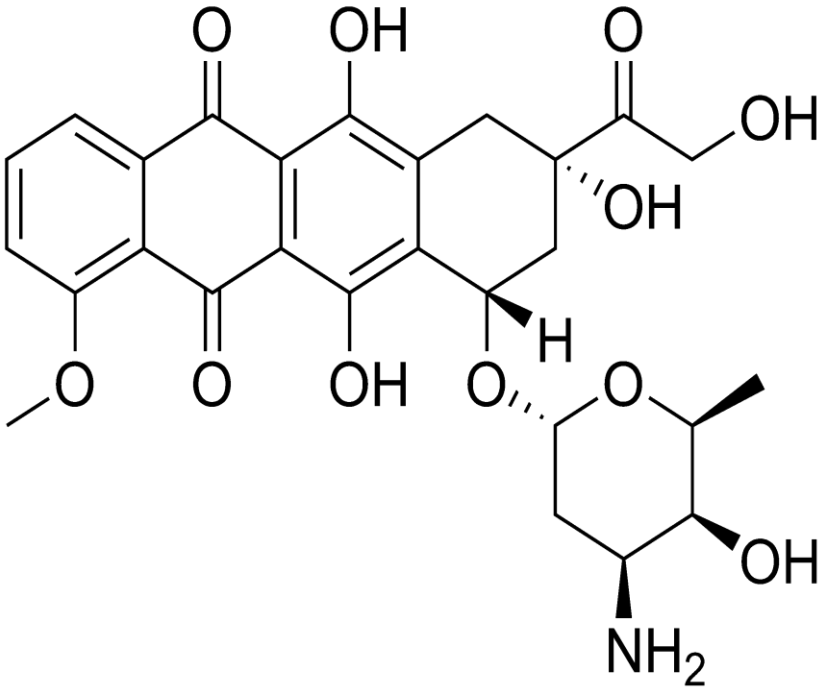
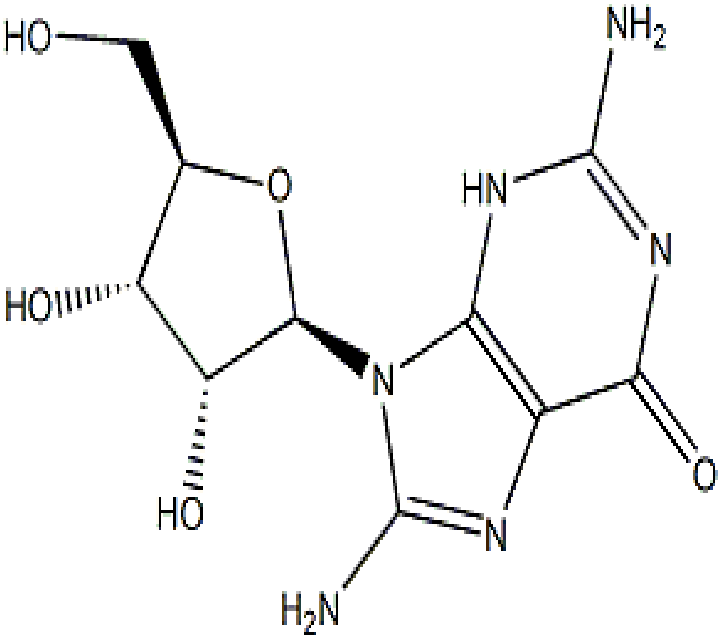
CARDIO-ONCOLOGY: NEW CHALLENGES FOR CLINICAL ONCOLOGICAL PHARMACISTS

Eduard Fort
Out-Patient Unit
Pharmacy Service
Hospital Duran y Reynals
Catalan Intitute of Oncology

