Masterclass 2013 Meeting Report

Standards

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Knowledge and progress – on the importance of multi-professional collaboration

In 2003, ESOP became a member of the European movement against cancer. At first the organization was named FECS (Federation of European Cancer Societies) and then ECCO (the European CanCer Organisation).

Nurses and physicians from different disciplines worked together. They understood that learning never ends and that the exchange of knowledge would bring benefit into the treatment of cancer.

One of its members, the European School of Oncology (ESO), was founded by Professor Umberto Veronesi and Laudomia Del Drago in 1982, with the aim of contributing to the reduction of deaths from cancer due to late diagnosis and/or inadequate treatment. Leading oncologists from around the world played a key role in the founding of this school.

Taught by these impressions, ESOP understood that an educational programme for establishing a specialization for its members would be necessary.

In countries like Germany and the UK, a postgraduate programme was intalled. But for the smaller European countries ESOP decided to build a European course. Since 2007, a Masterclass of 40 hours for basic and intermediate oncology pharmacy was installed yearly. In addition, ESOP and ESO discussed to hold a 40-hour Advanced Masterclass to widen the knowledge of oncology pharmacists specially in relation to therapeutic and patient-related demands.

Klaus Meier
ESOP President

EJOP

In 2013, it happened, and the first Advanced Masterclass started. In this publication project, we collected impressions and teaching contents in order to show the progress, and to advertise the great collaboration which was mostly possible through the support and grant from ESO.

After this great success everybody understands that in the future we will be able to promote high-level education within multi-professional collaboration.

A special thank you to all lecturers and also the participants who have made this first event an adventure.

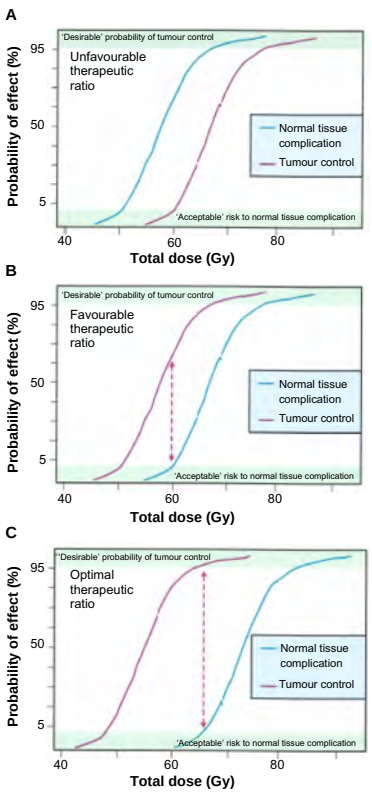
For more information, please visit the link below:
http://www.eso.net/events-2.html?e=ESOP-ESO_Advanced_Masterclass_in_Oncology_Pharmacy

Radiotherapy – principles and use in oncology

The most radiation sensitive part is the DNA with its double-helix. The ionizing radiation leads to breaks, partially to double-strand breaks whereby the former can be repaired, however the latter usually not. There are two types of biological cell deaths: on the one hand the necrosis, which begins relatively fast especially at high doses and on the other hand the so-called apoptosis. Here the cell divides several times more until the ability of cell division is abandoned due to the damage. Apart from the cell death there are also sub-lethal damages such as genetic mutations. The effect of rays depends on their quality, dose, fractionation, oxygen content, and temperature. These effects are measured by means of cell cultures whereby the cell number and doses are applied semi-logarithmically against each other.

Professor Dr med Wolfgang Wagner, MD, PhD

Figure 1: Holthusen-Graphs: the corridor between optimal tumour control and optimal protection of the normal tissue

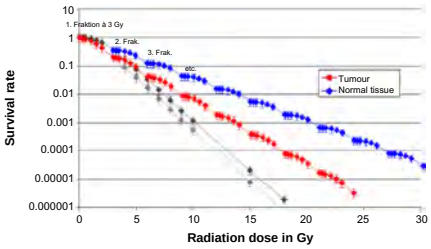


The graphs illustrate the concept of therapeutic ratio under conditions in which the relationship between the normal tissue tolerance and tumour control dose-response.
(**A**) curves are unfavourable; (**B**) favourable; (**C**) optimal.

The radiation effect depends from the cell cycle phase because cells within the mitosis – phase react in the most radiation-sensitive way.

Therapeutically different therapy regimen for different tumours are applied which means different radiation rhythms. It is distinguished between conventional radiotherapy and multiple radiations per day respectively a one-time radiation (radio-surgery). The radiotherapy can cause somatic and genetic damages. The application of 1 Sievert [Sv] increases purely mathematically the cancer mortality rate of 5%.

Figure 2: Fractionation 'extends' the corridor between tumour damage and normal tissue damage



Radiotherapy can produce cancer and can cure cancer. It is our challenge to treat the patient in an optimal way so that he will get a high chance of cure without severe late damage of the surrounding tissue.

Figure 1 shows the relationship between optimal tumour control and low risk of damage to the normal tissue.

Figure 2 demonstrates the diversity of tumour cells and of normal tissue; because of fractionation normal cell damage can be repaired by enzymes. Normal tissue recovers faster from radiation damages because of intact enzyme systems.

Interview

Where do you come from and where do you practise?
I come from Germany and I am working in Osnabrück.

How did you start this profession and why did you choose it?
I studied radiotherapy since the 1980s. I like this profession because for me, it is the most interesting job in the world.

What do you think about the past, present and future of oncology and input of oncology pharmacy?
We will go further in small steps but nowadays we are able to cure about 60% of the patients. Oncology pharmacy does a good job in helping and aiding oncologists.

Where do you see yourself in the development of ESOP and clinical pharmacy practice?
I am active in working on EJOP, and relatively often give talks at oncology pharmacy conferences.

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Epidemiology of carcinogenic factors influencing cancer development

Cancer statistics: the five most prevalent cancers

The five most prevalent cancers in men are lung, prostate, colorectal, stomach and liver cancers. In women, cancers of the breast, colorectum, cervix/uterus, lung and stomach are most prevalent. In both men and women, cancers of the lung, breast, colorectum, stomach and prostate are most prevalent. This data is generally worldwide, and in the whole group of population, without dividing countries and ages.

