possibly due to the high percentage of patients (31.6%) with ECOG > 1, who are not represented in the pivotal trial. Although in KEYNOTE-024 non-smokers showed worse outcomes to immunotherapy treatment, we found no difference in effectiveness between smokers/non-smokers in our study. In terms of safety, AE were as expected, with the exception of one death caused by pneumonitis. We consider that biomarkers to detect patients with rapid progression are missing. The combination of pembrolizumab with chemotherapy should be the option of choice in these patients.

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093

Lung cancer patients profile treated in a reference hospital in Rio de Janeiro: a descriptive analysis from 2009-2019

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Objective/Purpose: Lung cancer is the second in incidence (2.21 million of new cases) and first leading cause of cancer mortality worldwide (1.8 million of death) in 2020. In Brazil, lung cancer is third in incidence in men and fourth in women and first one in mortality, but the numbers are underestimated. Stage at diagnosis is a key for lung cancer survival, early detection cancer generates a higher survival rate than late stage diagnosis. Histology, socioeconomic conditions, access, quality of healthcare and local realities are related to lung cancer stages at diagnosis, and it has been influenced mortality. The population characterization of the healthcare system has been of great importance aiding to prioritize interventions that can lead to improvements in early detection, technological advances in diagnosis and treatment. We aim to describe lung cancer patients' profile at National Cancer Institute of Brazil.

Study Design/Methods: This is a retrospective study conducted with individuals diagnosed with lung cancer at Brazilian National Cancer Institute who were registered at the hospital-based cancer registry from January 2009 to December 2019. To represent malignant neoplasm of bronchus and lung, the International Classification of Diseases was used (CID10-C34) as a filter. The epidemiological and sociodemographic data were collected in July/2022. We organized and cleaned the database. The variables collected were: age, gender, race/color, high education, smoking status, stage at diagnosis and first treatment. A new variable was created - time to treatment - time between diagnosis and treatment in days.

Results/Key Findings: Among 5,286 patients, most patients were male (57.6%) and white (61.7%), with median age of 64 years (IQR 51–74); 83.3% of them were current and former smokers, only 7.6% had a high education level, most of them (86%) were diagnosed at a late stage, either clinical stages 3 or 4. Late diagnosis remains high during ten years of the study which is observed a stability standard. In 34.1% of the cases the first treatment was chemotherapy, 25.2% was radiotherapy and in 5.1% it was surgery. However, 35.0% of the patients did not start a treatment and main reason was advanced disease (43.5%). Median time to treatment in early stage was 82 days (IQR 46-127) and in late stage was 57 (IQR 29-96).

Conclusion/Recommendations: These findings show that lung cancer, in Brazilian National Cancer Institute, is diagnosed in advanced stage. So, future directions must include improvements in early detection, in the same way that developed places (e.g., USA and Europe) that apply approach (low dose computed tomography lung screening) to diagnosis more individuals in early stage improving lung cancer survival patient and treatment. Also, it is necessary to enhance lung cancer treatment in Brazil, because, in public system molecular target therapy to lung cancer specified subtypes is not a reality. Furthermore, lung cancer has a development fast, so, when cancer is diagnosed, the treatment should be faster than observed.

Encore Presentation (EN)

094

Observational study of avelumab in a third level hospital

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Objective/Purpose: Avelumab is a monoclonal antibody targeted against PD-L1 and approved for the treatment of metastatic Merkel cell carcinoma (MCC) and maintenance treatment of urothelial carcinoma (UC) stage III or IV after having received a platinum-based regimen. Nonetheless, avelumab is funded only if PD-L1 expression is positive. The study's objective was to evaluate the effectiveness and safety profile of avelumab in a third level hospital.

Study Design/Methods: A retrospective observational study was carried out, including patients treated with avelumab, regardless of the PD-L1 expression, between January 2018 and July 2022. Demographic, effectiveness and safety data were obtained from the electronic medical history.

Results/Key Findings: For UC, 8 patients were included, all of them were in stage IV; 7 were men (87.5%), with a median age of 65 years-old (57-80). 89% of the patients were smokers and the PD-L1 expression was positive in 3 patients (37.5%). All of them had received platinum and gemcitabine-based regimens. The median number of avelumab cycles administered was 13.5 (2-22). 5 patients continue treatment at the time of writing this report and 3 of them had their treatment interrupted because of disease progression. 3 patients received a set dose of 800 mg and 4 patients had their dose adjusted by body weight. None of the patients reached complete response, 3 had a partial response (37.5%), 3 stable disease (37.5%), 1 disease progression (12.5%) and one could not be evaluated (12.5%). One of the 8 patients passed away in July 2022. For MCC, 2 patients were treated for MCC stage IV, a man and a woman, with a median age of 82 years-old (79-85). One of them had not been treated previously and received 4 avelumab cycles at a dose of 700 mg. He had the treatment interrupted because of disease progression. The other patient had received carboplatine and etoposide and pembrolizumab before starting treatment with avelumab in 2018 and had received 75 cycles at the time of writing this report.80% of patients reported some kind of adverse event: asthenia (40%), renal function deterioration (20%), thrombocytopenia (20%), herpes zoster reactivation (10%), hepatic alterations (10%), psoriasis reactivation (10%), nausea and vomiting (10%) and decreased appetite (10%). 70% of patients had their treatment delayed because of adverse events. One of the patients had their dose reduced and administrations spaced, but none of them had avelumab discontinued.