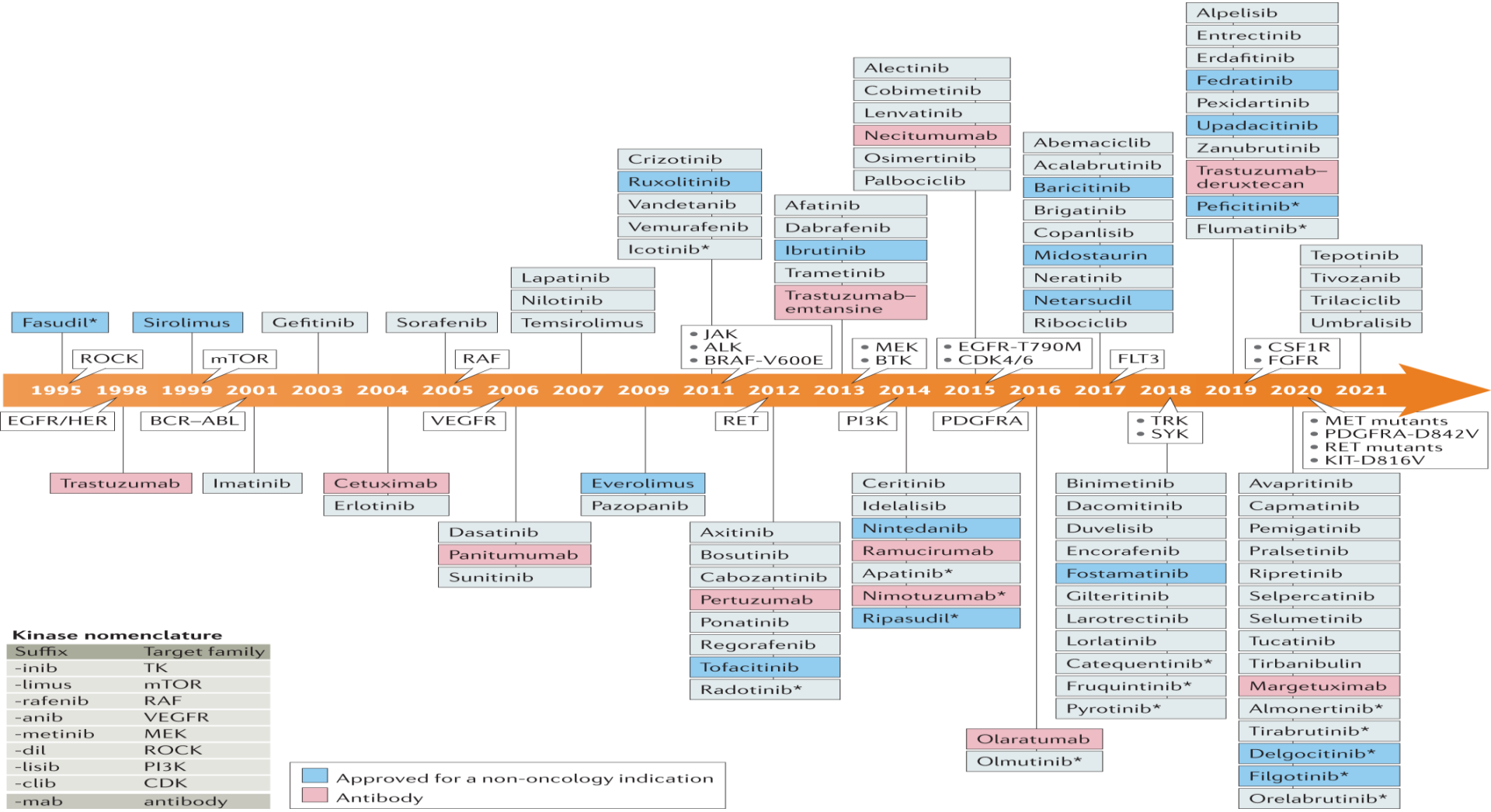
CARDIOTOXICITY

TYPE- I	TYPE- II
IRREVERSIBLE	REVERSIBLE
DOSE DEPENDENT	NOT DOSE DEPENDENT



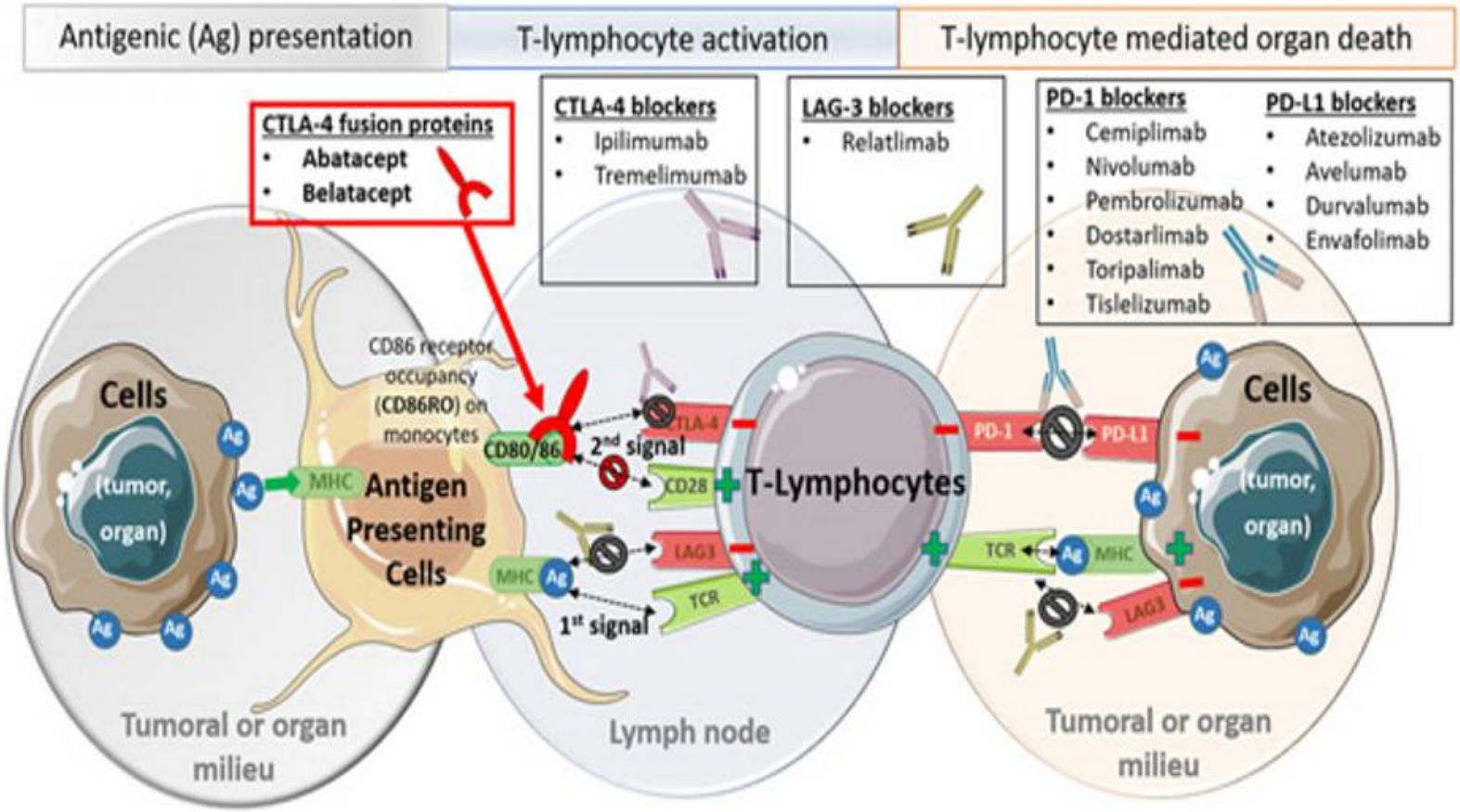


TIROSIN-KINASE INHIBITORS

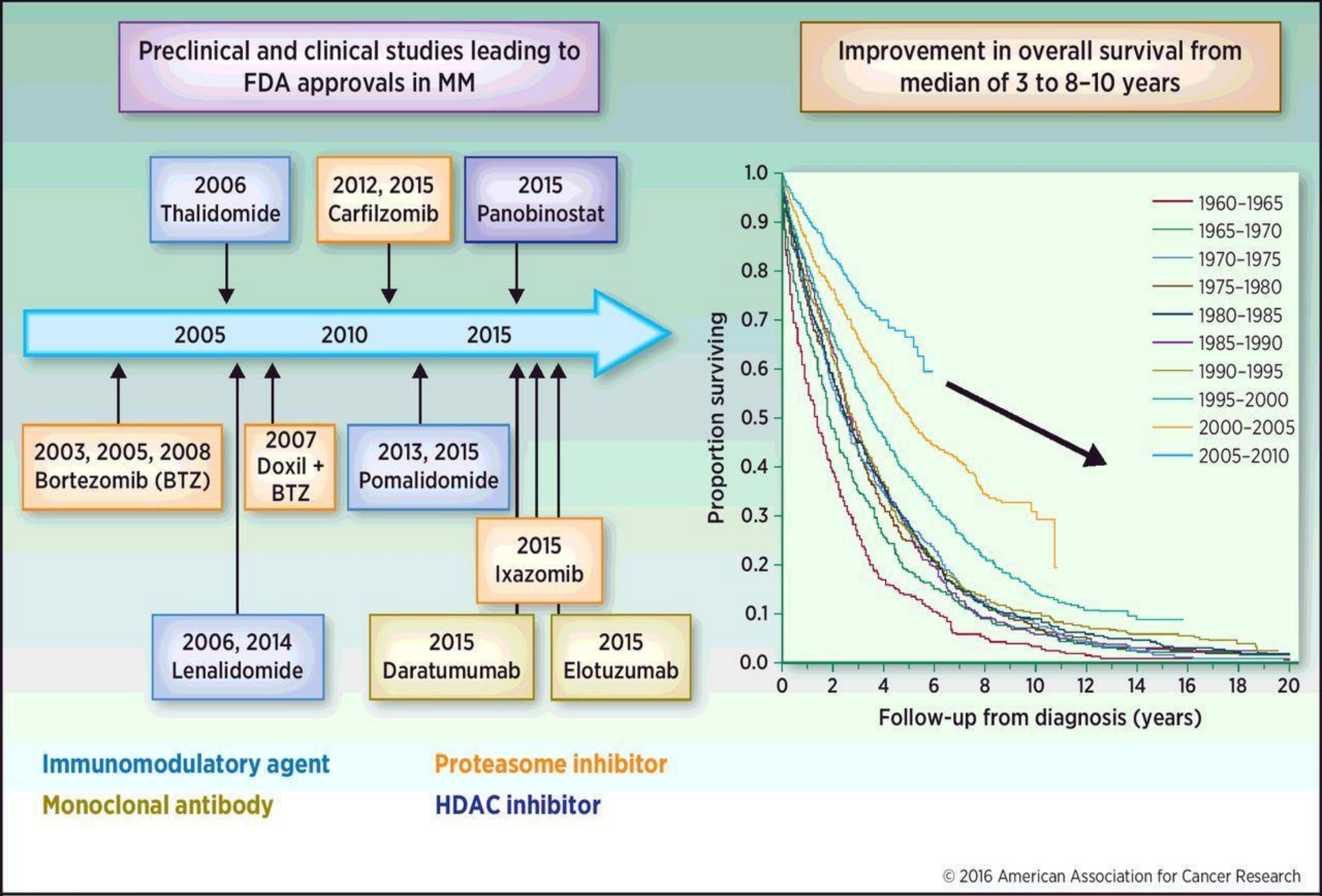


Misty M. Attwood et al. Trends in kinase drug discovery: targets, indications and inhibitor design. Nat Rev Drug Discov. 2021 Nov;20(11):839-861.

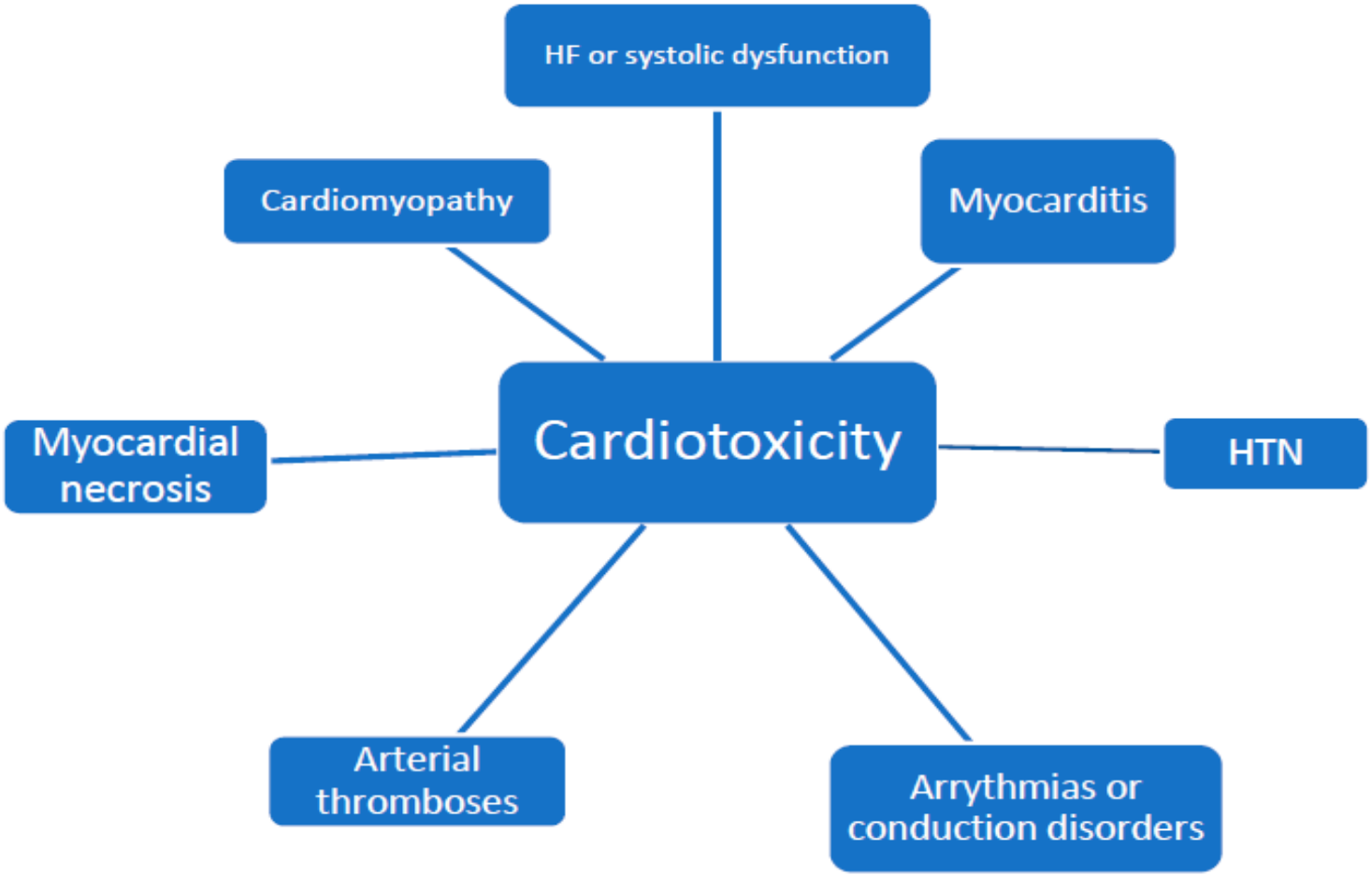
IMMUNE CHECKPOINT INHIBITORS (ICI)



Syed S. Mahmood et al. Myocarditis in Patients Treated With Immune Checkpoint Inhibitors. J Am Coll Cardiol. 2018 Apr, 71 (16) 1755–1764

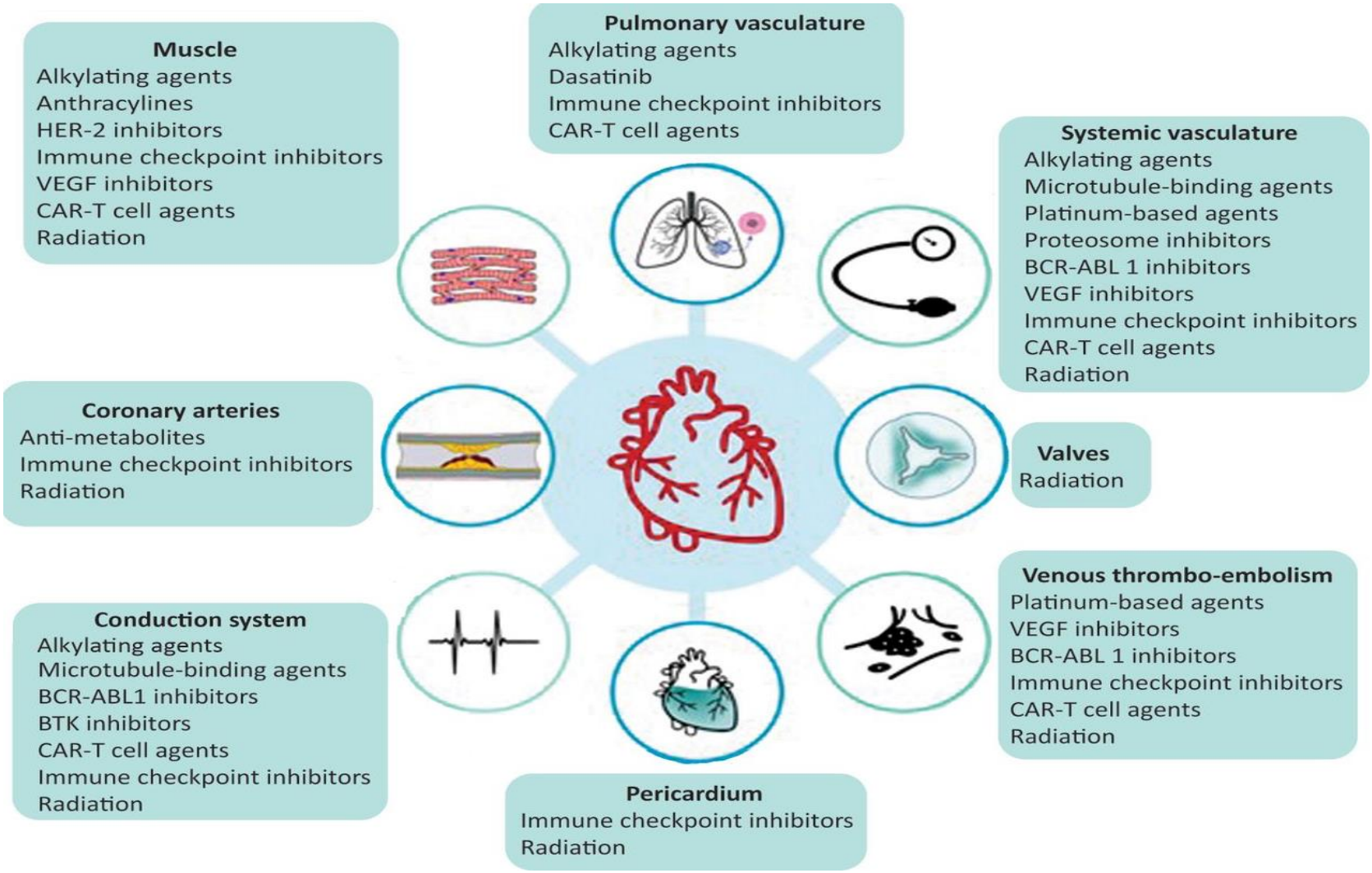

Preclinical and clinical studies leading to FDA approvals in MM
Improvement in overall survival from median of 3 to 8–10 years
2006 Thalidomide
2012, 2015 Carfilzomib
2015 Panobinostat
2005
2010
2015
2003, 2005, 2008 Bortezomib (BTZ)
2007 Doxil + BTZ
2013, 2015 Pomalidomide
2015 Ixazomib
2006, 2014 Lenalidomide
2015 Daratumumab
2015 Elotuzumab
Proportion surviving
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
2
4
6
8
10
12
14
16
18
20
Follow-up from diagnosis (years)
1960–1965
1965–1970
1970–1975
1975–1980
1980–1985
1985–1990
1990–1995
1995–2000
2000–2005
2005–2010
Immunomodulatory agent
Proteasome inhibitor
Monoclonal antibody
HDAC inhibitor
© 2016 American Association for Cancer Research
CCR Focus
AACR