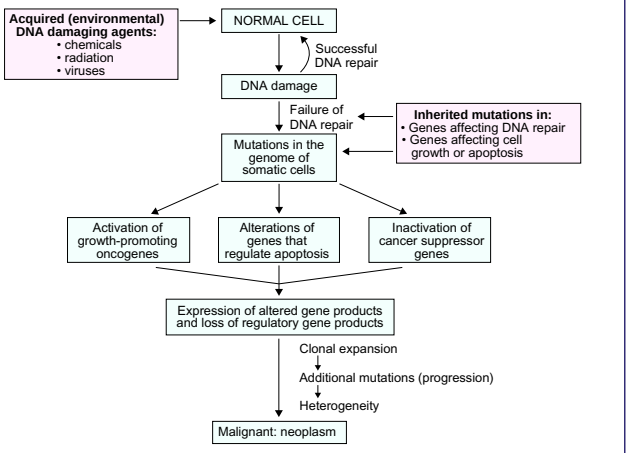
Joanna Stanislawiak-Rudowicz, MD, PhD

Lung cancer is one of the biggest public health problems in Europe, with tobacco as the risk factor. The incidence of colon cancer is growing in populations undergoing economic growth. The incidence of prostate cancer is growing in an ageing population in Europe. Breast cancer is the leading cause of death for women in Europe, with risk factors including genetic factors (10%), sex, age, previous breast cancer, family history, fibrocystic disease, ionizing radiation, hormonal aspects, body mass index (BMI).

There is great variation in the incidence of cervical cancer and mortality due to differing availability of screening programmes. The risk factor is human papilloma virus (HPV), with HPV 6 and HPV 18 mostly, and it is hoped that HPV vaccination will decrease incidence.

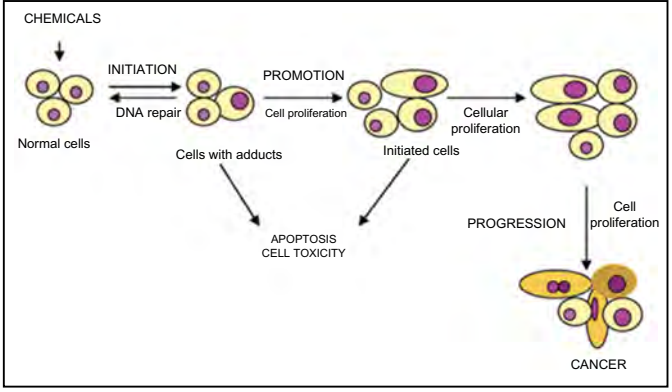
The risk factors for all cancers are:
- Genetics
- Nutrition
- Obesity
- Physical inactivity
- Hormones
- Environment-related factors: air pollution, radon, electromagnetic fields, ultra violet radiation, arsenic
- Viruses: hepatitis B virus, human papilloma virus, Epstein-Barr virus
- Smoking

Figure 1: The relationship between optimal tumour control and low risk of damage to the normal tissue



DNA: deoxyribonucleic acid.

Figure 2: Chemical carcinogenesis stages



Interview

Where do you come from and where do you practise?
University Hospital, Poznań, Poland

How did you start this profession and what is the reason you choose this profession?
I specialize in medical oncology. I participated in the oncology masterclass for medical students in Berlin, Germany in 2006, that was the moment I decided to specialize in oncology.

What do you think about the past, present and future of oncology pharmacy?
Oncology is a branch of medicine that is developing quickly, and cannot exist without pharmacy. It was thought many years ago that cancer patients could be cured but nowadays cancer is considered a chronic disease and everyone should have a chance to get treatment (no matter if they have diabetes mellitus or AIDS).

Where do you see yourself in the development of ESOP and clinical pharmacy practice?
It is important to develop comunication between doctors and pharmacies to understand both sides' point of view.

To continue on page 23.

Diagnosis and treatment: head and neck cancer

Head and neck cancer (HNC) refers to malignant tumours of the nasopharynx, nose, paranasal sinuses, mouth cavity, pharynx, larynx, lips, skin, salivary glands, thyroid gland, and soft tissue. Head and neck cancers are mostly squamous cell carcinomas – head and neck squamous cell carcinoma (HNSCC) – with high risk of lymphatic spread. They are strongly associated with certain environmental and lifestyle risk factors.

Professor Dr med Sven Koscielny, MD, PhD, MHBA

Many problems exist for the therapy of HNSCC:
1. ≥ 65% are diagnosed at an advanced stage
2. Most patients have notable co-morbid illnesses
3. Most patients have a poor social/cultural environment (poor quality of life [QoL] before treatment)
4. Most cases will require heavy combined therapies (leading to poor tolerance/compliance to therapy)
5. Many patients will relapse

Therapeutic options for HNSCC

Our first choice is surgery with or without post-operative radio- or radiochemotherapy. The indication to the postoperative radiotherapy depend on extension of tumour and lymph node metastasis. Radiochemotherapy is applicable in cases without possibility of operation. In palliative cases, we used a combination chemotherapy.

Figure 1: Risk factor for developing a head and neck squamous cell carcinoma (HNSCC)

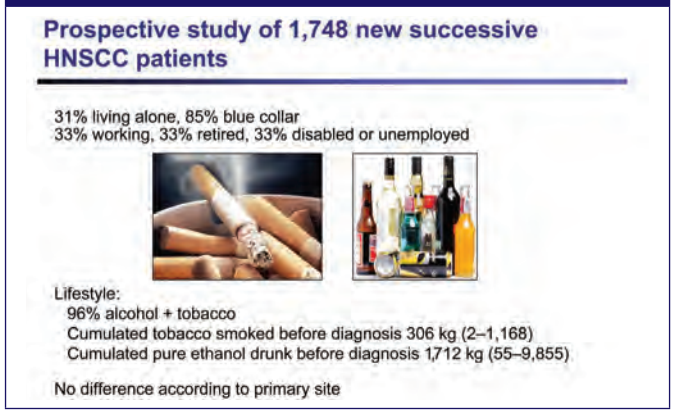


Figure 2: Chemo and antibody therapy

Interview

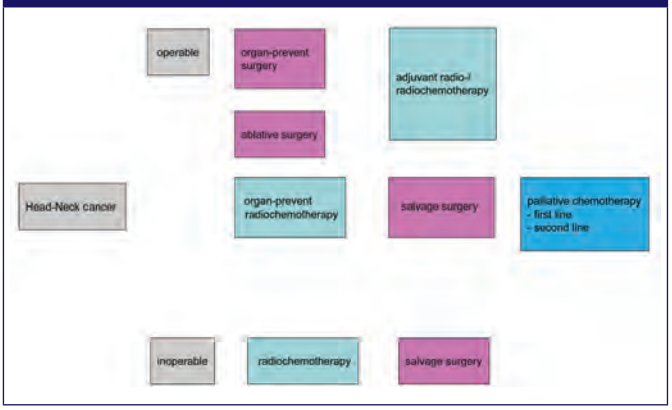
Where do you come from and where do you practise?

I come from Jena and I practise in the University Hospital of Jena.

How did you start this profession and why did you choose it?

I started training in 1989 and became a specialist in 1993. Today, I am the Vice Head of the Department of Otorhinolaryngology. I am very interested in tumour therapy.

Figure 3: Therapy flowchart for head and neck squamous cell carcinoma



What do you think about the past, present and future of oncology and input of oncology pharmacy?