Conclusion/Recommendations: Even though effectiveness data are not yet assessable because of the short follow-up and small sample size, our experience with avelumab is quite positive, with acceptable tolerance. There were adverse events directly related to immunotherapy, such as psoriasis and herpes simplex reactivation and hepatic alterations. It is necessary to increase follow-up time to obtain more robust results.

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095

Utilizing data visibility through a digital dashboard to optimize access to cancer care in Kenya

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Objective/Purpose: The National Cancer Control Program (NCCP) under Ministry of Health (MoH) aspires to utilize routine surveillance information to support efficient policymaking, cancer control planning, resource mobilization and allocation, and continuous quality improvement. Previously hospitals would submit paper-based monthly reports to the MoH; these were often late or missing, leaving NCCP without the necessary information to monitor cancer treatment services and plan timely interventions. The objective of the digital platforms was to

- Monitor treatment activities as well as commodity movement in the 11 regional centers
- Process commodity orders to central stores
- Guide technical working groups on policies around cancer treatment

Study Design/Methods: The NCCP in partnership with Clinton Health Access Initiative (CHAI) developed a digital platform to aggregate hospital level data in real time to provide insights into hospital performance and challenges, enable timely intervention, and inform national-level decision-making. Starting with data capture, the NCCP ensured that paper-based daily activity registers were available at hospitals. In parallel, the platform was developed and integrated within existing district health information system, hereby eliminating adoption hesitancy. To enhance data use**,** the platform was made open access, permitting all stakeholders to have visibility. The data is summarized in simple graphics to guide prompt decision-making. For sustainability, NCCP integrated data use into routine oncology technical working group (TWG) meetings. NCCP worked with the AIDS Control Program to allocate server space, eliminating recurring data storage costs.

Results/Key Findings: The oncology dashboard was launched in November 2020. The three referral cancer centres together with 12 regional cancer centres were trained on how to use the registers and upload to the Kenya Health Informatic System. This data would then be pulled to the oncology dashboard using the set indicators.

- More facilities have been reporting on the national register which is posted on the district health information system (DHIS)
- Commodity data for the past year informed the ministry on budgetary allocation for supply of 23 essential oncology drugs
- Facilities have placed orders on the system
- Facilities have uploaded delivery notes to facilitate reconciliation of orders

The Ministry has used the data to make decisions on which treatment interventions to develop at certain cancer centers. Such as Cervical Cancer Brachytherapy source was taken to centers which have reported high cases of cervical cancer as opposed to those with low cases.

Conclusion/Recommendations: Health system visibility aided by a digital platform enhanced responsiveness to program gaps and enabled rectification. Data visibility that addressed an information gap unlocked additional funding from the government. The system can be replicated both in-country and externally as it sits within DHIS2 – the health reporting system adopted by many countries in Africa.

Funding: Development of the system was funded by Clinton Health Access Initiative.

096

Quantifying chemotherapy wastage and exploring the development of a chemotherapy wastage calculator in an ambulatory cancer centre

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Objective/Purpose: To ensure an efficient use of chemotherapy drugs, chemotherapy wastage is an area that can be investigated. This study aims to quantify current parenteral chemotherapy wastage and estimate parenteral chemotherapy wastage when dose banding is executed, using a chemotherapy wastage calculator in an ambulatory cancer centre. The study also examines the variables that significantly predicts total cost of chemotherapy wastage, investigates the reasons for wastage, and explores opportunities to reduce wastage.

Study Design/Methods: Data was collected from the pharmacy in National Cancer Centre Singapore over 9 months retrospectively. Chemotherapy wastage is the sum of wastage in the preparation phase and potential wastage in the administration phase. The calculator was created using Microsoft Excel and generated chemotherapy wastage in terms of cost and amount and analysed the reasons for potential wastage.

Results/Key Findings: The calculator reported a total of 2.22 million mg of chemotherapy wastage generated over 9 months, amounting to $2.05 million. Regression analysis found that cost of drug was the only independent variable that significantly predicted total cost of chemotherapy wastage (p=0.004). The study also identified low blood count (625 [29.06%]) as the top reason for potential wastage and no show ($128,715.94 [15.97%]) as the reason that incurred the highest cost of potential wastage.