CARDIOTOXICITY



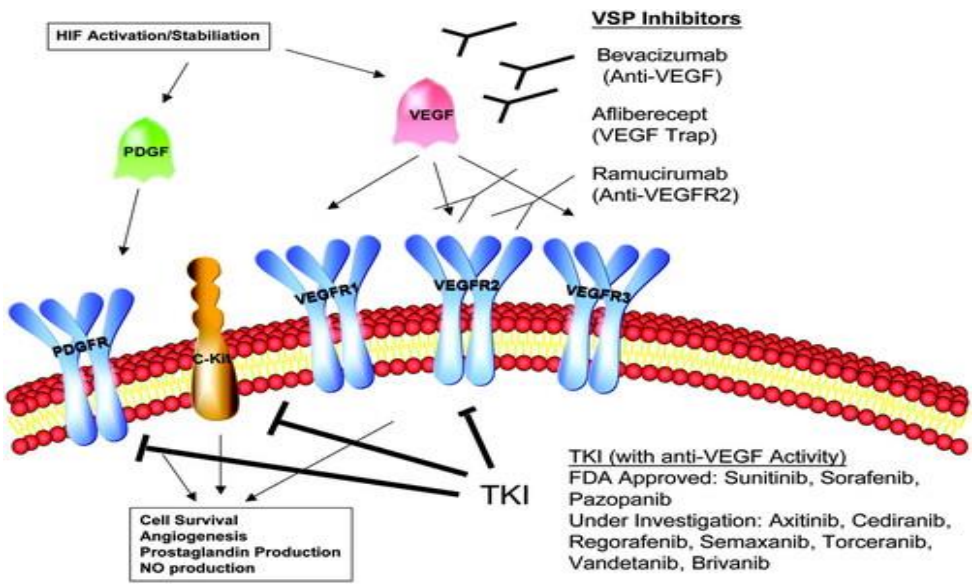
Briasoulis et al. Cardiotoxicity of Non-Anthracycline Cancer Chemotherapy Agents. J Cardiovasc Dev Dis. 2022 Mar; 9(3): 66

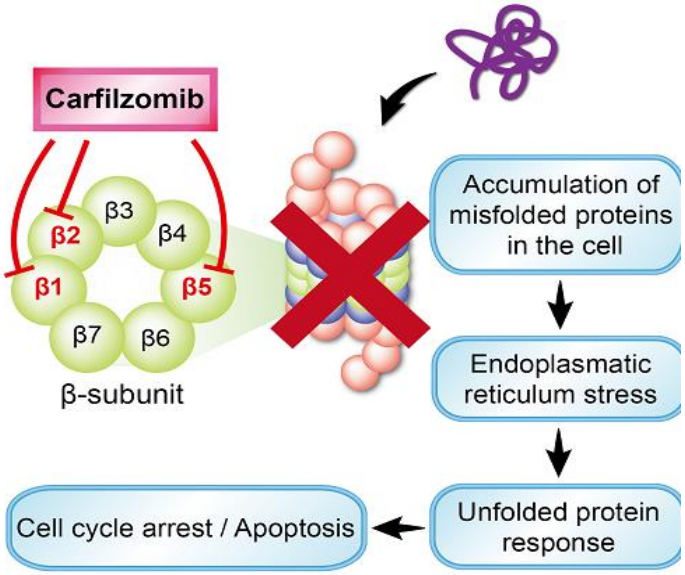
OVERVIEW OF INDUCED CARDIOTOXICY

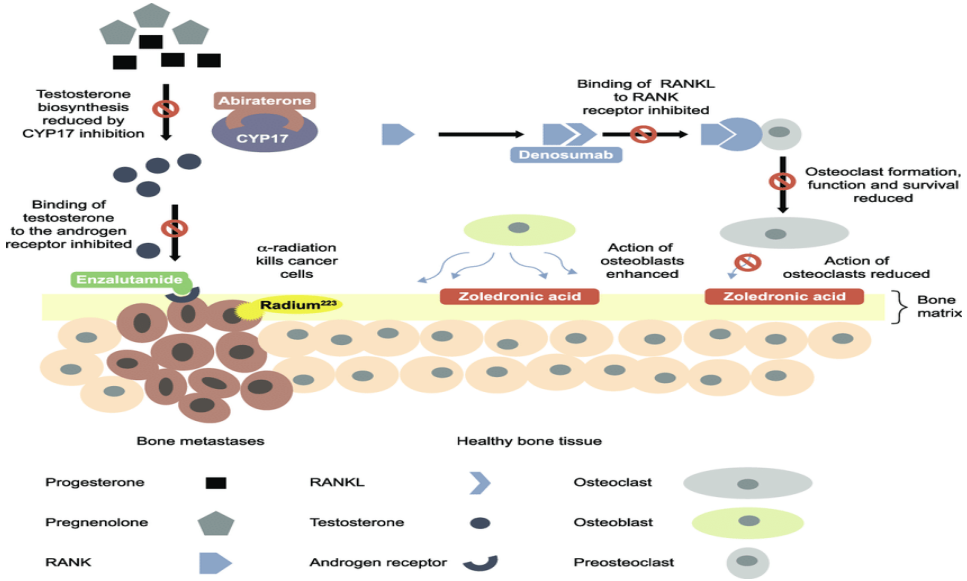


Ferreira VV, Ghosh AK. Essentials of cardio-oncology. Clin Med (Lond). 2023

HYPERTENSION

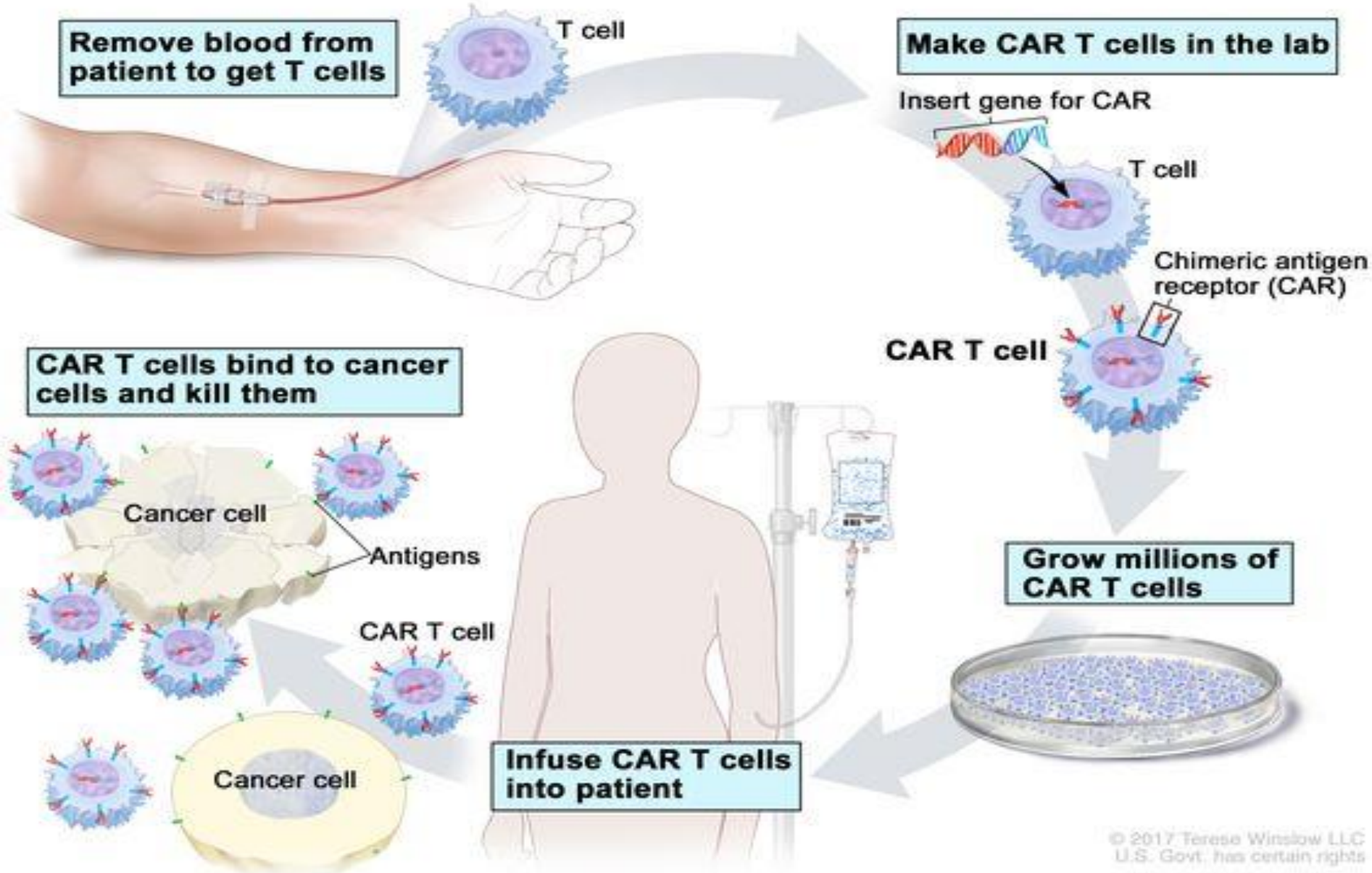




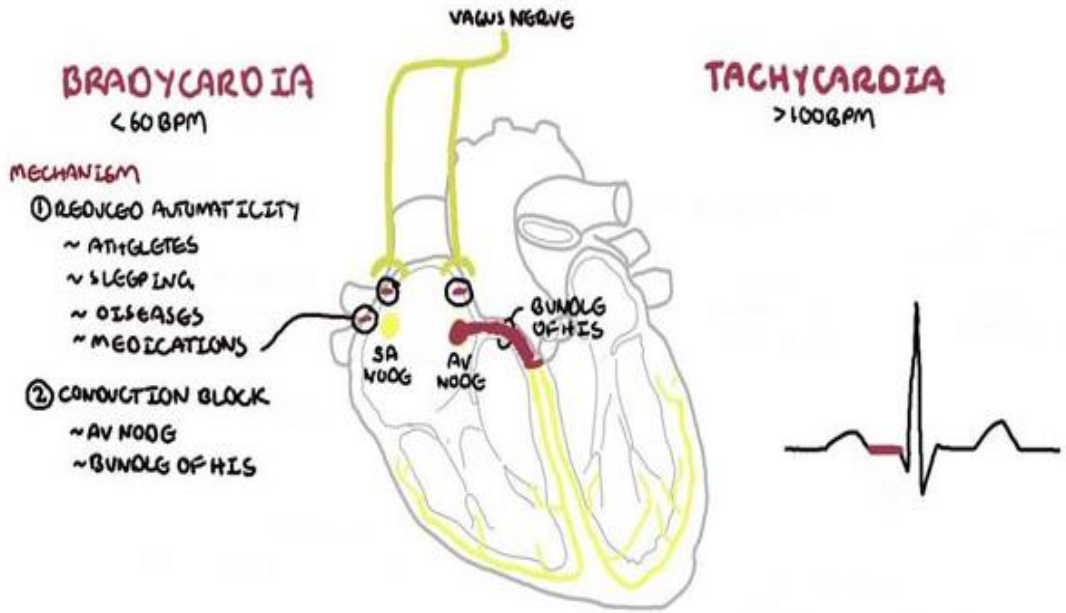


- Aleksandra Grela-Wojewoda et al. Cardiotoxicity Induced by Protein Kinase Inhibitors in Patients with Cancer. Int J Mol Sci. 2022 Mar 4;23 (5):2815
- Waxman et al. Carfilzomib-Associated Cardiovascular Adverse Events: A Systematic Review and Meta-analysis. JAMA Oncol. 2018, 4, e174519.
- Roberto Iacovelli et al. The Cardiovascular Toxicity of Abiraterone and Enzalutamide in Prostate Cancer. Clin Genitourin Cancer 2018 Jun;16(3):e645-e653