I think today we have the possibility to get balance between the quality of life of the patient after therapy and the functional deficit for the patients quality of life after therapy in long time follow up. I hope we can get better chemotherapy and better concepts for combination therapy to get better survival for the patient. Because the survival rate has not changed in the past 50 years, it is nearly the same as it was in the 1950s.

What are the highlights of your topic?

Patients with head and neck cancer should come to the doctor earlier in order to get a better prognosis. Pharmacists should send patients with early symptoms to a doctor.

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Diagnosis and treatment: ovarian cancer

The majority of ovarian malignancies derive from epithelial cells; the remainder from other ovarian cell types, 75% of ovarian cancers are diagnosed at an advanced stage.

If diagnosis is made early in the disease and treatment is received before the cancer spreads outside the ovary, the 5-year survival rate is very high (FIGO stage I/II 80–90% stage III/IV 15–45%).

Donata Grimm, MD

Surgery is used to treat all stages of ovarian cancer, but is particularly crucial for the prognosis of patients with advanced disease. As these patients have a good prognosis, perioperative morbidity is the critical point for decision-making when the treatment strategy is developed and the primary surgical approach is defined. Patients should be treated in a gynaecologic cancer centre specializing in ovarian cancer. Surgery is followed by adjuvant chemotherapy. Anti-angiogenesis therapy in ovarian cancer can further improve patients' outcome. Bevacizumab is an important angiogenesis inhibitor in the primary treatment of ovarian cancer. Since December 2011, patients with FIGO stage IIIB, IIIC and IV ovarian cancers have been given six cycles of carboplatin + paclitaxel and bevacizumab (15 mg/kg) maintenance for 15 months.

Diagnostics and treatment: cervical cancer

Bevacizumab was the first targeted agent to improve overall survival (OS) in gynaecologic cancer, and treatment with bevacizumab is not accompanied by a decrease in quality of life (QoL). A combination of cituximab incorporated with anti-VEGF is a novel therapeutic approach. Gynecologic Oncology Group (GOG) 240 interim analysis showed Bevacizumab plus CTX

To continue on page 21.

Figure 1: Prognostic factors of ovarian carcinoma

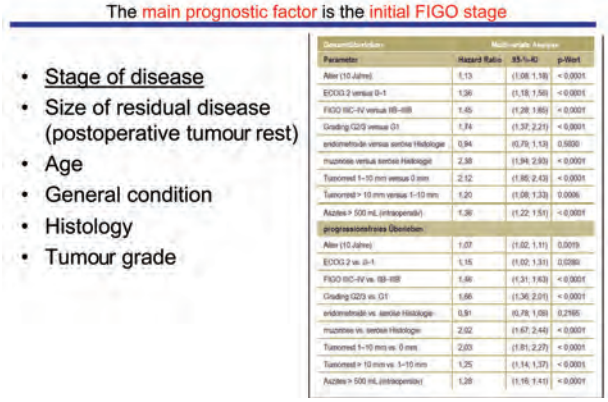


Figure 2: Therapy for epithelial ovarian cancer

Category of OC based on surgical staging	Recommended (standard) therapy
Early OC	
Low risk (stages IA, G1)	Total abdominal hysterectomy (TAH), bilateral salpingo-oophorectomy (BSO), staging
High risk (stages IA and IB, G2, G3; stages IC, IIA, IIB, and IIC, no residual)	TAH, BSO, staging, adjuvant therapy with a combination of carboplatin and paclitaxel or carboplatin mono
Advanced OC	
Stage III/IV	Maximal surgical cytoreduction, CTX

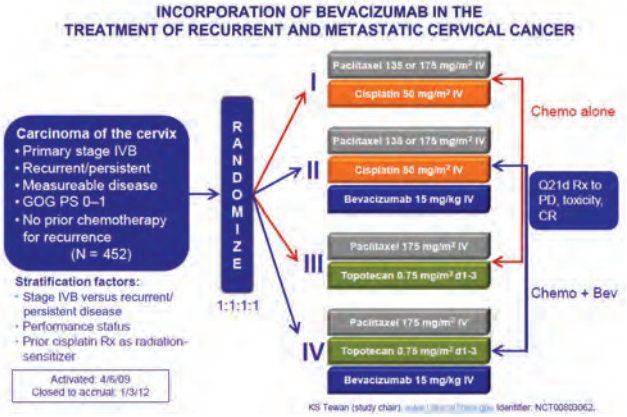
OC: ovarian cancer.

Figure 3: GOG 240: Demographics and baseline characteristics

Characteristic	Chemo Alone (n = 225), %	Chemo + Bev (n=227), %
Median age, years (range)	46 (20–83)	48 (22–85)
Histology, %		
Squamous	68	70
AdenoCa, unspec.	20	19
Race, %		
White	80	75
African American	11	16
Asian	3	5
Pacific Islander	0	0
Stage of disease, %		
Recurrent	73	70
Persistent	10	12
Advanced	16	17
Performance status, %		
0	58	58
1	42	42
Prior platinum, %	74	75
Pelvic disease, %	53	54

KS. Tewari, et al. J Clin Oncol 31, 2013 (suppl; abstr 3)

Figure 4: GOG 240: Schema



CR: computed radiography.

Diagnosis and treatment: gastric cancer and colorectal cancer

Progress against colorectal cancer: Flexible sigmoidoscopy and colonoscopy led to earlier detection of precancerous polyps and surgically curable colorectal cancer.

Local or loco-regional rectal cancer: Total excision of the mesorectum reduced significantly the rate of recurrences. It is now the standard surgical procedure to remove rectal cancer. 5-flourouracil (5FU) with radiation after surgery is the standard adjuvant treatment.

Local or loco-regional colon cancer: Oxaliplatin combined with 5FU and folinic acid (FOLFOX) is the standard adjuvant chemotherapy combination, reducing significantly the rate of local recurrences and metastatic disease.

Diagnosis and treatment: Esophageal and esophagogastric junction cancer

Gastric adenocarcinoma: Surgical removal of the complete tumour with resection of adjacent lymph nodes offers the only chance for cure.

Gastric adenocarcinoma is a relatively radioresistant tumour.

