

13th Norddeutsche Zytostatika Workshop

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Oncology pharmacy practise is still on the move in Europe. During the last weekend of January 2005 more than 500 delegates mostly from Germany were assembled in Harburg just south from Hamburg for the 13th Norddeutsche Zytostatika Workshop, NZW and the Onkologische Pharmazeutischer FachKongress. This event constitutes the yearly symposium of DGOP, Deutsche Gruppe Onkologische Pharmazie. The group is very active and successful in promoting quality standards, certification of oncology pharmacists, education and symposia in oncology pharmacy practice to the benefit of the cancer patient and optimal cancer therapy. DGOP also hold a yearly autumn conference which is named "post-ASCO conference" and highlights events of the big international conference held just before.

A large group of Polish hospital and oncology pharmacists also attended the conference as the two countries have had joint meetings for the last few years. A number of delegates of the European organisation ESOP, European Society of Oncology Pharmacy took part in the conference and also contributed to the program ESOP has now gathered representatives from 22 countries in Europe. Most important from the ESOPconference meeting was the launching of a document The Kopernikus Agenda with the hope to increase impact of the activities of clinical pharmacists. In all areas of European oncology pharmacy practice you can note the influence of Klaus Meier, former ISOPP President.

Many technicians were also attracted to the workshop and congress. They had a special program particularly designed to their tasks in cytotoxic drug preparation in German hospital pharmacies. The conference had a broad coverage from new treatment principles in certain cancer types, oral drugs designed for children and procedures for cost negotiations. It was possible to attend only a small part and an abstract book would have helped.

Lectures and a workshop on Chronobiology was given by Prof William Huskey from South Carolina, US received great interest. Many cells are regulated by biologic rythms and it is estimated that 5 to 10% of cancer cells are modulated by clock controlled genes. Cancer cells are sensitive to time for surgery and treatment. Some cytotoxics are more effective at certain times of day e.g. cisplatin is better in the evening whereas the effect of doxorubicin is superior in the morning. Immunoactivity is decreased in sun-light and melatonin (a hormone produced during hours of darkness) has shown an effect on cancer cells. In the north of Europe, people are greatly affected by light and dark, summer and winter and I urge pharmacists to learn more on the dependence of biology on time. A session on "Mechanisms of cytotoxic induced emesis" explained why nausea and vomiting still persists days and up to a week following cytotoxic drug administration. Better understanding of the mechanisms for emesis allows development of more efficient drugs for

supportive care in cancer.

Other topics included new drugs in supportive care (although there are no effective drugs to treat cytotoxic induced fatigue), automatic syringe filling, progress in oncology pharmacy in Cyprus, France and the Czech Republic, progress in quality assurance and complementary medicine with herbal drugs completed the program.

As always, the meeting provided an update on the progress in oncology pharmacy and was an excellent occasion for renewal of contacts with European colleagues.

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Editorial

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The aim of this newsletter is to paint a picture of the cancer situation in Europe and more specifically in France. Cancer is the leading cause of premature death in France. Every year, it kills 150 000 people (French population is 60 million). The French government has launched a five-year nation wide mobilization plan to fight against cancer. Set up in May 2005, the French National Cancer Institute is intended for expertise and resources. The purpose of this new institute is to improve care quality and to coordinate all players involved in cancer's fight. The fund allocated to this C plan will reach 640 million euros in 2007.

This new organization has direct consequences in the daily life of every hospital in France. Hospital pharmacists are particularly concerned by this C plan. Indeed, cytotoxic drug funding has been correlated with "proper use contract" to enhance efficiency. Centralized preparation unit, multidisciplinary meeting and participation in an oncology care network are a sine qua non for taking care of cancer patients.