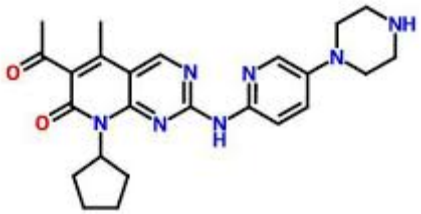
CAR T-cell Therapy

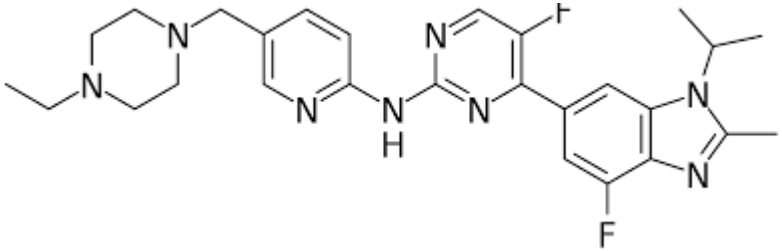


ARRHYTMIA

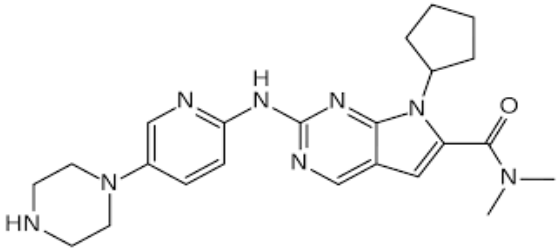


VANDETANIB 16.4-18%
RIBOCICLIB 7-16%
OSIMERTINIB 1.2-11%
VEMURAFENIB 1-10%
LENVATINIB 9%
CRIZOTINIB 8%
CAR-T CELLS 7-7,5%
NILOTINIB <5%





PALBOCICLIB/ABEMACICLIB VERY RARE

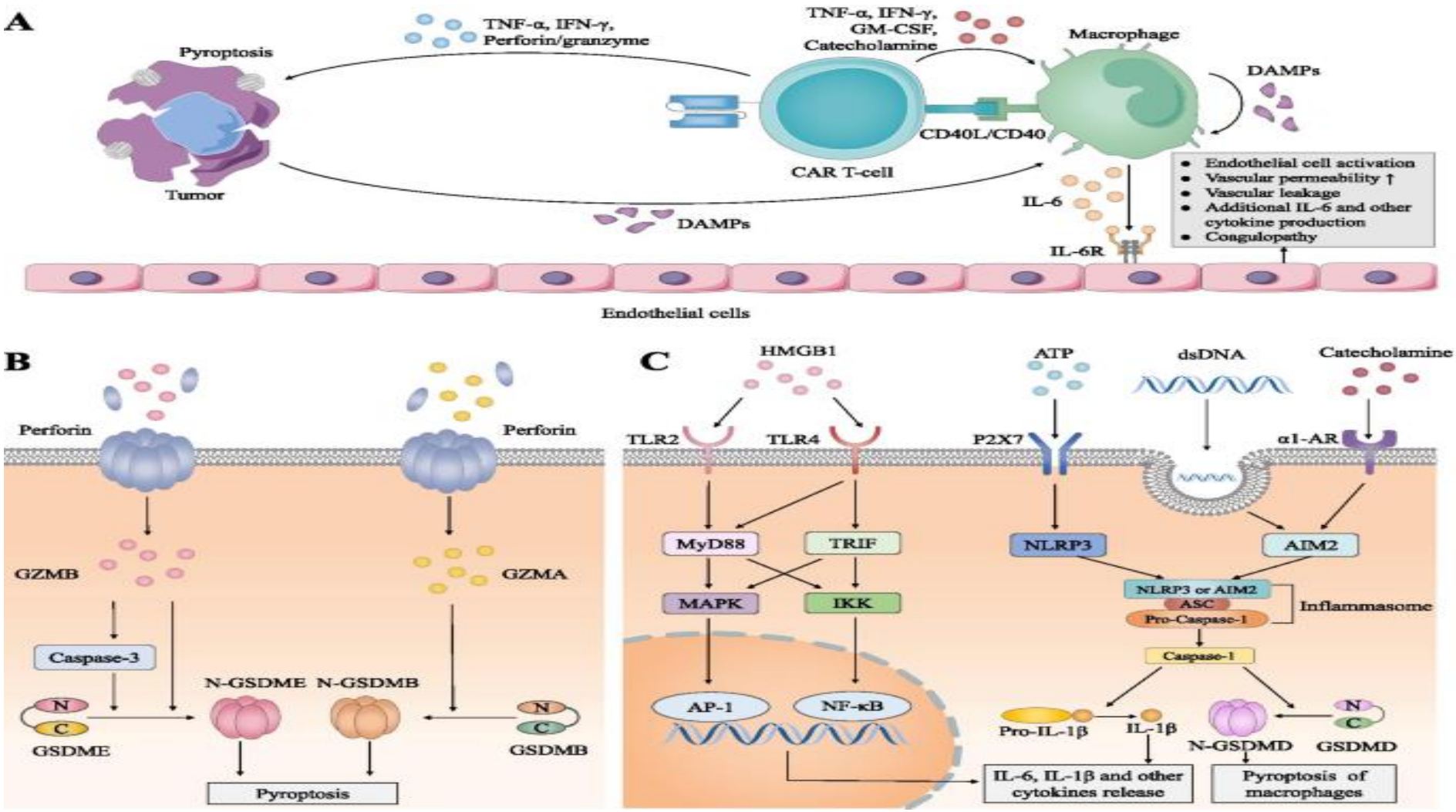


RIBOCICLIB 7-16%

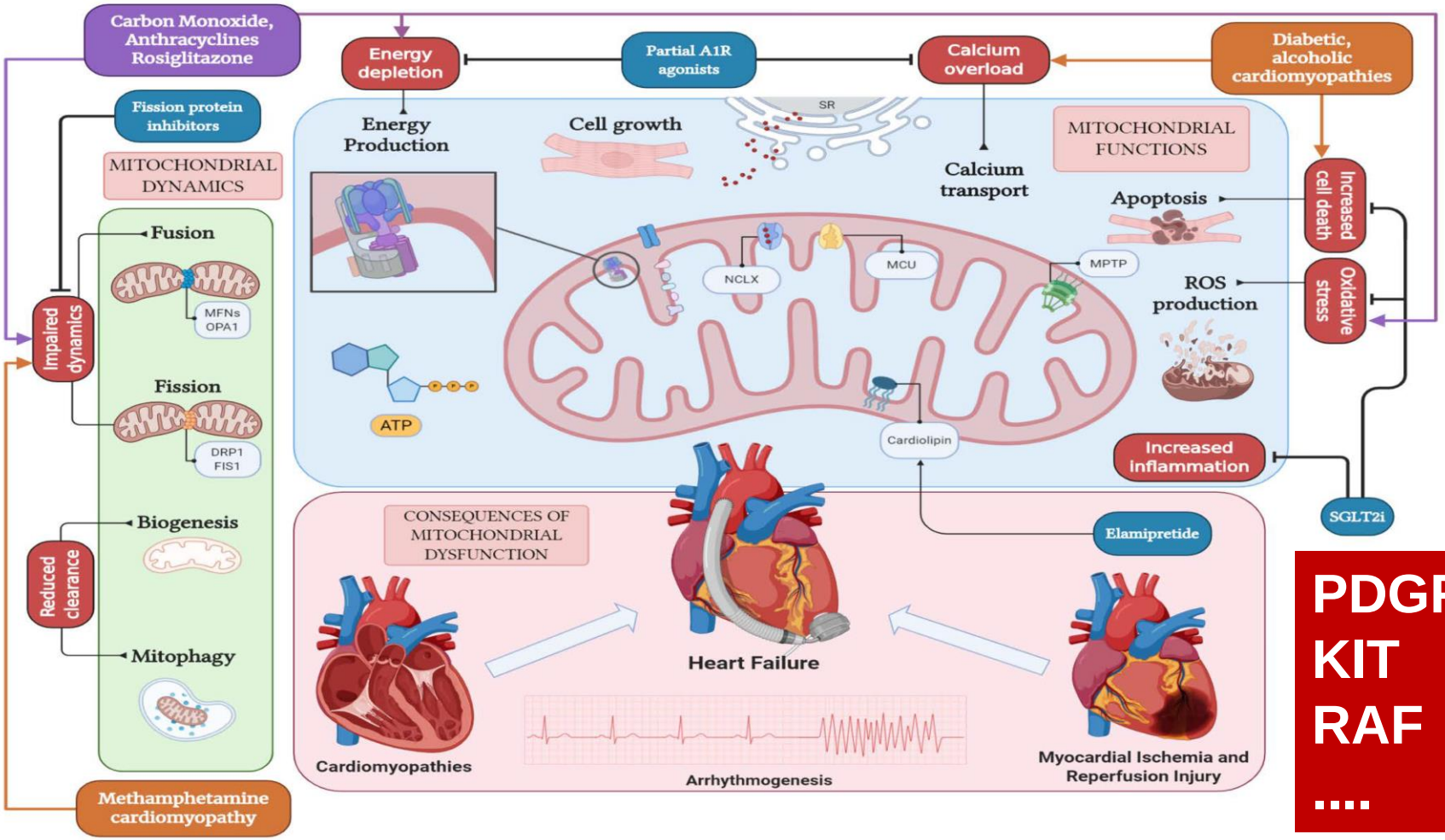
Aleksandra Grela-Wojewoda et al. Cardiotoxicity Induced by Protein Kinase Inhibitors in Patients with Cancer. Int J Mol Sci. 2022 Mar 4;23 (5):2815

Lefebvre, B.; Kang, Y.; Smith, A.M.; Frey, N.V.; Carver, J.R.; Scherrer-Crosbie, M. Cardiovascular Effects of CAR T Cell Therapy: A Retrospective Study. JACC CardioOncol. 2020, 2, 193–203.

CYTOKINE RELEASE SYNDROME



CARDIAC DISFUNCTYON



PDGFR
KIT
RAF
....

Hahn, V.S.; Lenihan, D.J.; Ky, B. Cancer Therapy-Induced Cardiotoxicity: Basic Mechanisms and Potential Cardioprotective Therapies. J. Am. Hear. Assoc. 2014, 3, e000665.

CARDIAC DISFUNCTYON

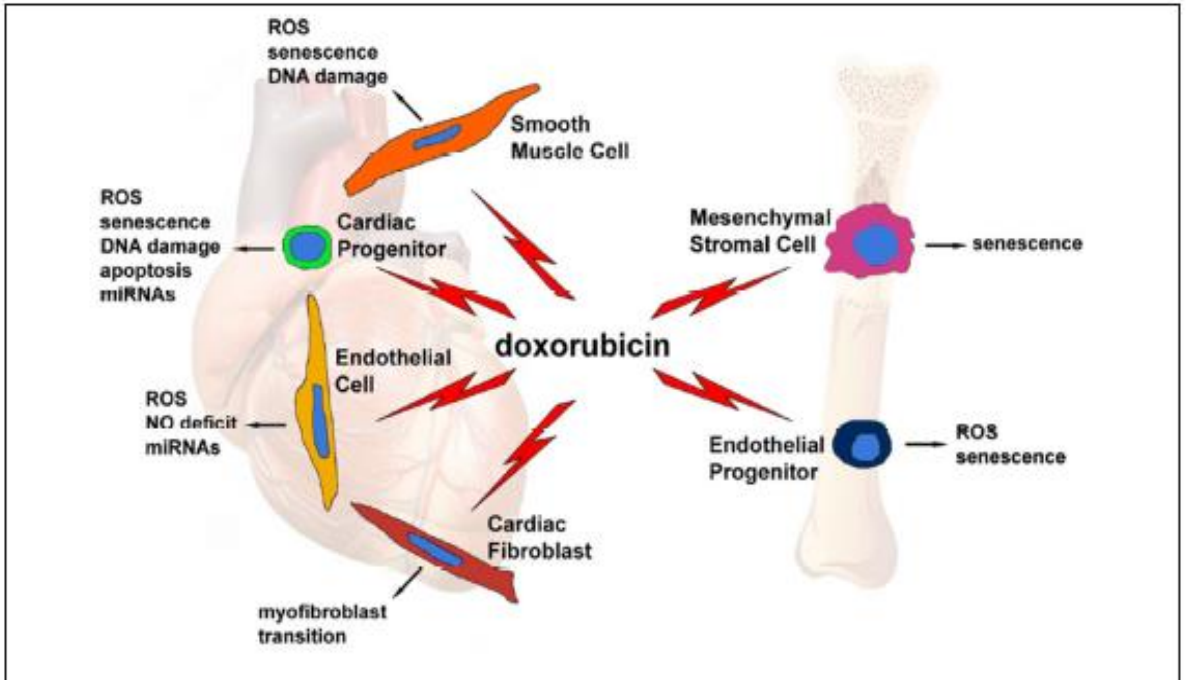


FIGURE 1 | Graphical representation of several doxorubicin-targeted cell types, with potential side effects and cellular and molecular events evoked by the drug. From Cappetta et al. (11).