Professor Dr med Günther J Wiedemann, MD, PhD

Figure 1: Colorectal cancer: stage IV

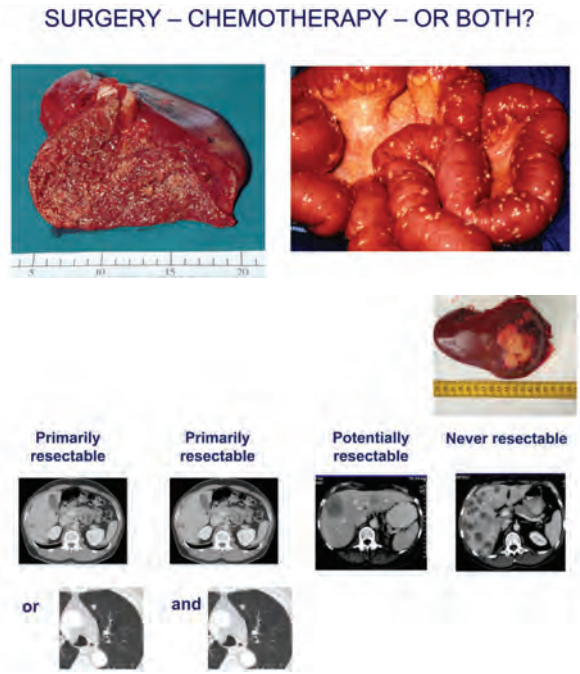


Figure 2: Metastatic colorectal carcinoma: 'limited metastatic disease' can be cured by surgical resection

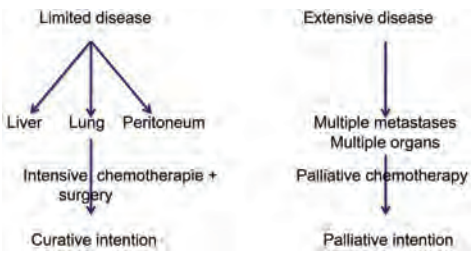
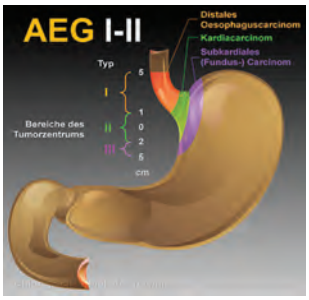
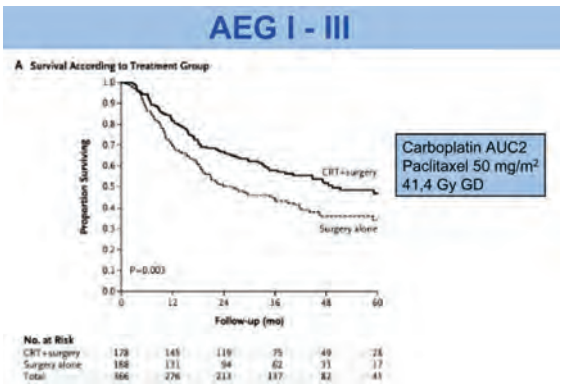


Figure 3: Adenocarcinoma of the oesophagus and gastro-oesophageal junction





The administration of combinations of cytotoxic drugs neoadjuvantely and/or adjuvantely has been associated with tumour reductions of greater than 50 per cent.

Interview

Where do you come from and where do you practise?
Internal Medicine Specialist. Specialist in Laboratory Medicine. Specialist in Oncology and Palliative Therapy. Oberschwabenklinik in Ravensburg, Germany.

How did you start this profession and why did you choose it?
Because of my interest in essentially working with people.

What do you think about the past, present and future of oncology and input of oncology pharmacy?
Impressive progress; increasing problems, increasing demand of contacts with patient, decreasing economical possibilities. Teamwork pharmacist <-----> physician.

What are the highlights of your topics?
Quality management of applying cytotoxic drugs.

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Diagnosis and treatment: urologic neoplasms

Professor Michael Fröhner, MD

Urological cancers represent a large proportion of malignant diseases, particularly in men. With early detection, most cases can be cured. In advanced disease, high cure rates are only seen in testicular germ cell tumours, of which 40–50% of patients are curable even in the most advanced metastatic stages, see Figure 1. The question of screening (or early detection) of prostate cancer, and optimal management when this tumour is diagnosed, is still controversial. Prostate cancer screening will undoubtedly save lives, but it is still unknown whether over-detection and impairment of quality of life caused by treatment outweigh the benefits of screening. Surgery for advanced renal cell carcinoma may be challenging, and thoracotomy may be needed. Cardiac arrest may be required in some cases, with tumour thrombi extending into the right cardiac atrium, see Figure 2. Bladder substitution by ileum neobladder formation is another challenging field in genitourinary surgery, see Figure 3. In recent years, several new and promising medical treatment options have become available for the systemic treatment of metastatic renal cell carcinoma and castration-resistant prostate cancer. Although these substances may prolong life by several months, cure is still unlikely in these advanced-staged tumours. Further research is needed on the optimal sequence of these new drugs and on the timing of treatment.

Figure 1: Lung metastases in a patient with advanced testicular germ cell tumour

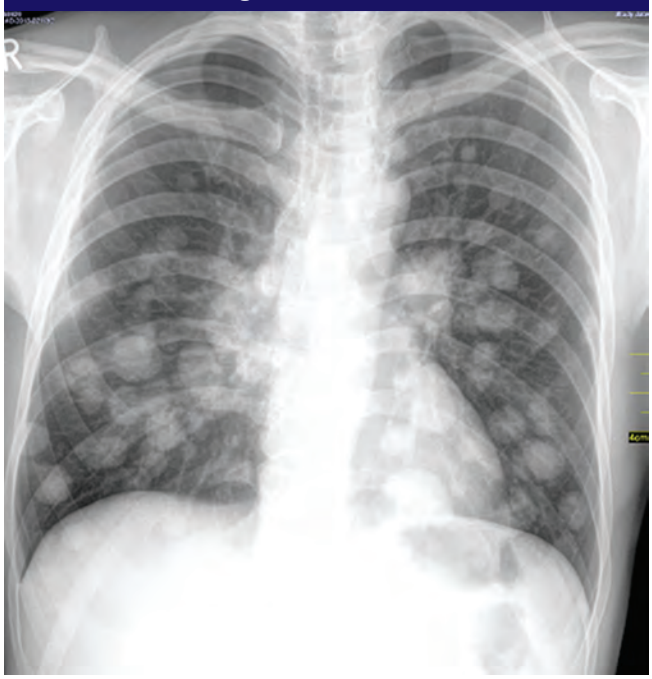
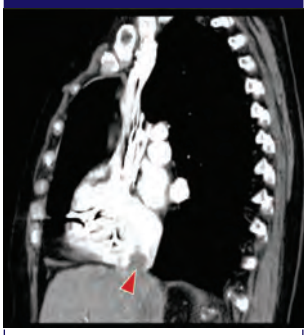
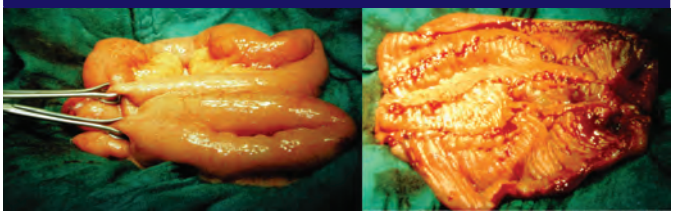


Figure 2: Renal tumour with tumour thrombus



Renal tumour with tumour thrombus reaching the right cardiac atrium, female, 76 years, liver cirrhosis.