Conclusion/Recommendations: The pharmacy has generated a considerable amount of chemotherapy wastage over 9 months. Interventions in both the preparation and administration phase are required to reduce chemotherapy wastage. The use of the chemotherapy wastage calculator in the pharmacy operations could guide efforts to reduce chemotherapy wastage.

097

Determining acceptance and perceptions of chemotherapy dose banding in an ambulatory cancer centre

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Objective/Purpose: Despite the advantages of dose banding (DB) and numerous plans to adopt this practice, worldwide uptake of DB is still poor. As opinions of healthcare professionals were deemed essential in DB's acceptance in the West, this study targeted these key stakeholders in chemotherapy. Acceptance, facilitators, and barriers of DB were obtained to make recommendations to improve its implementation.

Study Design/Methods: A cross-sectional study in the National Cancer Centre Singapore, involving 93 physicians, nurses, pharmacists, and pharmacy technicians, was conducted in February 2022. The Theory of Planned Behaviour was revised to design a survey questionnaire to obtain the acceptance, facilitators, and barriers of DB. Additional questions on maximum acceptable dose variance and essential criteria for selecting drugs for DB were included.

Results/Key Findings: A total of 93 participants responded, with a mean 9.75 ± 7.37 years of clinical experience. Less than half have heard of DB while few had prior experience. Drug cost was the top selection criteria for DB, followed by toxicity, therapeutic index, frequency of use and drug wastage. Acceptance rate of DB was 41.9%, with majority agreeing to use DB in various drugs but to determine patient suitability before usage. Being greatly affected by subjective norms, having a positive outlook for DB's impacts, and no effect on toxicity significantly influenced acceptance.

Conclusion/Recommendations: Prior to implementing DB at the institutional level, training particularly the pharmacy and nursing staff, addressing concerns over toxicity, and providing technological support can help improve acceptance. Future studies can involve patients' perspectives and more institutions for greater diversity in opinions.

098

Systematic review of the adverse effects of ipilimumab monotherapy and in combination with nivolumab

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Objective/Purpose: To analyze adverse reactions registered in melanoma and renal cells cancer diagnosed patients treated with ipilimumab monotherapy and in combination with nivolumab.

Study Design/Methods:

- Retrospective observational and descriptive study
- January 2010 – August 2022
- Information was collected via electronic clinic history
- Variables: sex, age, treatment line, administered cycles number and toxicity
- Toxicity: Adverse effects in the 6 months following the treatment according to CATCAE (V5.0/2017) classification

Results/Key Findings: 15 patients in treatment with ipilimumab where identified, either in monotherapy or in combination with nivolumab. 9 (60%) of them where men, age median being 59 years old (37-91) and 8 (53,3%) with ipilimumab as first-line treatment. 9 (60%). Of those 15 patients, 9 (60%) showed adverse effects in the first 6 months following the treatment, which consisted in gastrointestinal pathology (diarrhea) in 7 (46,6%) patients, cutaneous exanthema in 1 (6,67%), bad diabetes control in 1 (6,67%), and secondary to ipilimumab hypophysitis in 1 (6,67%) of the patients. Of the 4 patients treated with ipilimumab + nivolumab, 2 (50%) showed adverse effects that required hospitalisation: 1 of them presented peritonitis in the next month following the treatment and the other one developed an immunotherapy secondary hypophysitis.9 patients developed adverse effects that required hospitalisation after ipilimumab monotherapy or in combination with nivolumab. Adverse effects where predominantly gastrointestinal-related, requiring 2 (22,2%) of them surgery.

Conclusion/Recommendations: The only difference between ipilimumab monotherapy and in combination with nivolumab treatment founded was hypophysitis, which is not registered as a possible adverse effect of the ipilimumab monotherapy treatment. It is important to highlight that peritonitis happened to 2 of the 9 patients that showed adverse effects (22,2%) although it is registered as a very rare adverse effect in ipilimumab's SmPc à Necessity of more studies with a bigger sample in order to evaluate a possible estimation of this adverse effect.

099

An exploratory study to examine differences in adverse drug reactions experienced by male and female patients taking tyrosine kinase inhibitors at a tertiary cancer centre

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Objective/Purpose: Female patients continue to be underrepresented in oncology clinical trials, owing to the thalidomide tragedy in the 1950s and interpretation of subsequent guidance to exclude women of child-bearing age. Studies have shown that this lack of female inclusion has led to suboptimal healthcare, adverse medical outcomes, and higher reporting of adverse drug reactions (ADRs). There are significant physiological differences between female and male patients that impact the pharmacokinetics and pharmacodynamics of drugs. Tyrosine kinase inhibitors (TKIs) are an effective targeted treatment of many malignancies. Adverse drug reactions include haematological adverse effects, fatigue, oedema, nausea, hypothyroidism, diarrhoea, and cardiac toxicity. Severity of ADRs can vary; from mild and self-limiting through to life-threatening symptoms requiring urgent intervention. Despite the emphasis on personalised medicine, little is understood about the impact of sex on the nature and severity of ADRs. The aims and objectives of this study:1. To identify if there are any differences in adverse drugs reactions specific to sex for patients TKIs.2. To evaluate the rate (%) of adverse drug reactions by grade experienced by male and female patients initiated on TKIs between January and December 2021 across solid tumour and haematological cancers.