PONATINIB 5-20%
TRAMETINIB 11%
CARFILZOMIB 3,4 – 7,2%
PAZOPANIB 6,7%
OSIMERTINIB 3-5%
SUNITINIB 4,1%
TRASTUZUMAB 3%
VGEF INHIBITORS 2,4%
DASATINIB 1,6%

LVEF < 50%

Somaira Nowsheen et al. Incidence, Diagnosis, and Treatment of Cardiac Toxicity from Trastuzumab in Patients with Breast Cancer. Curr Breast Cancer Rep. 2017 September ; 9(3): 173–182

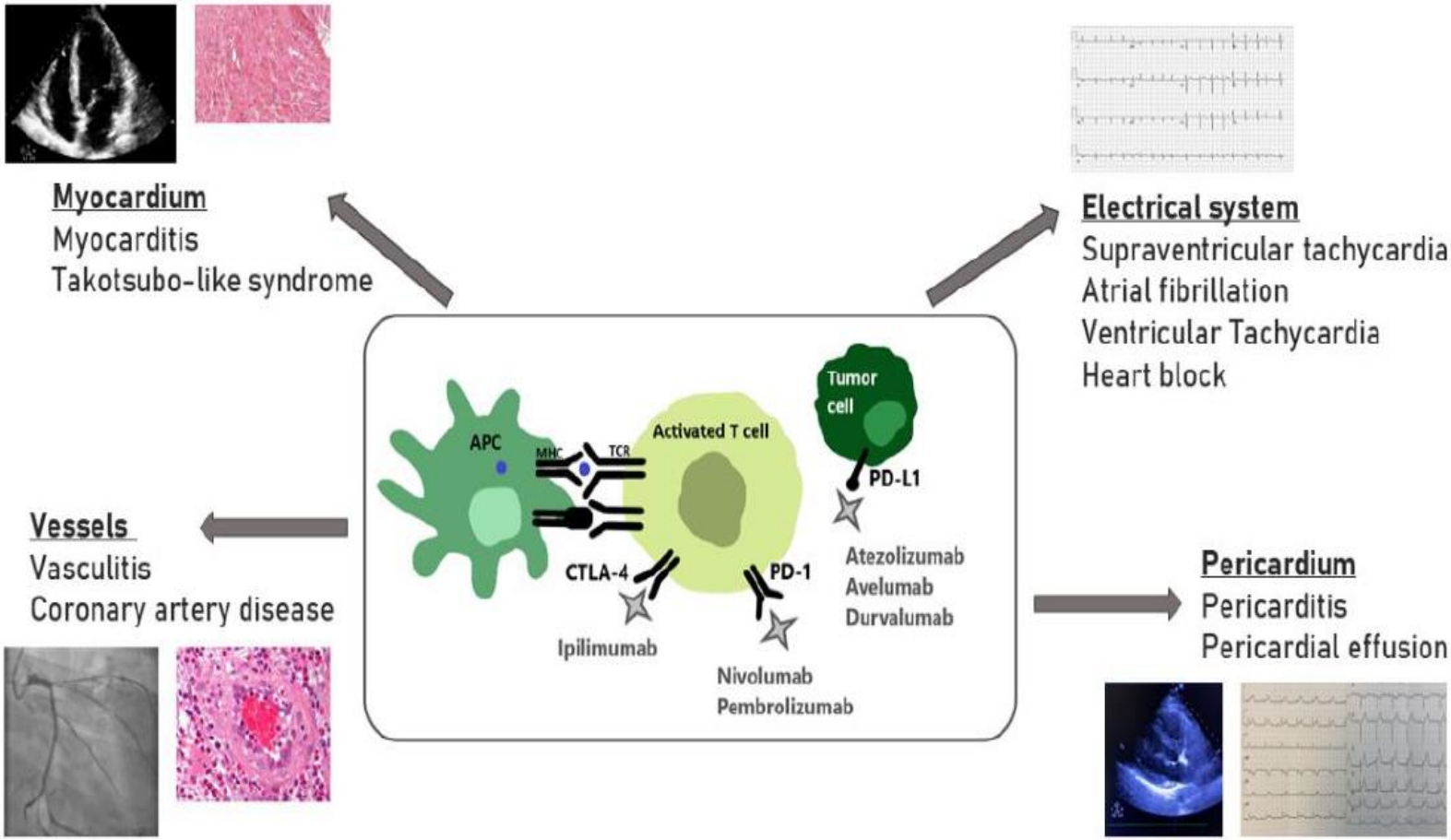
CARDIOVASCULAR TOXICITY

Table 2. The target sites of Bcr-Abl tyrosine kinase inhibitors and cardiotoxicity in patients with chronic myelogenous leukemia

Kinase/TKI	Imatinib	Nilotinib	Dasatinib	Bostinib	Ponatinb
Bcr-Abl	+	++	++	++	++
Bcr-Abl (T315I)					++
VEGFR				++	++
FGFR				++	++
PDGFR	+	+	++		++
SRC			++	++	+
DDR1	+	+	++		
Tie2					++
cKIT	+	+	++		++
Cardiotoxicity/TKI	**Imatinib**	**Nilotinib**	**Dasatinib**	**Bostinib**	**Ponatinb**
PAOD		++		+/−	++
IHD/CVA		+			+
VTE					+
Pulmonary hypertension			+		
Platelet dysfunction			+		+
Hypertension				+	++
Hyperglycemia	a	+			
Dyslipidemia	a	+			

Mikio Mukai et al. Mechanism and Management of Cancer Chemotherapy-Induced Atherosclerosis. J Atheroscler Thromb. 2018 Oct 1;25(10):994-1002

CARDIOTOXICITY BY ICI



Inbar Nardi Agmon et al. **The Potential Cardiotoxicity of Immune Checkpoint Inhibitors. J Clin Med.** 2022 Feb 7;11(3):865

FACTORS

Table 1. Patients with higher risk for cardiotoxicity.

- High-dose anthracycline (e.g., doxorubicin $\geq$ 250 mg/m^2, epirubicin $\geq$ 600 mg/m^2)
- High-dose radiotherapy ($\geq$30 Gy) where the heart is in the treatment field
- Lower-dose anthracycline (e.g., doxorubicin < 250 mg/m^2, epirubicin < 600 mg/m^2) or HERis or VEGFis or proteasomeis or Bcr-Ablis and presence of any of the following factors:
  - Age $\geq$60 y
  - Lower-dose radiotherapy (<30 Gy) where the heart is in the treatment field
  - $\geq$2 risk factors including: smoking, hypertension, diabetes mellitus, dyslipidemia, chronic renal insufficiency, and obesity
- Previous heart disease
- Elevated cardiac biomarkers before initiation of anticancer therapy

Briasoulis A et al. Cardiotoxicity of Non-Anthracycline Cancer Chemotherapy Agents. J Cardiovasc Dev Dis. 2022 Feb 23;9(3):66.

GUIDELINES ON CARDIONCOLOGY

ESC European Society of Cardiology
European Heart Journal (2022) 43, 4229–4361
https://doi.org/10.1093/eurheartj/ehac244
ESC GUIDELINES

2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS)

Developed by the task force on cardio-oncology of the European Society of Cardiology (ESC)

Authors/Task Force Members: Alexander R. Lyon*† (Chairperson) (United Kingdom), Teresa López-Fernández*† (Chairperson) (Spain), Liam S. Couch (Task Force Coordinator) (United Kingdom), Riccardo Asteggiano (Italy), Marianne C. Aznar[1] (United Kingdom), Jutta Bergler-Klein (Austria), Giuseppe Boriani (Italy), Daniela Cardinale (Italy), Raul Cordoba[2] (Spain), Bernard Cosyns (Belgium), David J. Cutter (United Kingdom), Evandro de Azambuja (Belgium), Rudolf A. de Boer (Netherlands), Susan F. Dent[3] (United States of America), Dimitrios Farmakis (Cyprus), Sofie A. Gevaert (Belgium), Diana A. Gorog (United Kingdom), Joerg Herrmann[3] (United States of America), Daniel Lenihan[3] (United States of America), Javid Moslehi (United States of America), Brenda Moura (Portugal), Sonja S. Salinger (Serbia), Richard Stephens (United Kingdom), Thomas M. Suter (Switzerland), Sebastian Szmit (Poland), Juan Tamargo (Spain), Paaladinesh Thavendiranathan (Canada), Carlo G. Tocchetti (Italy), Peter van der Meer (Netherlands), Helena J.H. van der Pal (Netherlands), and ESC Scientific Document Group

Lyon AR, López-Fernández et al. 2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS). Eur Heart J. 2022 Nov 1;43(41):4229-4361.