The organisation of a French general hospital illustrated the consequence of this reform. The Saint-Denis Hospital is a 700-bed general hospital which has a moderate cancer activity. In 2004, 114 patients received a chemotherapy regimen. Cancer patient undertaking is already a multidisciplinary activity in this hospital. Pharmacy is involved in many points: not only the centralised preparation unit staff is engaged but



Saint-Denis Hospital Pharmacy Staff

also the control laboratory one. Risk management is a theme that concerns all oncology pharmacists. Many improvements have been made notably in personal protective equipment and preparation procedures. Nevertheless, cytotoxic drug contamination remains a preoccupation and forms the subject of many studies.

Thanks to Catherine Gammel for the rereading

Impact of Biological Therapies on Oncology Pharmacy Practice

Genoa, December 14th , 2004

Franca Goffredo, ISOPP Secretariat member

Franca Goffredo and
Graham Sewell



Every year, in December, Italian oncologists organise a meeting called "Grandangolo: a year of oncology" dealing with the most important innovations in oncological treatments for each type of cancer which have emerged during the year. Over the last few years nurses and pharmacists involved in oncology have run parallel meetings on related topics.

In 2004 Italian oncology pharmacists kept this appointment, with a meeting touching on an innovative theme: "The Effect of Biological Therapies on Oncology Pharmacy Practice". The development of molecular biology and new applications in oncology makes it essential for pharmacists to face this and address their interests in this direction. Specific education on these topics could help them to better meet patients' needs and give their proper contribution within the oncological team.

The main purpose of the meeting was to give an overview on these new themes and stimulate the interests of the

pharmacists to go into them more deeply. President of ISOPP, Professor Graham Sewell, was invited to present the possible effects that the use of these new therapeutic approaches could have on oncology pharmacy in the future (this lecture also gave the title to the meeting). Prof. Sewell spoke about possible drug interactions, drug stabilities, and potential risks for the patients and operators handling these new agents. Prof. Silvia Giordano, from the Institute of Cancer Research and Treatment of Candiolo (To) presented the effect that new techniques can have on both diagnosis and therapeutics, presenting results from trials including gene therapies. Prof. Luzzatto, from Genoa, had an enthusiastic audience as he presented the development of the Genoma project in which he was involved. The presentation of Dr. Mario Bardelli, from the Institute of Candiolo, on practical applications for individualised therapies, seemed nearer to the present. The moderation conducted by Doctor Bertetto, who

summarised the session by pointing out the main message, was much appreciated.

The interesting afternoon sessions were more structured on discussion. The topics raised: off label use of oncological drugs together with the ethical problems related to the management of the bio-banks presented by Dr.ssa Franca Dana Bricarello, from Gaslini Hospital in Genoa. She involved in the discussion not only the audience, with examples of her vast experience at the hospital for children, but also the oncologists, Prof. Siena, Prof. Aglietta and Dr. Montemurro, who were speaking at the meeting.

The 2004 meeting was a great success, even if the topics faced were very difficult and very specialised, it was valuable and made the participants enthusiastic, laying the basis for future developments. We had the sensation of being projected into the near future, and this was confirmed by the evaluations collected from the participating pharmacists.

Pharmacists and France's Cancer

Muriel Dahan, public health pharmacist,
French national cancer institute



France's nation-wide mobilization plan to fight cancer is a strategic program for the five coming years, focused on patients.

This plan has six operational and priority chapters: covering prevention, screening, treatment, support, teaching, and understanding and discovering. An ambitious plan, the cancer plan combines 70 quite different steps, including the creation of the French National Cancer Institute (INCA), which was officially inaugurated on May, 24th, and will work in very close connection with scientists, health care professionals and patient representatives so as to facilitate the implementation of the plan.

The plan aims to impact our whole health care system with a renewed vision, where the fight against cancer is fought by patients, their families and friends, and the medical and nursing teams alike.