Study Design/Methods: A retrospective pilot study of male and female patients started on TKIs during the study period was conducted. Patients were identified using a custom-made report on the electronic health record system. Clinician's notes and bloods results were reviewed to identify ADRs throughout treatment. Adverse drug reactions were grouped/categorised by System Organ Class and graded according to CTCAE v5. Data collected included nature and grading of ADRs, age, sex, ethnicity, treatment, and treatment intent. Patients receiving treatment within a clinical trial, in combination with other agents, or those diagnosed with acute myeloid leukaemia were excluded.

Results/Key Findings: A total of 48 patients were included (median age 60.5 years [21-86]), 54.1% female rate. Patients of black ethnic background were not equally represented in both groups: 4.5% of males compared with 15.4% of females. The frequency and grading of ADRs for patients included in this study is summarised in table 1. Overall, 26.9% and 15.4% of female patients experienced grade 2 and grade 3 ADRs compared with 18.2% and 0% of male patients. The most common ADRs for females were gastrointestinal, general malaise, and respiratory in nature whereas males experienced gastrointestinal events, blood disorders or other effects.

Conclusion/Recommendations: Differences observed may be due to increased reporting of ADRs, although this is unlikely for higher severity ADRs. Limitations to this study include that data collection relied on the reporting of ADRs by patients and subsequent documentation by clinicians. It was noted that there was a variation in detail of documentation between clinicians. This study indicates there may be sex specific characteristics that impact patient tolerability of TKIs. Further collaborative data collection is required to help draw robust conclusions. Knowledge of the impact of sex on ADRs could influence how patients are managed, for example, sex-specific dosing, monitoring and provision of supportive care for those at greater risk of certain adverse effects and patient education.

100

Quality and economic value of returned unused oral targeted anticancer medication from patients and measures to reduce medication waste

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Objective/Purpose:

1. To examine the use and economic value of treatments with targeted oral anticancer medication; protein kinase inhibitors (PKI), lenalidomide, thalidomide and pomalidomide (LTP).
2. To examine the quantity, quality and economic value of unused returned medication of PKI and LTP medication, and reasons for their return.
3. To examine the attitudes of cancer patients and healthcare professionals towards medication waste, return of medication, re-dispensing and willingness to use unused medication returned to the pharmacy by another patient and activities to reduce medication waste.
4. To propose procedures to reduce medication waste and suggestions for re-dispensing of unused medication.

Study Design/Methods: This single center multifaceted study was divided into four parts:

A retrospective data collection was done for a period of one year in 2020, including the use and economic value of treatments for adult cancer patients with targeted oral anticancer medication; protein kinase inhibitors (PKI) and lenalidomide, thalidomide and pomalidomide (LTP).

A prospective data collection was done over a three month period from January to March 2021, for the quantity and quality of unused returned PKI and LTP medications, reasons for their return and the economic value of the medications calculated.

A standardized **questionnaire** was sent to the appropriate cancer out- patients and all healthcare professionals at Landspitali hospital to examine their attitudes towards medication waste, return of medications, re-dispensing and willingness to use unused medication returned to the pharmacy by another patient and activities to reduce medication waste.

Procedures to reduce medication waste and suggestions for re-dispensing of unused medication were proposed by the researcher.

Results/Key Findings:

1. A total of 453 treatments with PKI and LTP medications were issued in 2020 for 283 individual cancer patients. The total economic value of the medication dispensed in 2020 was 4.3 million EUR.
2. A total of 2,193 prescription units of returned medication was collected and the total economic value of 170.000 EUR calculated. Around 71% of the returned medication was reusable according to specific quality criteria, which could have saved up to 75% of the economic resources. The most common reasons for return of medication was discontinuation of treatment due to adverse effects and progress of cancer.
3. The attitude of cancer patients and healthcare professionals and willingness to re-dispense and use returned unused medication was very positive under the condition its quality was guaranteed.
4. The vast majority of healthcare professionals suggested that improvements were needed in procedures in order to be able to reduce medication waste.

Conclusion/Recommendations:

1. The economic value of medication treatment with PKI and LTP for cancer patients is very high.
2. The quality of most returned unused medication, by cancer patients who discontinue treatment, is satisfactory and suitable for re-dispensing.
3. The results of this study suggests that the perspectives of cancer patients and healthcare professionals are

very positive and supportive for the implementation of procedures to minimise medication waste, through re-dispensing of unused returned medication.

4. There are opportunities to collaborate with health authorities, relevant institutions and entities, to evaluate procedures and work on proposals to review and amend regulations, to make re-dispensing and reuse of returned medications possible.