Figure 3: Bladder cancer: bladder substitution by ileum neobladder



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Diagnosis and treatment: breast cancer

Gender and age are very important risk factors for breast cancer. The percentage of hereditary breast cancers is less than 15%. Women with mutations of the tumour suppressor genes BRCA1 and BRCA2 have a considerable high risk of developing breast cancer. These cancer types occur mainly in younger patients. Breast cancer prevention is possible by increased physical activity, avoiding overweight, and by special antihormonal drugs (Tamoxifen, aromatase inhibitors).

Professor Dr med Kurt Possinger, MD, PhD

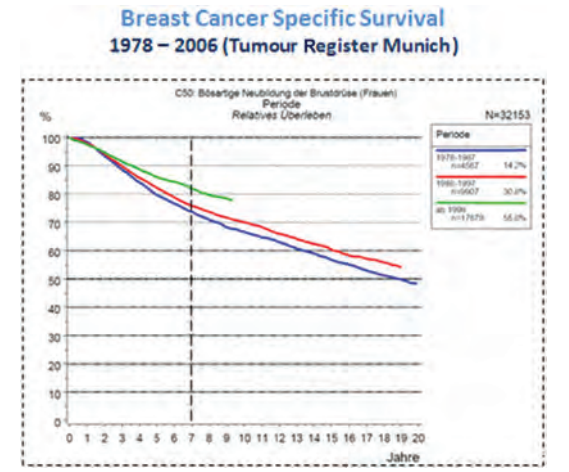
At present we discriminate between four types of breast cancer (luminal A, luminal B, HER2, basal-type). They differ both at prognosis and response to medical treatment:

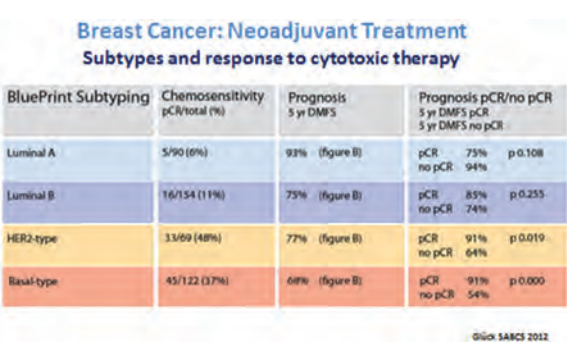
- Luminal-A and B-tumours are characterized by their synthesis of steroidal hormone receptor, oestrogen receptor (ER), progesterone receptor (PR). Selective oestrogen receptor modulators like tamoxifen block the activation of these receptors. Aromatase inhibitors (letrozole, anastrozole, exemestane) and gonadotropin-releasing analogues (GnRH-A) like goserelin suppress the production of the activating ligand estradiol. GnRH-A are effective in premenopausal, aromatase inhibitors in postmenopausal patients
- HER2-tumours synthesize HER2-receptors. These receptors need no activation by a ligand and continuously stimulate the proliferation of the tumour cells. Drugs like trastuzumab and pertuzumab inhibit the receptor activation.
- Basal-type tumours are very proliferative, active and express neither steroidal nor growth factor receptors (so-called triple negative tumours). They respond especially to cytotoxic drugs.

The choice of the individual treatment depends on tumour type, size, lymph node involvement, histologic grading, and the receptor status.

The chance to survive breast cancer improved significantly during the last years.

Figure 1: Improvement of breast cancer specific survival by early detection, (neo)adjuvant therapy





Interview

Can you introduce yourself briefly?

I started my medical career at the University Hospital in Munich, and was then appointed to Chairman and Director of the Department of Medical Oncology and Haematology of the University Hospital 'Charite' in Berlin. In June 2013, I retired and now live in Bavaria.

How did you start this profession and why did you choose it?

I started my profession as a medical doctor because my Latin professor persuaded me, and I looked for a combination of research and treatment of patients.

What do you think about the past, present and future of oncology and oncology pharmacy?

At present we live in a very interesting and very stimulating time. Day by day we learn more and more facts about the tumour cell biology and find ways to block very specific cellular growth pathways. I think that in the next 10–20 years the treatment modalities of breast cancer will dramatically change.

Where do you see yourself in the development of ESOP and oncology pharmacy?

I think that we have a considerable knowledge deficit about the interaction of drugs, and in this situation pharmacy can help us foresee favourable and unfavourable treatment situations.

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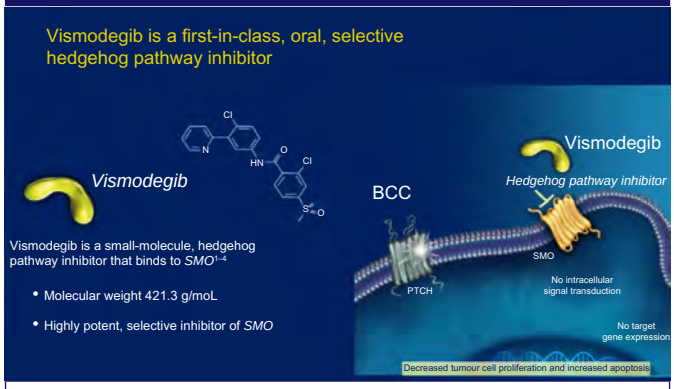
Diagnosis and treatment: non-melanoma skin cancers and melanoma

The take-home message from these two talks on non-melanoma and melanoma skin cancer is that a variety of effective drugs are available to treat actinic keratosis. A new drug Erivedge (vismodegib) was approved in the US in February 2012, and in Europe in July 2013, for the treatment of basal cell carcinoma. This is a highly effective drug but we must learn how to use it to avoid the many side effects and prevent poor compliance.

Dr med Peter Mohr, MD PhD

In melanoma treatment, adjuvant interferon significantly improves disease-free survival and, in some prospective randomized trials, overall survival [1]. New drugs for metastatic melanomas have been approved in the last years. Yervoy (ipilimumab) is a monoclonal antibody that antagonizes cytotoxic T lymphocyte antigen-4, a negative regulator of the immune system. Other drugs, such as the BRAF-Inhibitor, Vemurafinib (Roche) and BRAF- + MEK-Inhibitor (Dabrafenib + Trametenib) (GSK) are currently undergoing adjuvant phase III trials in melanoma.

Figure 1: Erivedge (vismodegib) inhibitor in advanced basal cell carcinoma: STEVIE study interim analysis in 300 patients*



*presented as a poster at ASCO 2013.

Figure 2: Result of treatment of large basal cell carcinoma lesion with Erivedge (visomodegib)

Interview

How did you start this profession and why did you choose it?

I started way back in 1990 and the reason was that we had a very talented professor who was giving excellent lectures in dermatology. We could see a lot of patients in his lessons. Live pictures of the dermatologic lessons were projected in the whole room. His lecture was usually on Friday morning at 8 o'clock and the lecture was always completely packed. He was a charismatic, fascinating man, and I thought dermatology was the field of my interest.