TEAM BUILDING

ONCOLOGICAL PHARMACY SERVICE

INFECTIOUS UNIT

PALLILATIVE CARE

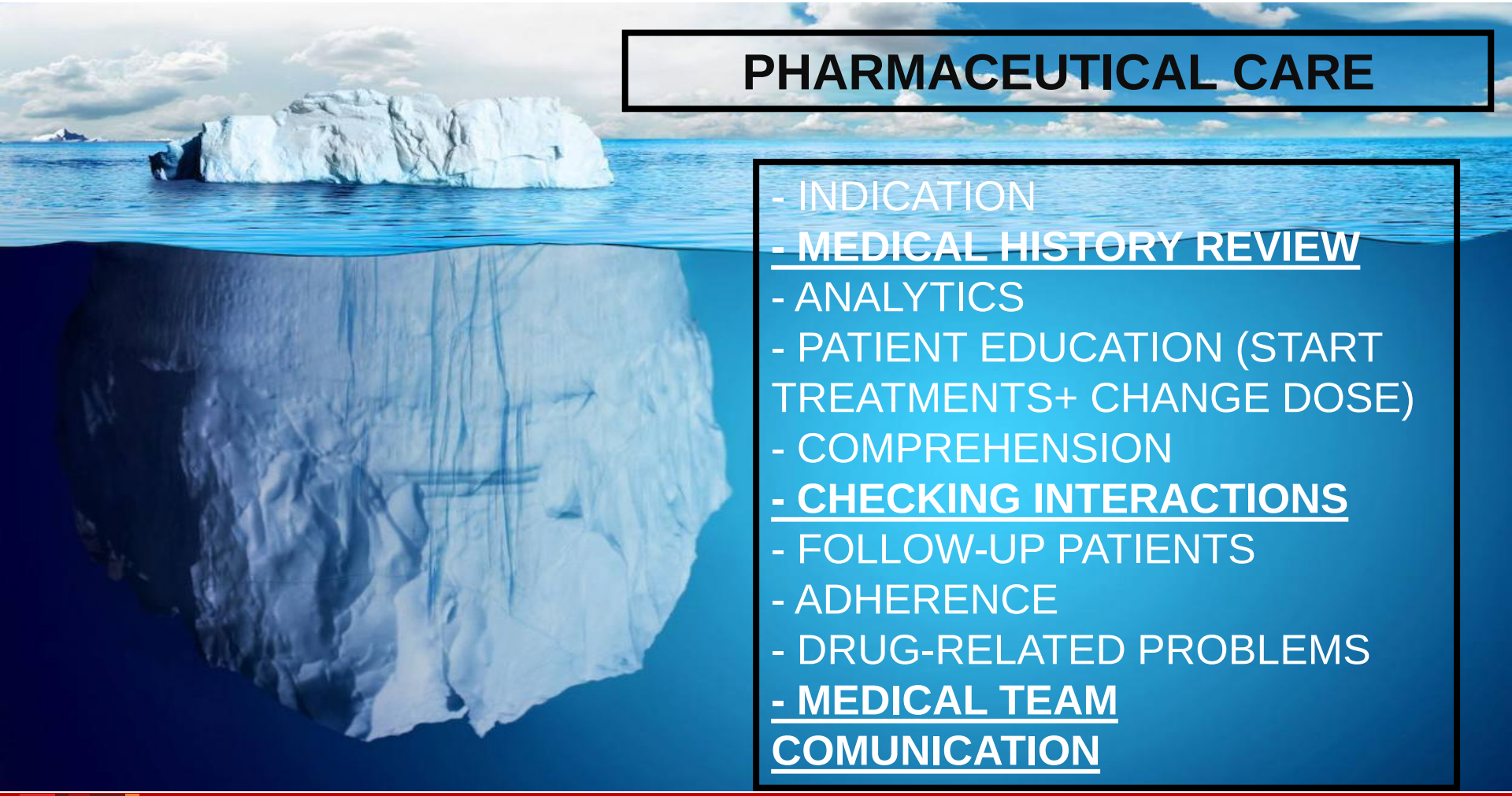
RADIOTHERAPY ONCOLOGY

MEDICAL ONCOLOGY

CLINICAL HAEMATOLOGY

PHARMACEUTICAL CARE

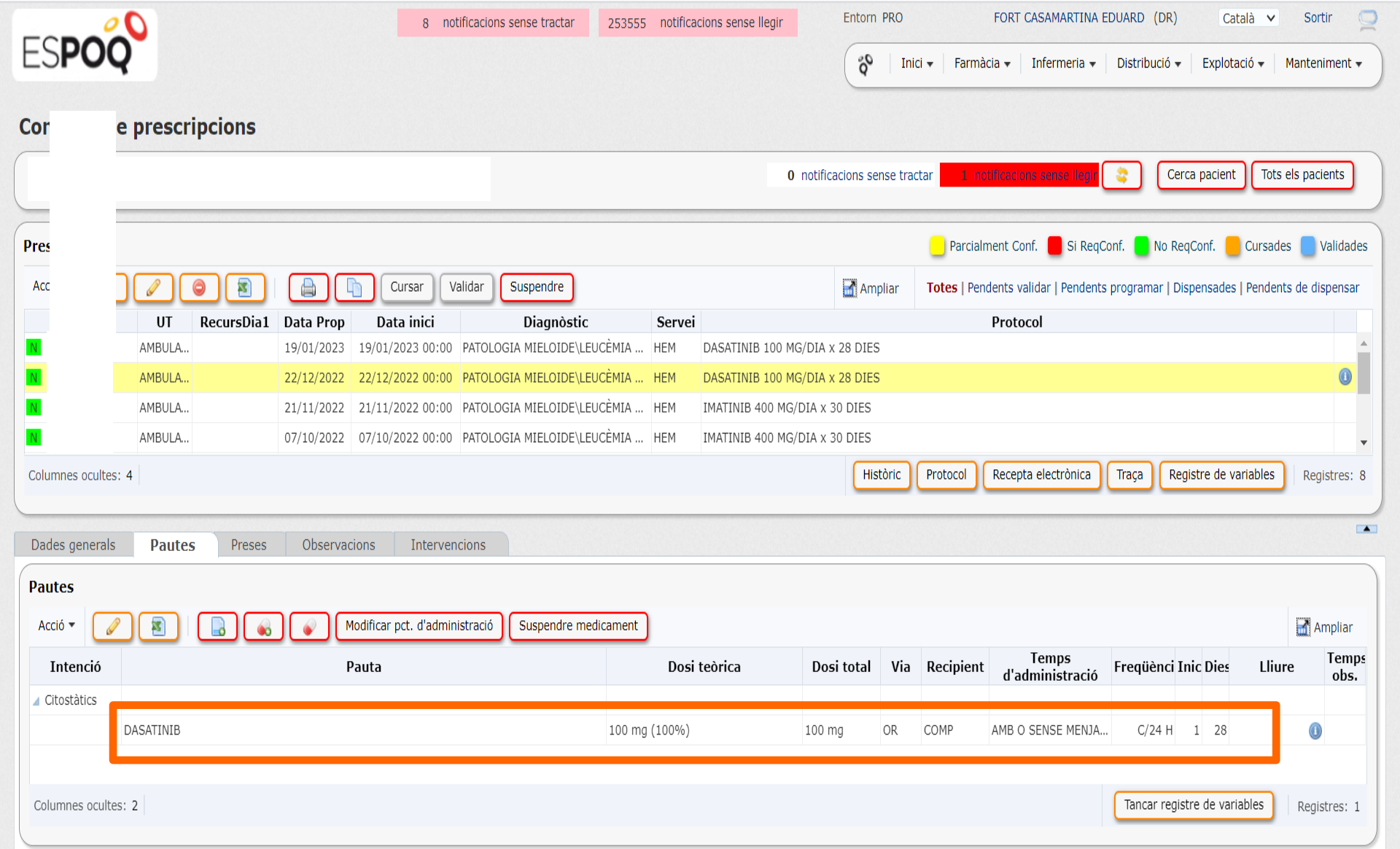
ONCOLOGICAL PHARMACY SERVICE



PHARMACEUTICAL CARE

- INDICATION
- **MEDICAL HISTORY REVIEW**
- ANALYTICS
- PATIENT EDUCATION (START TREATMENTS+ CHANGE DOSE)
- COMPREHENSION
- **CHECKING INTERACTIONS**
- FOLLOW-UP PATIENTS
- ADHERENCE
- DRUG-RELATED PROBLEMS
- **MEDICAL TEAM COMUNICATION**

VALIDATION (SOFTWARE)



MEDICAL HISTORY

MALE 65 YEARS OLD
EX-SMOKER
HYPERTENSION
DYSLIPEMIA
DIABETES MELLITUS
CAROTIDE VASCULOPATHY (60-70%)
CHRONIC LOW BACK PAIN (2 SURGERIES)

NILOTINIB

DASATINIB

CHRONIC MEDICATION

Pla de medicació comunitària

Tornar a la ETC

Institut Català de la Salut

Actualitzacions | Pàgina de test de Signatura

Pla de Medicació de F

108119596 FORT CASAMARTINA, EDUARD

Al·lèrgies (1) / Reaccions adverses significatives (0)

AL·LÈRGIA:
FENTANILO

Servei Actual | Tots els serveis

Prefaseg

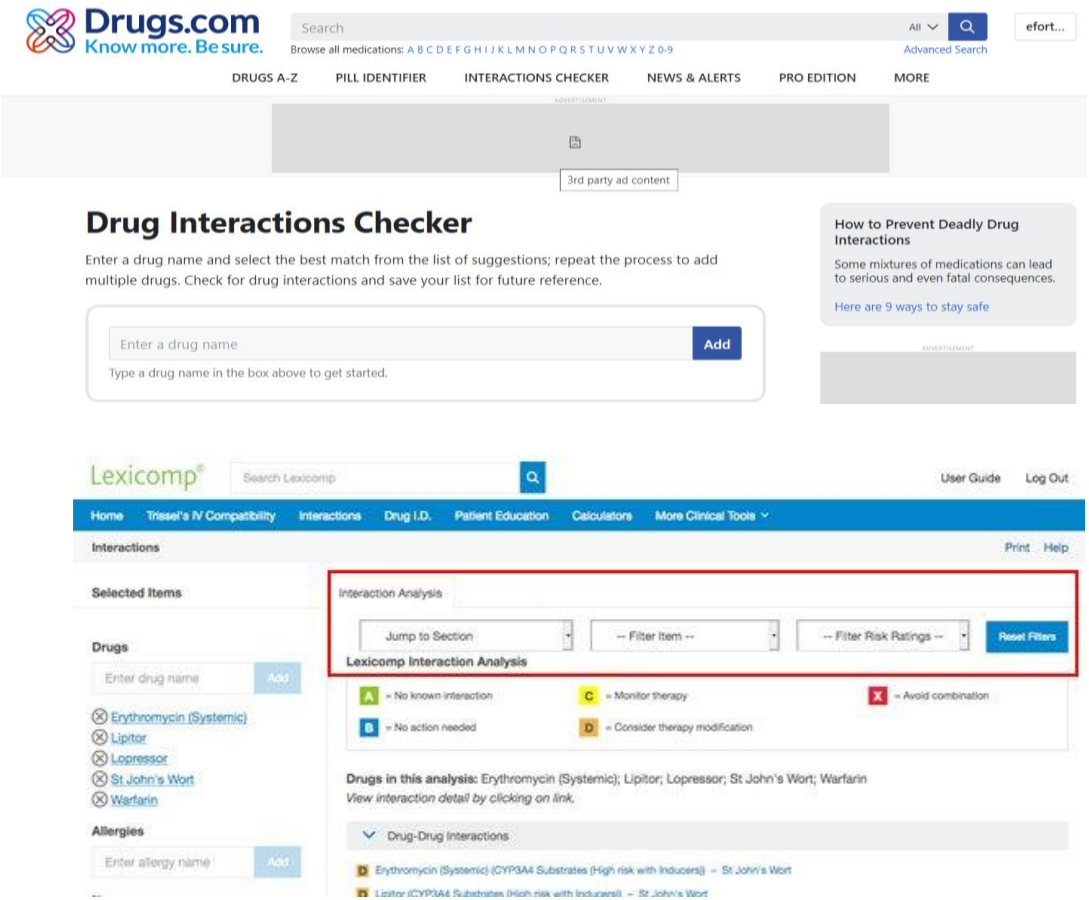
			Medicament	Principi Actiu	Via	Posologia	Durada	Envàs	x dies	Vigència	S
			SUMIAL 10MG 50 COMPRIMIDOS RECUBIERTOS CON PELICULA (MFC)	PROPRANOLOL, CLORHIDRAT	Oral	2 x 24 h.	Indefinida	1	25	RE-131	
			TAMSULOSINA EDIGEN 0.4MG 30 CAPSULAS DURAS LIBERACION MODIFICADA EFG (MFC)	TAMSULOSINA, CLORHIDRAT	Oral	1 x 24 h.	Indefinida	1	30	RE-339	
			TEBETANE COMPUESTO 30MG 60 CAPSULAS (MFC)	PYGEUM AFRICANUM	Oral	2 x 12 h.	Indefinida	1	15	RE-339	
			TRAMADOL ARISTO 50MG 60 CAPSULAS EFG (MFC)	TRAMADOL, CLORHIDRAT DE	Oral	2 x 8 h.	Indefinida	1	10	RE-339	
			TRULICITY 1.5MG 4 PLUMAS PRECARGADAS SOLUCION INYECTABLE (MFC)	DULAGLUTIDA	Subcutanea	1 x 1 s.	Indefinida	1	28	RE-339	
			XIGDUO 5MG/850MG 56 COMPRIMIDOS RECUBIERTOS CON PELICULA (MFC)	METFORMINA + DAPAGLIFLOZINA	Oral	1 x 12 h.	Indefinida	1	28	RE-339	
			DEXKETOPROFENO TEVA 25MG 20 COMPRIMIDOS RECUBIERTOS PELICULA EFG (MFC)	DEXKETOPROFEN, TROMETAMOL	Oral	1 x 8 h.	Si cal	1	365	RE-362	
			BESITRAN 50MG 30 COMPRIMIDOS RECUBIERTOS CON PELICULA (MFC)	SERTRALINA	Oral	Segons pau	183 dies	1	30	RE-157	
			DECENTAN 8MG 50 COMPRIMIDOS (MFC)	PERFENAZINA	Oral	2 x 24 h.	360 dies	1	25	RE-334	
			DIAZEPAM NORMON 5MG 40 COMPRIMIDOS (MFC)	DIAZEPAM	Oral	5 x 24 h.	360 dies	1	8	RE-334	
			MIRTAZAPINA NORMON 15MG 60 COMPRIMID RECUB PEL EFG (MFC)	MIRTAZAPINA	Oral	1 x 24 h.	60 dies	1	60	RE-34	

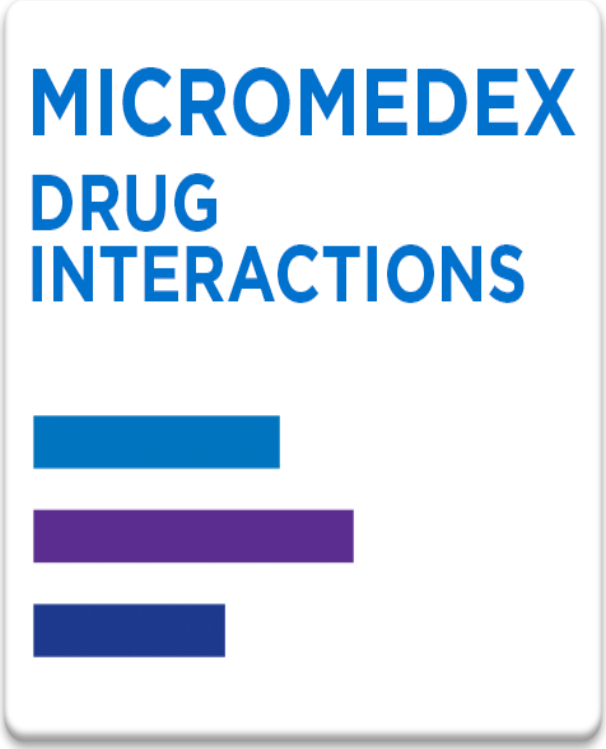
12

Missatgeria

Escriu aquí per cercar

INTERACTION CHECKER





Medscape

PHARMACOLOGICAL INTERACTION

Moderate

traMADol ⇄ dasatinib

Applies to: tramadol, dasatinib

Using dasatinib together with traMADol can increase the risk of an irregular heart rhythm that may be serious and potentially life-threatening, although it is a relatively rare side effect. You may be more susceptible if you have a heart condition called congenital long QT syndrome, other cardiac diseases, conduction abnormalities, or electrolyte disturbances (for example, magnesium or potassium loss due to severe or prolonged diarrhea or vomiting). Talk to your doctor if you have any questions or concerns. You should seek immediate medical attention if you develop sudden dizziness, lightheadedness, fainting, shortness of breath, or heart palpitations during treatment with these medications, whether together or alone. It is important to tell your doctor about all other medications you use, including vitamins and herbs. Do not stop using any medications without first talking to your doctor.