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Indication, safety and adherence to oral targeted anticancer medication in Iceland

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Objective/Purpose: To review the use and indications of oral anticancer therapies with tyrosine kinase inhibitors (TKI's)To evaluate the quality and safety of TKI therapies with respect to adverse events (AEs) and drug interactions. To evaluate adherence to TKI therapies and risk factors associated with adherence.

Study Design/Methods: This single-center study was conducted at Landspitali – The National University Hospital of Iceland and is divided into two parts: **A retrospective study** as a descriptive chart review of patient cases between January 1st and December 31st 2019. **A prospective study** from January to March 2020 as patient interviews with a standard questionnaire. The study population included cancer patients, 18 years and older receiving TKI therapy during the above time periods. Data collection included a review of the use and indications of oral anticancer therapies with TKI's to evaluate the quality and safety with respect to adverse events (AEs) and drug interactions, and to evaluate adherence to TKI therapies and risk factors associated with adherence.

Results/Key Findings: Retrospectively, a total number of 252 cancer patients participated and the most common TKI therapy was palbociclib with the indication breast cancer. **Prospectively**, 42 cancer patients participated and the most common TKI therapy was ribociclib with the indication breast cancer. All patients reported that they had experienced an AE at some point in their TKI therapy and the AEs were mostly mild or moderate and tolerable. Clinical relevant drug-drug interactions were 5 and for 7 patients (16,7%). Medication adherence was generally very good for the majority of patients (98%) and no risk factors were directly linked to adherence.

Conclusion/Recommendations: The results indicate that the majority of cancer patients at Landspitali Hospital that receive therapy with TKI´s are women being treated for breast cancer. Generally, most AEs experienced are mild to moderate and tolerable. Clinical relevant drug-drug interactions were few, which indicates that patients are not at high risk due to drug-drug interactions. Medication adherence to TKI therapy indicates good adherence overall with no risk factors predicting the adherence.

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A nationwide review of immune checkpoint inhibitor therapy in Iceland: indications and tolerance

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Objective/Purpose: The main objectives were to document the indication for Immune checkpoint inhibitor (ICPI) therapy and patient tolerance to the ICPI therapy with regards to side effects and if any, how they were treated.

Study Design/Methods: This single center retro- and prospective study was conducted at Landspitali – The National University Hospital of Iceland, covering the period from January 1st to December 31st 2019 and from January 1st to March 15th 2020, respectively. The study population included cancer patients, 18 years and older, which had received a minimum of one dose of Immune checkpoint inhibitor (ICPI) therapy during the above time periods. Data for the retrospective study was collected through the patient medical records, whereas interviews using a standard questionnaire were conducted prospectively with patients by weekly telephone calls.

Results/Key Findings: In total, 141 patients participated in the study, 94 retrospectively and 47 prospectively. The most common indications for ICPI therapy in both studies were non-small cell lung cancer (NSCLC) and melanoma. In the **retrospective study**, the majority of the patients (64%) experienced a specific side effect, a total of 120 instances. The most common side effects were thyroid disorders, dermatological reactions and arthritis. Roughly 13% of patients had to stop therapy due to severe side effects (grade 3–4). In the **prospective study,** nearly all patients experienced side effects (96%), a total of 369 instances. The most common side effects were fatigue, shortness of breath and cough. Most patient reported side effects were moderate (94%), with only 6% severe (grade 3). One patient (2%) took a break from therapy due to severe side effects (grade 3). In both studies, side effects were most commonly treated with the oral corticosteroid prednisolon.

Conclusion/Recommendations: The results indicate that the vast majority of patients receiving ICPI therapy will experience side effects. Generally, the side effects are moderate and manageable, with most patients being able to continue ICPI therapy. The side effects can however be severe and resulting in discontinuation of ICPI therapy. The results indicate that asking focused questions weekly, to patients receiving ICPI therapy, may prevent development of serious immune-related adverse events, thus enabling continuation of therapy.

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What's the risk? Update on the safe use of medicines in patients with G6PD deficiency

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Objective/Purpose: Glucose-6-phosphate dehydrogenase (G6PD) deficiency predisposes individuals to develop hemolytic anemia in the presence of oxidative stress when exposed to certain medications (e.g., rasburicase and tafenoquine). Regulatory agencies warn against the use of some medications in the setting of G6PD deficiency, but this information may be conflicting and the peer-reviewed clinical evidence may be scarce. The expanded Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for medication use in the context of *G6PD* genotype was recently published. The guideline author group performed a systematic review of the evidence for 48 medications cited by one or more primary and tertiary resources as being potentially unsafe in the setting of G6PD deficiency. The update to the guideline classifies these medications as high, medium, or low-to-no risk based on the published evidence of the gene-drug associations and regulatory warnings. Based on this review, high risk medications now include dapsone, methylene blue, pegloticase, standard primaquine, rasburicase, tafenoquine, and toluidine blue. In patients with G6PD deficiency, high risk medications should be avoided, medium risk medications should be used with caution, and low-to-no risk medications can be used without regard to G6PD phenotype.