What do you think about the past, present and future of oncology and input of oncology pharmacy?

We are now in a very unique time because we have had a lot of basic research within the last 10, 20 years. Now we have new, effective drugs in targeted therapy as well as in immuno therapy, and I think these two fields will be the fields of the future. The most interesting part will be to combine the targeted therapy agents so that patients can tolerate them and to develop and combine new immunological drugs in cancer.

Where do you see yourself in the development of ESOP and oncology pharmacy?

This is my first time here at ESOP, and I think it is a great honour and a pleasure to give a lecture here. It is a good development that pharmacists and medical doctors are coming together because there is a high need of collaboration especially regarding side effect management and the combination with non-oncology drugs. In many cases, the treating physicians have difficulties with the drug interactions, so we need the pharmacists to assist us for the safety of our patients.

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Reference

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Diagnosis and treatment: soft tissue sarcoma

Professor Dr med Peter Reichardt MD, PhD

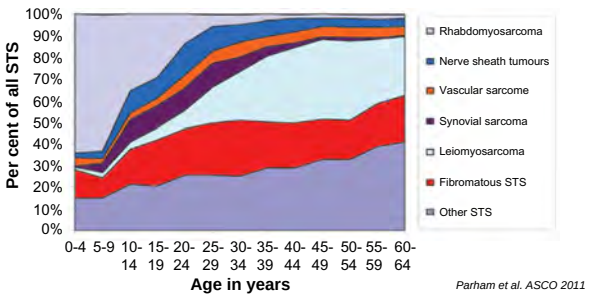
Soft tissue sarcomas consist of more than 70 different histological subtypes. Altogether, they are rare tumours, with an incidence of 4–5 per 100,000, representing about 1% of all adult cancers with equal gender distribution. The prognosis depends on several factors, including the patient's age and performance status, histological type, size, and grade of the tumour. About 10% of patients present with metastatic disease at the time of diagnosis, whereas 40–60% of patients with localized, high-grade soft tissue sarcoma will develop metastases predominantly in the lungs, despite local control of the tumour. Median survival from time of diagnosis of metastatic disease has been reported to be around 12 months.

Complete surgical removal followed by radiotherapy is the gold standard for the treatment of localized resectable soft tissue sarcomas. Where preservation of function is not possible, preoperative treatment should be considered. Options are isolated limb perfusion for unresectable sarcomas of the extremities, regional hyperthermia in conjunction with chemotherapy or radiotherapy, and chemotherapy or radiotherapy given alone.

Only a few drugs have shown single-agent activity and gained approval in this indication, including doxorubicin, epirubicin, ifosfamide, dacarbazine, trabectedin, and, recently, pazopanib. Combination chemotherapy has improved both response rate and progression-free survival compared with single-agent therapy without affecting overall survival in first-line therapy.

Although adult soft tissue sarcomas have been treated uniformly until recently, new strategies aim to develop specific treatment modalities for well-defined subgroups of sarcomas.

Figure 1: Individual sarcoma histologies as proportion of all soft tissue sarcoma



Individual sarcoma histologies as proportion of all soft tissue sarcoma by age according to surveillance, epidemiology and end results (SEER) data, 1975–1999.

Figure 2: Systemic therapy

Classical active agents:

- Anthracyclines, ifosfamide, DTIC

More recent agents:

- Trabectedin, pazopanib

Unregistered agents:

- Gemcitabine, docetaxel, trofosfamide, temozolomide

Figure 3: Soft tissue sarcoma – subtype-specific treatment

- Combination chemotherapy with curative intent
- Infosfamide in synovial sarcoma
- Trofosfamide in elderly/unfit patients
- Paclitaxel in angiosarcoma
- Hormonal therapy in endometrial stromal sarcoma of uterus
- Gemcitabin/docetaxel in leiomyosarcoma (uterus)
- Trabectedin in leiomyosarcoma and liposarcomas
- Trabectedin, sunitinib, everolimus and cediranib in ASPS
- Topo I – inhibitors in rhabdomyosarkoma and ewing tumours
- Imatinib in GIST/DFSP
- Sorafenib in angiosarcoma
- mTOR inhibitors in PEComa
- Crizotinib in inflammatory myofibroblastic tumour associated with ALK translacations
- IGF1RAB in ewing tumours

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Treatment of oncology patients with organ dysfunction: renal and liver impairment

Dose modification in the case of renal dysfunction

Accurate dose modification in the case of renal impairment is a great challenge when cancer patients receive cytotoxic drugs that are primarily excreted in active form through the kidneys. Commonly, mathematical glomerular filtration rate (GFR) calculation is preferred in routine practice, however, significant under- and overestimation of the real situation has to be expected by most formulas in the lower and higher constitutive GFR range, respectively. This background of experience has to be kept in mind when Carboplatin dose individualization is calculated by the Calvert formula: Carboplatin dose [mg] = AUC × (GFR + 25). As a consequence, the use of AUC = 4 mg × min/mL may be associated with subtherapeutic Carboplatin levels in case of an inaccurate mathematical GFR calculation. On the other hand, absolute Carboplatin dose should be limited to 900 mg in case of AUC = 6 mg × min/mL, because calculated GFR values should not exceed 125 mL/min.

Professor Hans-Peter Lipp PharmD, PhD

Different GFR calculation formulas are used in everyday clinical practice. However, there is significant over- and underestimation of the real situation, see Table 1.

Dose modification in case of hepatic dysfunction

Most orally available tyrosine kinase inhibitors (TKI) as well as selected cytotoxic drugs, e.g. vincristine, undergo extensive metabolic degradation within hepatic and extrahepatic tissues mainly mediated by Cytochrome P450 isozymes, followed by biliary and faecal drug excretion.

Compared with GFR-based recommendations in case of renal dysfunction, accurate dose modification in patients with hepatic dysfunction receiving, e.g. dasatinib is far more complicated. Child Pugh Scores which have been derived from patients with liver cirrhosis can only roughly reflect individual Cyp3A activity and are primarily recommended for regulatory reasons. However, Cyp isozyme-based phenotyping has not yet been established. In the case of hyperbilirubinemia, one has to consider biliary obstruction as a reason that necessitates dose modification in case of conventional anthracyclines or irinotecan.

Accurate assessment of metabolic clearance in the case of liver dysfunction is very difficult despite parameters like the Child-Pugh or MELD Score, see Table 2.

Interview

Where do you come from and where do you practise?

I live near Tübingen, which is located in the south of Germany. There is a large university clinic and I am the Director of Hospital Pharmacy. There are many tasks to do.