Pharmacists, especially, are proximity health professionals, easily and equally accessible, without appointments, wherever the patient is located, and are likely to play an important role in each of the six chapters of the plan:

1. PREVENTION: The prevention of cancer focuses on studying and modifying behaviors that increase risk, mitigating the influence of genetic and environmental risk factors. Pharmacists are central actors of prevention. They give advice to patients about quit-smoking and quit-alcohol programs, and promote food hygiene and nutrition. National information campaigns organised regularly are broadcasted by pharmacists and biological laboratories. The retail pharmacists relay at a local level, through their windows accommodations, brochures and advice provided to patients, national actions launched in cancer plan framework.

2. SCREENING: The plan aims to develop screening for those types of cancer where screening has been proved to be truly useful, by making it easier for all to access the required testing. The pharmacists can encourage individual screening and help the patients who wish to be informed and directed towards appropriate structures. Moreover, in France, pharmacists can be

biologists, playing a key role among screening stakeholders.

3. TREATMENT: The plan aims to give the patients the best possible chances of recovery, regardless of where they are treated. This involves coordinating care around the patient, complying with good clinical practices, and ensuring maximum access to innovative equipment and therapies. Especially, the steps 46 & 47 of the cancer plan expect:

- Equal access to expensive and innovative drugs & facilities in the private and public sectors
- Access for all patients, within a secure frame; no patient, hospital, district discrimination
- Developing the evaluation of new molecules in oncology, via public follow-up of post-AMM studies.

Pharmacists will be foreground actors, particularly through the evolutions of retrocession¹ and at-home chemotherapy legislations, the new funding system and the creation of innovations observatories "OMIT"²

- Besides their basic and current missions, which target to ensure safe and effective use of medications, provide close advice, information and listening, pharmacists involving oncology care **networks** will take a major place in at-home care. Coordination between different care structures can't be implemented without pharmacists, community as retailers. Especially, **coordination** between hospital pharmacist/ retail pharmacist/ GP / hospital doctor, and circulation of information are part of the conditions to improve **quality of care, at home and within the hospital**
- A specific funding mechanism is created for a list of drugs & facilities based on real cost for all institutions and all patients, but prescriptions & dispensations must comply with national recommendations, provided by INCA for cancer concerns, for best practices (e.g. centralised reconstitution) and proper use; **regulation through « Proper use contracts ».**

- In relation to proper use contracts, **inter-regional innovations prescriptions observatories OMIT** will soon be created over the country, first in cancer field (INCA pilot), in order to follow-up proper use and costs of cancer therapies, especially innovative ones.

4. SUPPORT: retail and community pharmacies can be a privileged place of listening and psychological assistance. They can also be considered as relays for national or local information on possibilities, methods and places where patients will find supports implemented within the cancer plan steps.

5. TEACHING: implementing initial and ongoing training specific in oncology for pharmacists is necessary to improve patients monitoring and proper use of medications, particularly within the facilitating at-home chemotherapy program.

6. UNDERSTANDING & DISCOVERING: In order to define the best benefit-risk and cost-benefit ratios frame of using innovative molecules, INCA will propose that post-AMM studies are undertaken, or formalize experts opinions regarding real conditions of use and patients concerned. All pharmacists, of course industrials, but also community, biologists, and retailers can be involved in research, particularly in pharmaco-epidemiology and costs-benefits studies. Indeed, their own unique databases on medications use, their skills and their proximity to patients can be used to assess effects, risks, observance and costs of medications in real situation.

For all these reasons, pharmacists are major stakeholders and must be involved in cancer nation-wide plan steps. They will take an important place among the health professional interlocutors, as well as intervention and information relays for the **new National Cancer Institute INCA.**

¹ Only a specific list of medications can be sold ("retroceded") to non-hospitalized patients by community pharmacists.

² Observatoires des médicaments et des innovations thérapeutiques

Oncology Pharmacist Point of View

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Oncology is one of the areas where the pharmacist has to participate actively in order to provide optimal drug therapy to the cancer patient.