Study Design/Methods: As part of the pre-emptive Clinical Pharmacogenomics Program at St. Jude Children's Research Hospital (St. Jude), gene/drug pairs with sufficient evidence for implementation are introduced into the electronic health record (EHR) utilizing CPIC guidelines. Results are integrated into the EHR and coupled with clinical decision support (CDS). Clinical *G6PD* genotype results are integrated into St. Jude's EHR, and CDS alerts for G6PD deficient patients have been developed to guide pharmacotherapy.

Results/Key Findings: Based on the CPIC author group's systematic review of published literature, many drugs previously labeled as potentially hazardous in G6PD deficiency do not have published evidence supporting those labeled hazards. For the pediatric hematology/oncology population, the most relevant practice-changing reclassifications are the downgrading of trimethoprim-sulfamethoxazole to a low-to-no risk medication which can be used without regard to a patient's G6PD phenotype, and nitrofurantoin to a medium risk medication. As of September 2022, 2309 St. Jude patients were genotyped for *G6PD*; 2% (n = 47) were G6PD deficient and should avoid the aforementioned high risk medications due to the risk of hemolysis.

Conclusion/Recommendations: *G6PD*-guided medication therapy has the potential to prevent drug-induced hemolytic anemia. The updated CPIC guideline provides clear evidence-based recommendations for personalizing patients' therapy in the context of G6PD deficiency. This implementation by St. Jude's Clinical Pharmacogenomics Program serves as a model for other institutions that are considering integrating *G6PD* genotype or G6PD activity testing into their medication selection workflow EHR to improve patient outcomes.

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Managing opioids and mitigating opioid risks in patients with cancer: an environmental scan of the attitudes, confidence, and practices of pharmacists practicing in Canada

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Objective/Purpose: Describe the attitudes, confidence, and practices among pharmacists in Canada when providing care for patients using opioids for cancer pain (CP) management.

Study Design/Methods: An environmental scan of pharmacists who provide direct patient care in Canada. An electronic questionnaire was distributed via email by pharmacy organizations, and online platforms. It consisted of Likert-scale and open-ended questions and was open for 6 weeks. Analysis was conducted using descriptive statistics and qualitative content analysis.

Results/Key Findings: Eighty-one responses from 9 provinces were included in analysis. Respondents endorsed limited and varied practices when caring for patients with CP managed by opioids. Pharmacists were more confident in their ability to assess and provide education compared to managing these patients. Pharmacists' attitudes were generally discordant with available literature. Education and resources were the most commonly reported facilitators and barriers to resource use.

Conclusion/Recommendations: Pharmacists in Canada report employing opioid risk mitigation practices with low but varied frequency when caring for patients receiving opioids for CP. They endorsed varied confidence and limited awareness of available provider and patient education. These findings can help inform development of education models and guidelines which will serve to support pharmacists in their care of this patient population.

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Describing oncology visits to a tertiary care emergency department: a pilot project

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Objective/Purpose: To describe emergency department (ED) usage by oncology patients by identifying characteristics including oncology diagnoses, reason for visit, services consulted, and communication between ED and oncology services.

Study Design/Methods: This pilot project was conducted at a 965-bed Canadian tertiary care and trauma centre. Patients (18 years and older) who presented to the ED between January 1st and December 31st in 2017, with a confirmed cancer diagnoses prior to the unplanned ED visit, were included. Patients' electronic health records were reviewed for data extraction.

Results/Key Findings: A total of 2150 encounters were identified for review and 827 were included in the study. Based on the Canadian Triage and Acuity Scale, 64.5% of these encounters were classified as level 2, while 30.5% were level 3. In total, 80.5% of patients had a current cancer-associated treatment. While 93.5% of the ED visits documented their cancer diagnosis, only 35.1% of subsequent clinic visits documented the ED visit. The 5 most common chief complaints were fever, shortness of breath, abdominal pain, post-operative complications, and general weakness.

Conclusion/Recommendations: Characteristics of oncology patients presenting to ED were identified, improving the understanding of the unmet care needs for this vulnerable patient population, and informing the development of targeted pharmacist-interventions.

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Clinical pharmacy services in ambulatory oncology: an environmental scan of the Canadian practice landscape

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Objective/Purpose: To describe the current landscape of pharmacy services in ambulatory oncology in Canada and to identify perspectives related to the development and implementation of cpKPIs in this practice setting.

Study Design/Methods: In this national cross-sectional study, a web-based questionnaire was distributed to pharmacists working in ambulatory oncology settings. Potential participants who self-identified as pharmacists practising in an ambulatory oncology setting were eligible. Survey questions focused on participants' demographic characteristics, oncology pharmacy services provided, metrics captured, and pharmacists' perceptions of cpKPIs. All data were analyzed using descriptive statistics.