Moderate

buprenorphine ⇄ dasatinib

Applies to: buprenorphine, dasatinib

Using buprenorphine together with dasatinib can increase the risk of an irregular heart rhythm that may be serious and potentially life-threatening, although it is a relatively rare side effect. You may be more susceptible if you have a heart condition called congenital long QT syndrome, other cardiac diseases, conduction abnormalities, or electrolyte disturbances (for example, magnesium or potassium loss due to severe or prolonged diarrhea or vomiting). In addition, dasatinib may increase the blood levels of buprenorphine. This can increase the risk and/or severity of other side effects such as drowsiness, dizziness, lightheadedness, difficulty concentrating, and impairment in thinking and judgment. In severe cases, low blood pressure, respiratory distress, fainting, coma, or even death may occur. You may need a dose adjustment or more frequent monitoring by your doctor to safely use both medications. Talk to your doctor if you have any questions or concerns. You should seek immediate medical attention if you develop sudden or excessive drowsiness, dizziness, lightheadedness, fainting, confusion, shortness of breath, heart palpitations, and/or shallow or difficult breathing during treatment with these medications. Do not drink alcohol during treatment with buprenorphine, and do not use more than the dose prescribed by your doctor. Also, avoid activities requiring mental alertness such as driving or operating hazardous machinery until you know how these medications affect you, and use caution when getting up from a sitting or lying position. It is important to tell your doctor about all other medications you use, including vitamins and herbs. Do not stop using any medications without first talking to your doctor.

Major

aspirin ⇄ dasatinib

Applies to: aspirin, Aspirin Low Strength (aspirin), dasatinib

Using dasatinib together with aspirin may increase the risk of bleeding. The interaction may be more likely if you are elderly or have kidney or liver disease. In clinical studies, treatment with dasatinib alone has been associated with severe and sometimes fatal hemorrhage. Talk to your doctor if you have any questions or concerns. Your doctor may already be aware of the risks, but has determined that this is the best course of treatment for you and has taken appropriate precautions and is monitoring you closely for any potential complications. You should seek immediate medical attention if you experience any unusual bleeding or bruising, or have other signs and symptoms of bleeding such as dizziness; lightheadedness; red or black, tarry stools; coughing up or vomiting fresh or dried blood that looks like coffee grounds; severe headache; and weakness. It is important to tell your doctor about all other medications you use, including vitamins and herbs. Do not stop using any medications without first talking to your doctor.

Moderate

mirtazapine ⇄ dasatinib

Applies to: mirtazapine, dasatinib

Using mirtazapine together with dasatinib can increase the risk of an irregular heart rhythm that may be serious and potentially life-threatening, although it is a relatively rare side effect. You may be more susceptible if you have a heart condition called congenital long QT syndrome, other cardiac diseases, conduction abnormalities, or electrolyte disturbances (for example, magnesium or potassium loss due to severe or prolonged diarrhea or vomiting). Talk to your doctor if you have any questions or concerns. You should seek immediate medical attention if you develop sudden dizziness, lightheadedness, fainting, shortness of breath, or heart palpitations during treatment with these medications, whether together or alone. It is important to tell your doctor about all other medications you use, including vitamins and herbs. Do not stop using any medications without first talking to your doctor.

COMUNICATION

CC 22/12/2022 16:29 **Eduard Fort Casamartina** FARMACIA ICO / CEX FARMACIA ICO (DR) Metge Farmacèutic

Paciente de 65 años con diagnóstico de LMC de debut. Sokal 0,75 bajo riesgo; ELTS 1.5821 Riesgo intermedio

23/06/2022 Inicia imatinib 400 mg/24h (1 comp de 400 mg).

Tras visita de hoy se inicia nuevo linea de tartamiento por regular tolerancia y falta de respuesta. Dasatinib 100mg c/24h (2 comp de 50mg una sola toma diaria x la mañana)

Se detectan multiples interacciones potenciales con medicacion cronica del paciente: tramadol, mirtazapina, aspirina, sertralina, buprenorfina, diazepam. Se aconseja monitorizacion cardiaca y de coagulacion y sangrados

Acude esposa impactada por falta de respuesta a imatinib, se dispensa medicacion. Realizamos educacion sanitaria y entregamos informacion escrita, reforzando esquema de tratamiento asi como efectos adversos

CC 29/12/2022 12:11 CARDIOLOGIA / CEX U.F.Insuf.Card. (BE) Metge Cardiologia

Unidad de Cardio-Oncología - Consulta virtual

Varón de 65 años. Exfumador, HTA, dislipemia y diabetes mellitus. Lumbociatalgia crónica, intervenido en 1988 con desquectomía y artrodesis, con dos relQ poseriores por infección. Nueva IQ en raquis en 2013. Seguimiento en clínica del dolor y tratamiento habitual con múltiples medicaciones. Vasculopatía carotídea. EcoTSA en nov/2022 con estenosis significativa (60-70%) de carótida interna derecha. En tratamiento habitual con AAS.

LMC con tratamiento con Imatinib desde Junio/2022. Tras progresión se realiza cambio de linea a dasatinib. Nos avisan desde farmacia por multiples interacciones potenciales con medicacion cronica del paciente (tramadol, mirtazapina, aspirina, sertralina, buprenorfina, diazepam).

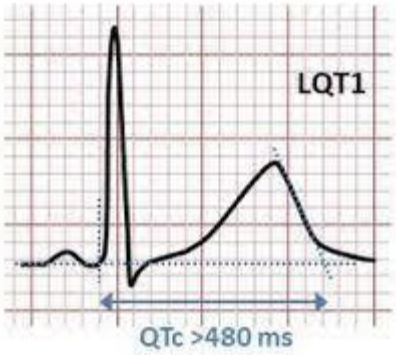
Plan
-Paciente con indicación de AAS por criterios de prevención cardiovascular secundaria en relación a su vasculopatía carotídea. Recomiendo mantener en la medida de lo posible mientras no presente eventos hemorrágicos relevantes o plaquetopenia.
-Se han descrito casos de prolongación del íntervalo QT en relación con el Dasatinib, aunque se trata de un evento poco frecuente y la asociación con eventos arrítmicos no está clara. Se recomienda utilizar con precaución en paicnetes que tomen otra medicación con potencial riesgo de prolongar el QT. En este caso, paciente en tratamiento con mirtazapina y sertralina que podrían influir en este sentido. No considero que de entrada suponga una contraindicación para el tratamiento. Solicito ECG y control virtual para revisar.
-Dasatinib se asocia a reaciones adversas cardíacas. En este caso paciente con FRCV pero sin diagnóstico de cardiopatía previa. No considero que haya contraindicación cardiológica. Recomiendo seguimiento clínico estrecho por parte de hematología y comentar con cardio-oncología en caso de progresión de signos de disnea, dolor torácico o sospecha de insuficiencia cardíaca.

CLINICAL REPORT

MALE 42 YEARS OLD
SMOKER
HEROIN/COCAIN ADDICT
METASTATIC MELANOMA BRAF MUTATION
PULMONAR, HEPATIC ANS PERITONEAL M

- METHADONE 25MG C/12H
- QUETIAPINE 50MGC/24H
- OMEPRAZOL 20MG C/24H
- DIAZEPAM 10MG C/24H
- FUROSEMIDE 40MG C/24H
- DEXAMETASONE 4MG 1-1-0
- METOCLOPRAMIDE IF NEDEED