Since the new mode of public and private hospital funding, all French hospitals have to conclude an agreement with the regional administration of health (ARH). This draft agreement called “proper use contract” intends to ensure the good use of oncology drugs and other very expensive drugs and medical devices. Hospital pharmacists are likely to play an important role in each of the parts of contract. The most important points of this contract are:

1. Drug use system:

In the field of this contract the quality assurance of the drug use system of hospitals became a priority. Computerization of this hospital drug use system process seems to be a

necessity for both patients and healthcare professionals. Accreditation reports or clinical practice survey are successful at identifying the weaknesses of the system. Hospitals have to explain their plan to establish corrective actions if necessary.

2. Multidisciplinary meeting and oncology care network

Treatment of cancer patients should be decided during a multidisciplinary meeting composed of one oncologist, surgeons, one therapy radiographer, several physicians and one pharmacist. Physicians and the pharmacist determine the drugs and dosage to be used and the schedule of the cure according to medical local or international consensus. Hospitals involving oncology care network help healthcare professionals improving patient management. Staff with physicians and pharmacist working in oncology care network benefited from teaching experience. Healthcare professionals from smaller centres felt more confident caring for cancer patients and checking chemotherapy orders, which they generally do infrequently.

3. Centralized handling of cytotoxic drugs

This part of the contract involves more specifically the pharmacist.

The aims of centralized handling of cytotoxic drugs are to enhance the quality of preparations and the security of technicians. The charges related to the central unit are generally balanced by

the reduction of the treatment cost.

4. Proper use of oncology drugs

For especially innovative and very expensive drugs (specific list of medication), physicians and pharmacist should explain their uses and choice, to obtain their financing. The French Drug Agency (AFSSAPS) designates proven indications as “labelled” and manufacturers are allowed to list labelled indications only if the drug efficacy has been demonstrated in clinical trials using their preparations.

Labelled indications are the base of medical prescription, but extra-labelled uses are possible if the drugs are mentioned for a number of diseases listed under “possible benefit”. In each hospital, Drugs and Sterile Medical Devices Committee (COMEDIMS) follow up the use of oncology drugs, especially extra-labelled indications, in order to explain their use to the ARH.

Hospital pharmacists are also likely to play an important role in improving the quality of care of at-home patients. Use of oral oncology drugs or drugs to increase cancer treatment’s tolerance, at home is more and more frequent thereby improving cancer patients’ quality of life and reducing public health costs. Coordination between hospital pharmacist and retail pharmacist is important to share professional experience and to avoid breaking in treatment.

Cytotoxic Drug Contamination on the Outside of Vials

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During the preparation and administration of cytotoxic drugs there are several events that may result in environmental contamination and exposure of pharmacy technicians and nurses.

In order to protect the workers handling antineoplastic agents, protective measures were taken and safety guidelines were developed. Cytotoxic drugs were prepared in isolators or in a clean room with laminar air flow and preparation procedures were improved. Despite of safety guidelines and standard protective measures, pharmacy technicians continue to be exposed to neoplastic agents. Several studies have shown that these agents were detected in the air and on work surfaces in drug

manufacturing areas, and administration area. It has been suggested that this level of contamination may be related to some level of contamination of the drugs vials delivered from manufacturers. In Sweden, Nygren¹ observed cisplatin contamination on the outside of drugs vials. The elevated platinum levels showed that the vials were most probably contaminated during the manufacture or packing process. Although the number of samples was limited, it indicates that contaminated drug vials may be delivered from manufacturers. In the United Kingdom, Mason² investigated the level of cytotoxic drug contamination on the external surfaces of drug vials (cisplatin, carboplatin, cyclophosphamide, ifosfamide and methotrexate). And a significant number

of vials had a quantifiable level of external contamination.

A study was carried out about chemical contamination in isolators in France in two hospital pharmacies³. About outside isolator, in one pharmacy, a contamination was observed on the surface of the table used for entrance of the drugs. No more contamination was found on this location after usual cleaning (isopropyl alcohol) and after special cleaning (tensio-active detergent). In the other pharmacy, only worktop and floor were contaminated. Both locations are on the entrance way of cytotoxic drugs. The authors explained contamination could be due to the external contamination of vials and the possibility of spreading contamination during the removal of the « flip off » of the vials.