Results/Key Findings: A total of 44 responses were received, with most respondents practising in community hospitals in British Columbia, Ontario, and Atlantic Canada. The services most commonly provided were chemotherapy order verification, laboratory monitoring, identification and resolution of drug therapy problems, and counselling on anticancer medications. Twenty-six of the 44 respondents (59%) indicated that performance metrics or patient outcomes were tracked at their respective institutions, with none being universally captured. Overall, 43 (98%) of the respondents favoured the development of cpKPIs for ambulatory oncology practice.

Conclusion/Recommendations: Despite growing patient care needs in ambulatory oncology, there is significant heterogeneity in the scope of pharmacy services offered and the outcomes used to qualify their impact within this setting across Canada. This study demonstrates a clear need for national consensus cpKPIs to inform pharmacy resource utilization and patient centred quality improvement initiatives.

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Engaging community pharmacists in a breast cancer survivorship shared care model in Singapore: a mixed-method report

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Objective/Purpose: Early-stage breast cancer (ESBC) is the most common cancer diagnosis among women in Singapore, with high survival rates. The unsustainable, extensive utilization of oncologist services could be mitigated by increasing community pharmacists' involvement in extended survivorship. In a pilot initiative, cancer survivorship care is jointly provided by oncologists, family physicians, and community pharmacists from a Singapore-based community pharmacy chain since 2021. This mixed-methods study aims to report on the preliminary feasibility and acceptability of this new shared care model in Singapore.

Study Design/Methods: This study recruited 35 ESBC survivors minimally three years post-primary treatment and ascertained to be 'low-risk' for recurrence by treating oncologists. Pharmacists offered tele-consults every three months, addressing survivorship care areas like monitoring for physical or psychosocial issues; managing chronic diseases; advising on medication, complementary and alternative medicine usage; and health promotion. Care provision was facilitated by a survivorship care plan shared among clinicians. Satisfaction surveys were completed by ESBC survivors who went through the shared care model and in-depth interviews were conducted to elicit their care experiences. Thematic saturation was achieved.

Results/Key Findings: Preliminary qualitative feedback reinforced pharmacists' strengths in addressing health-related queries on medications and supplements. Survivors found the pharmacists friendly and were keen to extend the rapport built. Among survivors who completed quantitative surveys, the majority (64%) found the consult frequency to be appropriate, with pharmacists usually providing the desired amount of health-related information (64%) in an understandable manner (73%). Most survivors reported higher confidence in self-management (82%) and were willing to continue with the model (91%)

Conclusion/Recommendations: This pilot clarified the roles that community pharmacists could play in cancer survivorship care – an area traditionally managed exclusively by oncologists. This initiative expanded survivors' awareness of pharmacists' clinical care expertise to manage survivors in the community and created interprofessional collaborative opportunities across care settings.

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Trimethoprim-sulfamethoxazole as PJP prevention in patients undergoing methotrexate therapy for haematological malignancies: A review of the literature

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Objective/Purpose: Methotrexate is a cytotoxic agent that is commonly used to treat autoimmune diseases and both solid and haematological malignancies. Drug interactions are of particular concern during methotrexate therapy, as they have the potential to alter the pharmacokinetics of methotrexate and lead to significant toxicity. One agent that has the potential to interact with methotrexate is the antimicrobial agent trimethoprim/sulfamethoxazole. Consideration of this interaction is of importance in patients that are undergoing high dose methotrexate therapy for haematological malignancies as trimethoprim/sulfamethoxazole is the preferred agent for Pneumocystis Jiroveci pneumonia (PJP) prophylaxis. Current Australian guidelines recommend avoiding concurrent administration of high dose methotrexate and trimethoprim/sulfamethoxazole, yet evidence to support this recommendation is unclear.

Study Design/Methods: A search of PubMed/Medline, Embase and Cochrane Database of Systematic reviews was conducted. Keywords used in the search included methotrexate and trimethoprim/sulfamethoxazole, trimethoprim/sulfamethoxazole in cancer and drug interaction of methotrexate and sulfamethoxazole. Synonyms for methotrexate (e.g. MTX, Methoblastin) and trimethoprim/sulfamethoxazole (e.g. TMP/SMX, Bactrim, co-trimoxazole) were included in the search. The search identified one case study and eight clinical studies that were included in the review.

Results/Key Findings: Of the eight clinical studies, five either recommended the use of trimethoprim/sulfamethoxazole during high dose methotrexate treatment or found no interaction between the combination. Furthermore, this review identified a potential link between dose frequency of trimethoprim/sulfamethoxazole and methotrexate toxicity in this patient population. With all clinical studies that utilised intermittent dosing (two or three days weekly) supporting the use of trimethoprim/sulfamethoxazole with high dose methotrexate.