Table 1: Bias of renal function for low, normal and high levels of GFR [1]

Formula	GFR Bias (%)	GFR < 50 mL/min	GFR: 50–100 mL/min	GFR > 100 mL/min
Wright	+2% (p = 0.11)	+39% (p = 0.03)	+5% (p = 0.15)	–18% (p < 0.001)
Martin	+1% (p = 0.14)	+30% (p = 0.05)	+4% (p = 0.33)	–16% (p < 0.001)
Cockcroft-Gault	–10% (p < 0.001)	+11% (p = 0.38)	–7% (p = 0.002)	–24% (p < 0.001)
Jeliffe	17% (p < 0.001)	+14% (p = 0.34)	–15% (p < 0.001)	–32% (p < 0.001)

GFR: glomerular filtration rate.

Table 2: Comparison of Midazolam-Clearance: Child-Pugh and MELD Score

Parameter	Control	Child-Pugh A	Child-Pugh B	Child-Pugh C	Mean
Bilirubin (mg/dL)	0.62 (0.3–1.1)	1.30 (0.7–2.5)	1.74 (0.7–3.8)	4.65 (1.4–9.4)	2.88 (0.7–9.4)
INR	1.04 (0.99–1.11)	1.19 (0.94–1.45)	1.51 (1.06–2.08)	1.3 (0.94–2.09)	1.09
Midazolam-Clearance	24.8 ± 8.1	25.8 ± 8.2	9.8 ± 6.6	8.4 ± 2.1	
Registered-Score	7.5 (6–10)	8.0 (7–11)	12.0 (7–16)	17.5 (11–24)	13.0 (7–24)

Albarmawi A et al. (Br J Clin Pharmacol 2013 epub)
MELD Score and Midazolam-Clearance (L/h); MELD < 10: 17.9 ± 10 L/h; MELD 10- < 15: 12.1 ± 8.5 L/h, MELD ≥ 15: 7.5 ± 2.2 L/h.

How did you start this profession and why did you choose it?
I started in 1992 as a hospital pharmacist in Tübingen focussing on the admixture service, especially for cytotoxics, and interdisciplinary cooperation with physicians and nurses on the wards with the education topics of clinical infectious diseases, oncology and haematology.

Where do you see yourself in the development of ESOP and oncology pharmacy?
I am working as a lecturer with ESOP, focussing on oncology pharmacy. Meanwhile, I have published more than 100 reviews and original papers with the topics in oncology concerning pharmacokinetics and pharmacoeconomics. I think it is interesting to bring my experience into international groups of colleagues in order to learn from each other. Therefore, I think that ESOP is a very important tool and interesting platform for colleagues from Germany, Spain, Italy, Turkey, and many other countries.

What are the highlights of your topic?
I focussed on needs for dose modification during the meeting. What shall we do with the anticancer drug in case of liver or renal impairment? Should the dose be modified and to what extent? There is ongoing research, there are many new publications, but also many unmet needs; I think it is interesting to discuss it on an international platform.

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Reference

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Interview with speaker of the Advanced Masterclass in Oncology Pharmacy 2013 Meeting

Can you introduce yourself briefly?
I come from Hamburg in Northern Germany. I now practise haematology in an outpatient setting, in Hamburg.


Professor Dr med Eckart Laack, MD

How did you start this profession and what is the reason you chose this profession?
I was a medical student at the University of Hamburg. There was a very young child. He had a haematological disease, and I thought it would be a reason for me to come back to this part of the treatment. It was not a malignant one, but it was a child. It was then in my mind to study haematology and oncology. After I finished my study in medicine, I started working in the general hospital in Hamburg in oncology. Two years later, I moved to the university hospital in Hamburg and Professor Hösveld influenced my education.

What do you think about the past, present and future of oncology and input of oncology pharmacy?
I think we have made a lot of steps to the past, present and future. We are more focused on targeted therapy. We know each tumour is individual so we are looking in oncologic driver. The input of oncology pharmacy in my opinion is very high. Due to the effect of the disease, the patient has to take a lot of medications. Because of the interactions between all these drugs it is very difficult to look at which drug I have to separate, and where I have to make dose reduction. When asking 100 different physicians you will receive a hundred different answers on which tablets to take. A lot of cancer patients take a lot of vitamins or alternative treatment options. If we mistreat, a lot of complications between all disease agents can happen and then we do not know much about the action. So I think a high input from oncology pharmacist is very important, Professor Dietel will say the same.

Where do you see yourself in development of ESOP and clinical pharmacy practice?
My role is that I was a speaker at ESOP courses and also the clinical pharmacy practice course, so I am a big player and a big supporter.

What are the highlights of your topic?
The highlight of my topic is that lung cancer is the best example for molecular targeted therapy treatment strategies.

Can you describe two or three most important slides of your presentation in one sentence?
More than 50% of adenocarcinomas of the lung had a mutation of an oncologic gene like K-RAS, EGFR, ALK and BRAF.

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Side effects of cytotoxic drugs

Introduction

Cytotoxic drugs have a plethora of side effects. They affect most tissues in the body and toxicity may also accumulate so that there is a summed dose limit for certain drugs that prevents further medication. There are side effects that are general for all or most cytotoxic drugs that are due to the action of the drugs on cell division and proliferation. These effects seen in many patients are blood dyscrasias, fatigue, pain, nausea, vomiting, alopecia, constipation, diarrhoea, mucositis and cachexia. There are also specific side effects for certain drugs like heart failure (anthracyclines), lung fibrosis (bleomycin), damage of sensory nerves (vinca alcaloids), cystitis (cyclophosphamide), and kidney failure (high doses of methotrexate). The side effects often influence and increase other side effects or symptoms seen in the patients.

Professor Per Hartvig-Honoré, PharmD, PhD

Much is done to prevent these side effects and care plans including supportive therapy are frequently employed. Supportive therapy is care given to improve the quality of life of patients who have a serious or life-threatening disease. The goal of supportive care is to prevent or treat as early as possible the symptoms of the disease, side effects caused by treatment of the disease, and psychological, social and spiritual problems related to the disease or its treatment. This care is also called palliative care, comfort care and symptom management. Clinical oncology pharmacists may have a great impact and give support to these initiatives.