A Day in the Life of a Quality Control Pharmacist or Microbial Contamination Monitoring in the Cytotoxic Drug Preparation Unit of Saint-Denis Hospital

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Cytotoxic drug preparation requires several steps and each step involves different personnel of the pharmacy of the Saint-Denis hospital

One person attends to cleaning installations, the sterilization unit prepares reconstitution kits, and the operator and the assistant operator validate cytotoxic drug prescriptions and then prepare them in the clean room. But pharmacists and personnel of the cytotoxic drug preparation unit are not the only persons involved in this work. Pharmacist and technicians of the control laboratory also have a role in the quality of the work practice, by monitoring microbial contamination during the preparation. This last step of control has been established in order to evaluate the work practice in the cytotoxic drug preparation unit. Cytotoxic drug preparations in the Saint-Denis hospital are made in condition of asepsis: the operator and the assistant operator work in a low pressure room, the preparation is made under a laminar air flow, the operator and the assistant operator wear sterile clothes (disposable gowns), mask, gloves, they have a surgical cleaning of hands before entering the clean room and the installation is cleaned every day and decontaminated every week. All of these conditions are specified in



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described procedures and are strictly applied so as to avoid contamination.

The microbial contamination monitoring permits to evaluate asepsis quality of the clean room and the laminar air flow. It also permits to detect technical problems or dysfunction in the application of cleaning or preparation process.

Every day, before and after preparation, the pharmacist of the control laboratory takes on culture medium surface and air sampling:

- air samplings are taken under the laminar air flow on a RCS High low (Biotest), a microbial air sampler which impacts onto an Agar media strip by centrifugal force
- Surface samplings are taken by contact plates of Agar Tryptic Soy + LTH (Biotest) on the work areas of the operator and the assistant operator.
- Gloves samplings of operator and assistant operator are taken on

contact plates of Blood sheep Agar 5% (Biotest) at the end of the manipulation.

Culture media are incubated 48h at 35°C then 48h at room temperature. The pharmacist gives the results by comparison with maximum acceptable levels (value in number of UFC per plate).

An increase of the number of bacteria colony up to the limit established values permits to detect any dysfunction in cleaning or manipulation and to correct the work practice.

For example, a three-year study on microbial contamination monitoring was made from 2001 to 2003 in the cytotoxic drug preparation unit of the Saint-Denis hospital. Analysis included 649 days of cytotoxic drug preparation and the interpretation of the results showed that positive microbial controls often happened when a new operator or assistant operator started to work. This monitoring also permitted to detect technical problems which occurred in the summer 2003.

A contamination assessment program helped to create awareness among personnel involved in cytotoxic drug preparation. It also permits very fast reaction after a potential problem of microbial contamination. Moreover, the knowledge of surface contamination needs to be detailed to develop corrective actions such as revision of aseptic technique and personnel training.

Cytotoxic drug contamination on the outside of vials

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Connor⁴ and Sessink realized three studies, two in the United States, and a third one in the Netherlands. They demonstrated that surface contamination of commercially available drug vials was detected with cyclophosphamide, ifosfamide and fluorouracil (sporadic contamination). It showed the possibility to reduce the contamination of drugs vials with cisplatin using decontamination equipment and sleeve (monoaxial, stretched, high-shrink polyethylene terephthalate film) protection of vials during the manufacturing process. The results of these studies show that

surface contamination exists in Europe and in the United States.

We must carry on developing safety guidelines about workers who handle vials. They must have appropriate personal protection to receive, control or distribute drug vials or packages. If the outside of vials is contaminated, contamination is also on the inside of the drug carton. The drug carton should be thrown like contaminated waste material.