Conclusion/Recommendations: In conclusion, the findings of this review suggest that concurrent use of trimethoprim/sulfamethoxazole, when dosed intermittently, during high dose methotrexate treatment for haematological malignancies appears to be safe and effective in the prevention of PJP. It is recommended that current Australian guidelines of PJP prophylaxis in this patient population be reviewed.

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Not normal for you? the design and evaluation of a cancer red flag referral intervention for community pharmacies

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Objective/Purpose: Community pharmacies may be an ideal setting in which to promote early cancer detection due to their accessibility, opening hours and familiarity with the local population. Research confirms that suspected red flag cancer symptoms are frequently seen within community pharmacies. This study is a prospective interventional proof of concept study investigating the acceptability and utility of a red flag referral intervention that incorporates a card given to pharmacy users following conversational intervention in the community pharmacy. The objectives of the study were to:

- Evaluate acceptability and perceptions of pharmacy teams
- Investigate the acceptability and perceptions of the pharmacy users
- Investigate the number of referrals conducted.

Study Design/Methods: This study was conducted within Devon. A convenience sampling approach was adopted. Pharmacy inclusion was based on willingness to participate and level of engagement in previous training. Pharmacy users were recruited upon elicitation of a suspected red flag cancer symptom in conversation with a member of the pharmacy team. The study was active for 6 months in each pharmacy. Those pharmacies who agreed to participate in the study were offered training to those staff who would be disseminating the red flag referral intervention. The training was delivered face to face using video and group training sessions at each pharmacy. Questionnaires were designed to capture the experience of pharmacy teams post training and post study, as well as the pharmacy users who received the intervention. Responses were analysed using descriptive statistics, facilitated by IBM SPSS Statistics 25.

Results/Key Findings: A total of 11 community pharmacies were approached to take part in this study and 10 agreed to participate. Between May and November 2019, a total of 38 pharmacy users were given the red flag referral intervention. The average number of cards administered per pharmacy was 3 (SD=3.2; Range 0-11). Top three reported symptoms were skin (n=16), persistent cough (12), indigestion (n=6). Representatives from each pharmacy (n=6) reported over 65% of their pharmacy users to be willing to discuss their red flag symptoms. The training enabled more than 79% of staff (n=13) to fully understand the intervention and when to refer people to their GP. After the training, over half of staff were confident in their ability to recognise red flag symptoms, refer people to their GP and have sensitive conversations about red flag symptoms. When reflecting on the extent to which elements of the intervention had encouraged pharmacy users to decide to visit the GP and discuss their symptoms, more than three-quarters of the sample (n= 18) felt that both the card and the conversation had helped or encouraged them fully to see their GP and discuss their symptoms. As a consequence 88% either had already met with their GP or had an appointment booked. Anecdotally one case of lung cancer and several urgent referrals for skin issues were made.

Conclusion/Recommendations: This proof of concept study suggests that a red flag referral intervention delivered by community pharmacies is acceptable to both pharmacy users and staff and leads to patients visiting their GP when they otherwise may not have.

Funding: Health Education Foundation/ National Pharmacy Association

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Patient perceptions of a pharmacist-delivered cannabis consultation service integrated into Canadian cancer care: a qualitative interview study among patients with cancer

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Objective/Purpose: Patients with cancer have expressed interest in using plant-derived medical cannabis (PMC) for symptom management. In response to patient and oncologist need, a Cannabis Consultation Service (CCS) was pioneered by pharmacists at the Sunnybrook Odette Cancer Centre. There is little known about the patient experience at the CCS, nor is there published literature regarding provision of PMC services by oncology pharmacists. As such, we sought to explore patient perceptions of this innovative service.

Study Design/Methods: This was a qualitative research study grounded in a post-positivist approach. A purposive sample of adult cancer patients who had accessed the CCS were invited to participate. We designed a self-reported questionnaire and semi-structured interview guide. Participants engaged in a 1:1 interview with a pharmacist researcher over videoconference. Interviews discussed the patient experience, including perceived barriers and facilitators and the role of the pharmacist with respect to PMC. Interviews were recorded, transcribed, and the text was inductively analyzed using content analysis.

Results/Key Findings: Ten interviews (three males, seven females) were conducted. Involvement of the most responsible oncology care provider in the provision of PMC therapy emerged as the prominent theme. Participants revealed that they valued a pharmacist-delivered consultation service within their circle of care, and held expectations of persistence with PMC to reach purported benefits. Product costs and lack of acceptance to support cannabis as a treatment alternative were frequently cited barriers by participants.

Conclusion/Recommendations: Patients with cancer appreciate the support of their oncology team, via the pharmacist, to provide information regarding the suitability, risks during their cancer journey. Administrative, scientific, educational, and economic challenges for patients remain even in jurisdictions where cannabis is accessible via legislation. Pharmacists have an opportunity to engage with patients to meet care gaps and ensure safe and appropriate PMC use. Future research should prioritize development of patient-centered educational resources about PMC and conduct formal program evaluations to improve service delivery.

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