ONCOLOGICAL TREATMENT OPTIONS



PRE QTc 560mseg

ENCORAFENIB 450MG C/24H
+ BINIMETINIB 45MG C/12H

QUETIAPINE
METHADONE

P-gp inhibitor

↑ BINIMETINIB

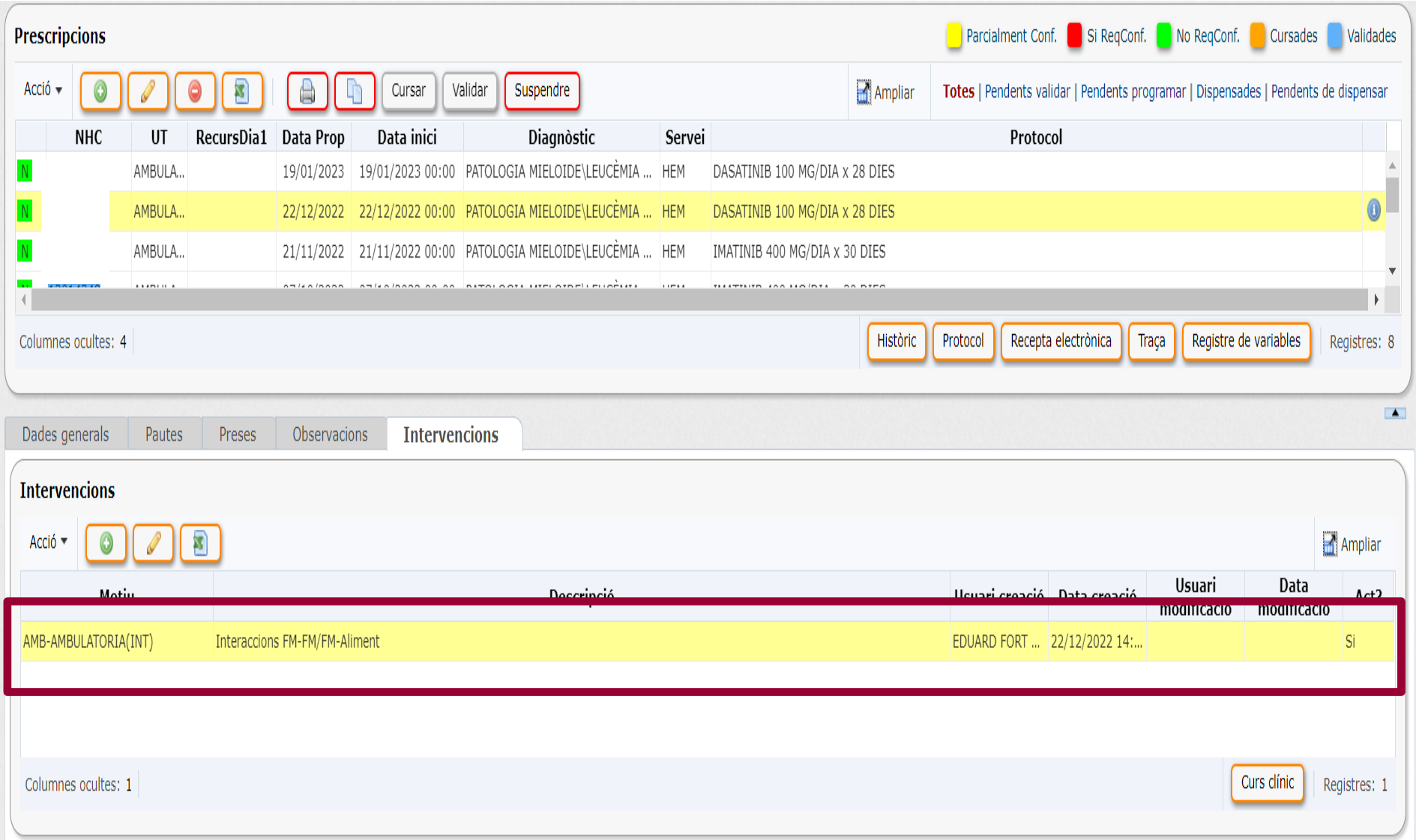
LVEF DYSFUNCTION

DABRAFENIB 150MG C/12H
+ TRAMETINIB 2MG C/24H

CYP450 INDUCER

↓ METHADONE
↓ QUETIAPINE

WORLD REAL DATA RESEARCH



F	G	H	I	J	K
Antineoplásico oral	Enfermedad oncohematológica	Medicamento concomitante	Drugs	Fort Casamartina, Eduard:	
IMATINIB	SARCOMES	Paracetamol	MODERADA	Riesgo hepatotoxicidad	Riesgo hepatotoxicidad
IMATINIB	SARCOMES	Roflumilast	MODERADA	Efecto adivo inmunosupresor	Efecto adivo inmunosupresor
OSIMERTINIB	PULMO CEL·LULA NO PETITA	Quetiapina	MAJOR	Riesgo prolongación intervalo QT	Riesgo prolongación intervalo QT
CAPECITABINA	RECTE	Hidroclorotiazida	MODERADA	Desconocido	Prolongación del efecto mielosupresor
PAZOPANIB	SARCOMES	Pantoprazol	MAJOR	solubilidad pazopanib ph dependiente, insoluble pH>4	reducción biodisponibilidad OR de pazopanib
PAZOPANIB	SARCOMES	Atorvastatina	MODERADA	Addición de hepatotoxicidad	Elevación ALT
PAZOPANIB	SARCOMES	Tacrolimus	MAJOR	inhibición transportadores P-gp o BCRP por carvedilol/Riesgo prolongación intervalo QT	aumento conc pazopanib/ Riesgo prolongación intervalo QT
BOSUTINIB	LMC	Espironolocatona	MODERADA	ESPIRO inhibitor of CYP450 3A4 and/or P-glycoprotein (P-gp)	Aumento concentraciones BOSUTINIB
ENCORAFENIB	COLON	Loperamida	MODERADA	Riesgo prolongación intervalo QT	Riesgo prolongación intervalo QT
OSIMERTINIB	PULMO CEL·LULA NO PETITA	Fentanilo	MODERADA	Riesgo prolongación intervalo QT	Riesgo prolongación intervalo QT
ENZALUTAMIDA	PROSTATA	Simvastatina	MODERADA	Inducción CYP450 3A4, 2C9, 2C19, and/or P-glycoprotein (P-gp) por enzalutamida	Disminución concentraciones SIMVASTATINA
ENZALUTAMIDA	PROSTATA	Sertralina	MODERADA	Riesgo prolongación intervalo QT	Riesgo prolongación intervalo QT
CAPECITABINA	COLON	Hidroclorotiazida	MODERADA	Desconocido	Prolongación del efecto mielosupresor
CAPECITABINA	MAMA	Hidroclorotiazida	MODERADA	Desconocido	Prolongación del efecto mielosupresor
IMATINIB	SARCOMES	Ticagrelor	MODERADA	Inhibición CYP3A4 por IMATINIB	Aumento concentraciones TICAGRELOR
IMATINIB	SARCOMES	Ivabradina	MAJOR	Inhibición CYP3A4 por IMATINIB	Aumento concentraciones IVABRADINA
IMATINIB	SARCOMES	Eplerenona	MAJOR	Inhibición CYP3A4 por IMATINIB	Aumento concentraciones EPLERENONA
IMATINIB	SARCOMES	Carvedilol	MODERADA	Inhibición CYP450 2C9, 2D6 and/or 3A4 por IMATINIB	Aumento concentraciones CARVEDILOL
IMATINIB	SARCOMES	Atorvastatina	MODERADA	Inhibición CYP3A4 por IMATINIB	Aumento concentraciones ATORVASTATINA
OLAPARIB	OVARI	Rosuvastatina	MODERADA	Inhibición CYP3A4 por OLAPARIB	Aumento concentraciones ROSUVASTATINA
POMALIDOMIDA	MIELOMA MULTIPLE	Amiodarona	MODERADA	inhibición CYP450 3A4, 1A2 y P-gp por amiodarona	Aumento concentración pomalidomida
DASATINIB	LMC	Dexametasona	MAJOR	Dexa inductor CYP3A4	Descenso concentraciones DASATINIB
LINEZOLID	SUPORT	Enalapril	MODERADA	IMAOs pueden potenciar efecto hipotensivo	Potenciación del efecto hipotensivo
ENTECAVIR	SUPORT	Metfomina	MODERADA	competitive inhibition of transporters in the renal tubules	Aumento C de ambos medicamentos
ENTECAVIR	SUPORT	Aciclovir	MODERADA	competitive inhibition of transporters in the renal tubules	Aumento C de ambos medicamentos
LENALIDOMIDA	MIELOMA MULTIPLE	Atorvastatina	MAJOR	Desconocido	Riesgo rabdomiolisis
RUXOLITINIB	MIELOFIBROSIS	Apixaban	MAJOR	Efecto aditivo anticoagulante o antiplaquetario	Aumento riesgo de hemorragia
VINORELBINA	PULMO CEL·LULA NO PETITA	Simvastatina	MODERADA	mismo EA	Riesgo de neuropatía
CAPECITABINA	RECTE	Hidroclorotiazida	MODERADA	Desconocido	Prolongación del efecto mielosupresor
RUCAPARIB	OVARI	Clonazepam	MODERADA	Inhibición CYP450 3A4 por rucaparib	aumento conc clonazepam
RUCAPARIB	OVARI	Diazepam	MODERADA	Inhibición CYP450 3A4 por rucaparib	

QT-PROLOGING INTERACTIONS

PREVALENCE OF DRUG-DRUG INTERACTIONS OF QT-PROLONGING DRUGS IN AN ONCO-HEMATOLOGICAL OUTPATIENT

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1: Pharmacy Service; 2: Cardioncology Unit; 3: Medical Oncology

BACKGROUND

Oral anticancer therapy is increasingly integrated into the care of patients (pts) with cancer. Recognition and management of pharmacodynamic drug-drug interactions is critical to provide efficacious and safe anticancer treatment.

PURPOSE

We aimed to gain insight into the real-world prevalence of potentially significant drug-drug interactions of QT-prolonging with oral antineoplastic agents used in an Oncohematological

METHODS

Prospective observational study between October 2020 – June 2021. Pts diagnosed with an oncohematological neoplasia and start treatment with an oral anticancer drug or suport treatment were included. Cancer treatment data were obtained from our prescription software System. Demographic data and concomitant medication were obtained from our electronic medical record software. Micromedex was used to find potencial QT-prolonging interactions between anticancer drugs and chronic medication, and were classified as major or moderate

RESULTS

Start treatment	1.217 patients
Global interactions	266
Pts QT interaction	37
Mean Age	66,6 years (40,9- 87,3)
Sex (M/F)	22/15
QT interactions	46
Mean interactions/patient	1,24 (1 - 3)
Cancer diagnostic	
Renal Cancer	12 (32,4%)
Non-small cell lung	9 (24,7%)
Prostate	4 (10,8%)

Figure I. Anticancer drugs

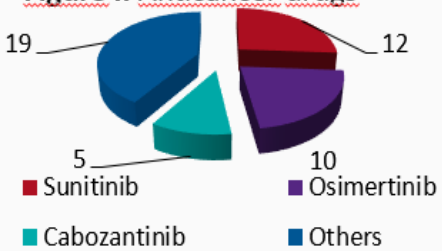
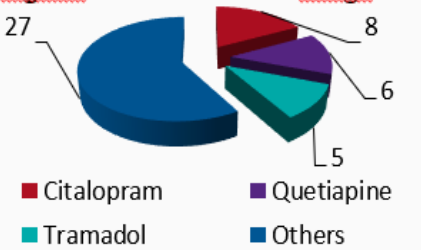


Figure II. Concomitant drugs



CONCLUSION

Drug-drug interactions can play a significant role in drugs' cardiac safety in oncohematological pts, specially in renal, lung and prostate cancers, with more than one potential interacting drug or at least one major interaction. Cardiac monitorizacion should be considered when potential drug drug interaction is detected.

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NO CONFLICT OF INTEREST TO DISCLOSE

INTERACCIONES FARMACOLÓGICAS IDENTIFICADAS EN PACIENTES CON CANCER DE PULMÓN CÉLULA NO PEQUEÑA AVANZADO EN TRATAMIENTO ORAL

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XI Educational Symposium

Tabla I. Descripción población

Variable	N=168
Interacción Farmacológica - Si/No	61 (36,3%)/107 (63,7%)
Interacciones totales	84
Severidad interaccion - Mayor/Moderada	22 (26,2%)/62 (73,8%)
Media interacciones/paciente	1,38 (1-3)
Edad media si interaccion	67,8 (42,3-85,7)
Sexo (H/M)	45%/55%

Gráfico II. Medicación concomitante

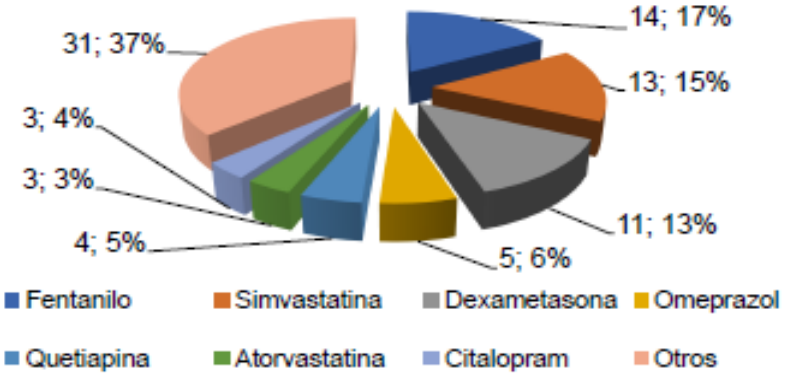

Gráfico II. Tratamiento oncológico CPCNPm

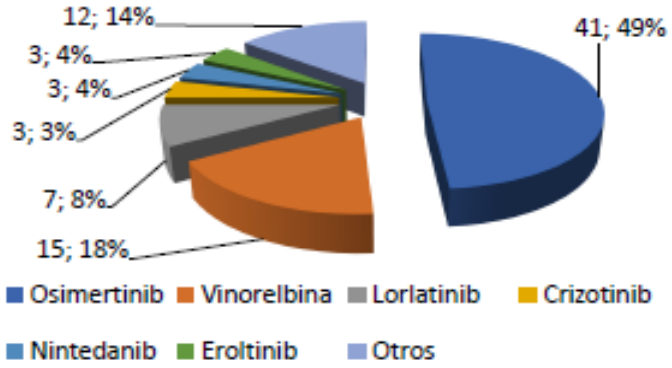

Tabla II. Efecto interacción

↓ efecto ITK	19 (22,6%)	↓ efecto MC	11 (39,2%%)
- Aumento pH gástrico	6 (31,6%)	- Inducción CYP3A4	10 (90,1%)
- Inducción CYP	12 (63,2%)	- Inducción CYP2D9	1 (9,9%)
- Inducción glicoproteína P	5 (26,3%)		
↑ toxicidad ITK	36 (42,8%)	↑ efecto MC	23 (82,14%)
- Cardíaca	22 (61,1%)	- Inhibición CYP3A4	18 (78,3%)
- Neuromusculares	8 (22,2%)	- Otros	8 (34,8%)
- Hematologicas	2 (5,5%)		
- Otras	4 (11,1%)		

CONCLUSIONS

CENTRAL ILLUSTRATION: Priorities Identified for Advancing the Field of Cardio-Oncology

Lenihan, D.J. et al. J Am Coll Cardiol CardioOnc. 2019;1(2):256–72.

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