In order to improve this situation, to limit chemical contamination anywhere, manufacturers should deliver clean vials. Some manufacturers have started to assess drug packaging.

¹ Nygren O, Gustavsson B, Ström L, Friberg A. Cisplatin contamination observed on the outside of drug vials. *Ann occup Hyg.* 2002;46(6) : 555-7.

² Masson HJ, Morton J, Garfitt SJ, Iqbal S, Jones K. Cytotoxic drug contamination on the outside of vials delivered to a hospital pharmacy. *Ann Occup Hyg.* 2003 ;47(8) :681-5.

³ Crauste-Manciet S, Sessink PJM, Ferrari S, Jomier JY, Brossard D. Studies chemical contamination in isolators in France. *Gerpac* 6-8 octobre 2004, Presqu'île de Giens.

⁴ Connor TH, Sessink PJ, Harrison BR, Pretty JR, Peters BG, Alfaro Rm, Bilos A, Beckmann G, Bing MR, Anderson LM, Dechristoforo R. Surface contamination of chemotherapy drugs vials and evaluation of new vial-cleaning techniques : results of three studies. *Am J Health Pharm.* 2005 ;62(5) :475-84.

A Day in the Day Ward or How we take care of cancer patients at the Saint-Denis' Hospital

When a new patient is admitted at the Saint-Denis Hospital for the treatment of a cancer, his medical history is studied during the weekly multidisciplinary meeting, each Thursday. This meeting is composed of an oncologist, a radiographer, an anatomical pathologist, surgeons, several physicians and a pharmacist. These experts decide on the treatment of their patient (surgery, radiotherapy, chemotherapy or other treatment). If chemotherapy is necessary, the physicians and the pharmacist determine the drugs and doses to be used with already published protocols. Moreover, they plan the schedule of the first cure. The first cure is generally realised during several days at the hospital in order to check the tolerance of the treatment. Afterwards, the patient can be hospitalised only for the day in the day ward and go back home in the evening. Thus, this kind of care-taking improves the quality of life of the patient.

Before the beginning of the treatment, the patient consults with the oncologist who explains to him chemotherapy and the possible side effects. Then, the oncologist writes the prescription.

After that, the pharmacist's task consists in validating this prescription i.e. drugs' associations, doses, drugs' compatibility and the duration of administration. The pharmacist with the aid of a pharmacist assistant makes out preparation sheets.

Hereafter, a typical day in the day ward:

At first, the patient is admitted in the day ward. A physician examines the patient, checks his pulse, his blood-pressure and his temperature. Thereafter, a blood test and an x-ray photography (to check the position of the central catheter) are realised before all treatment.

Then, the physician checks the results of the blood test and analyses the x-ray photography.

If the results are well, the chemotherapy can be made. In that case, a state registered nurse informs



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the pharmacy to prepare the chemotherapy. Sometimes, it is necessary to modify dosage or cancel the cure.

The preparation is realised in the centralized unit of cytotoxic reconstitution. This is a clean room with laminar flow boxes. This room is sterilized and offers a high security level for the technician. The technician always works with an assistant who controls each preparation. In the meantime, before the chemotherapy, the state registered nurse gives the patient special drugs in order to increase the treatment tolerance: antiemetics, corticoids, hyperhydration and other drugs if the chemotherapy induces other side effects.

Later, when the preparation is ready, a nurse's aid of the day ward goes to the pharmacy with a special box to carry the chemotherapy in safe conditions.

The state registered nurse checks the conformity of the chemotherapy before the administration. Then, the administration consists only in connecting the solution (bag or syringe) with the infusion system or the perfusor, which was previously filled with physiological solution. The chemotherapy can be administered during a few hours thanks to an infusor. So, the patient can go back home with the system. At the end, when the chemotherapy has been administered, the vein must be rinsed with physiological solution.

Before the end of the hospitalisation, the physician or the state registered nurse advises the patient on what he should do in case there were any complications. The physician writes a prescription with growth factors and/or antibiotics.