Figure 1: Interdisciplinary work together – teamwork

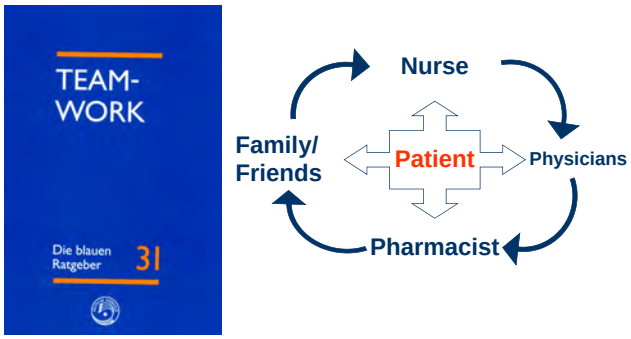
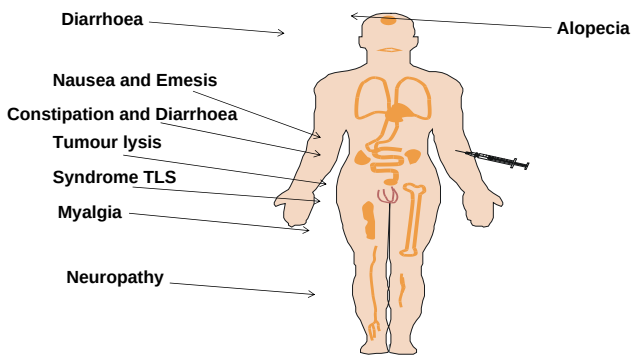
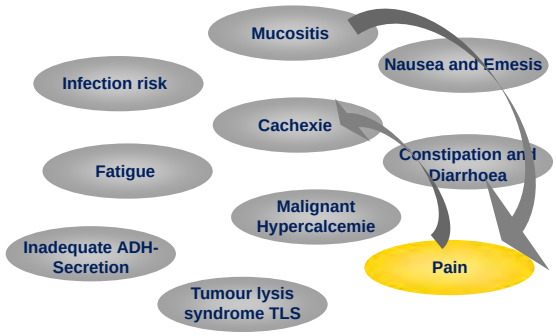


Figure 2: The most common side effects observed during and/or after cancer treatment



Source: The oncologist, 1999

Figure 3: The interconnection of cytotoxic drug induced side effects



Fatigue

Fatigue is today the most common and incapacitating side effect in patients with cancer. It affects both physical and psychosocial function and reduces the patients´ quality of life. Risk factors also include female gender and young age. The mechanisms explaining fatigue are still mostly unknown and there is no general treatment to alleviate the symptoms, although effective treatment of coexisting symptoms and easy exercise will make some benefit.

The National Comprehensive Cancer Network (NCCN) defines cancer-related fatigue (CRF) as 'a persistent, subjective sense of tiredness related to cancer or cancer treatments that interfere with usual functioning'. It differs from the fatigue of everyday life, which usually is temporary and is relieved by rest.

CRF is more severe, more distressing, and usually not relieved by rest. Fatigue may cause 'stress' and alterations of several neurotransmitter systems in the brain. The transmitter systems usually discussed are the serotonergic and noradrenergic ones. Both these systems are closely linked to the control of corticotropine releasing hormone (CRH) release and hence patients with fatigue have an increased CRH sensitivity. Low brain concentrations of serotonin, norepinephrine and dopamine, but also an activated hypothalamic-pituitary-adrenal axis (HPA-axis) is linked to the elevated glucocorticoid concentrations.

Cytokines are released in many diseases and during treatment. Of these, IL-1β, IL-2 and IL-6 have been of particular interest. Interleukins activate the hypothalamus-pituitary axis which controls CRH release, and is closely linked to serotonergic and noradrenergic neurotransmission.

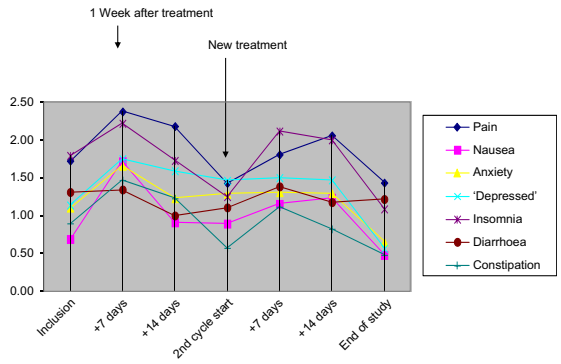
The limited knowledge about the mechanisms of CRF has led to a lack of efficient treatment of fatigue and inappropriate treatment have been tried. Most frequently used are based on dietary and vitamin support, in some cases pharmacologic treatment and in others complete rest. The pharmacological therapies tested to combat fatigue have not been rigorously evaluated in controlled trials. Nonetheless, there is evidence to support the use of several classes of drugs. In recent years, scientific evidence has dramatically changed the ideas about the relationship between physical activity, rest and fatigue. Convincing clinical evidence supports the management of fatigue with physical exercise. It is now overshadowing the symptom from cancer and cytotoxic drug treatment. Obviously, today unconventional treatment paradigms like light exercise are most successful.

Figure 4: Known and unknown mechanisms in fatigue

- **Cytokines as IL-1β and IL-6 with activation of the HPA axis and CRH**
- **Stress induced lower release of corticotropin releasing factor, CRH**
- **Central changes in serotonin and noradrenergic transmission**
- **The role of brain-derived neutrophic factor**

CRH: corticotropine releasing hormone.

Figure 5: Results – Side effects



Source: The Oncologist, 1999

Figure 6: Fatigue in the treatment plan of cancer patient

- **Patients must be informed about fatigue in cancer and cytotoxic drug treatment**
- **Fatigue must be included in a treatment plan**
- **Treatment of patient's side effects essential**
- **Exercise good alternative to combat fatigue**
- **Early and repeated information necessary to introduce exercise in daily life in cancer**

Nausea and vomiting

Effective prophylaxis and treatment of nausea and emesis is fundamental in cancer.

The emesis following cytotoxic drug administration occurs in different phases.This is highlighted in treatment schedules for cytotoxic drug-induced emesis.

The acute phase starts some hours after drug administration and lasts for one to two days.

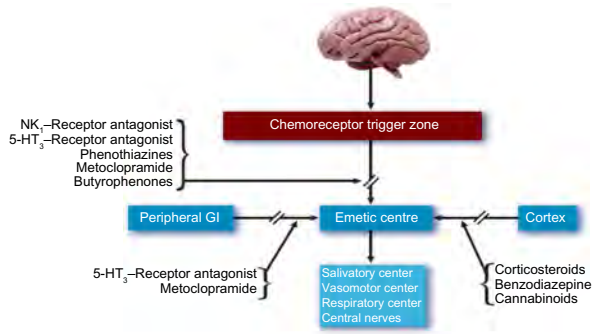
Setrons block these symptoms by acting on serotonin 5HT3 receptors. The acute emesis phase is thought to be due to cytotoxic drug-induced release of serotonin and other neurotransmitters from chromaffin cells in the fundus of the ventricle and in cells close to the vomiting centre. Selective blockade of these receptors explains the success of the 5HT3 receptor-blocking setrons. New setrons, e.g. palonosetron, which are eliminated slowly and have a higher affinity for 5HT3 serotonin receptors, offer some advantages but it is still obvious that the effect wears off after a few days.

The metabolism of another neuropeptide, substance P, is regulated by amidases and esterases in the body and is similarly involved in emesis. The action of substance P is inhibited by selective substance

Figure 7: Antiemetic supportive therapy

Emetogenic potential	Chemotherapy		Radiotherapy	
	Prophylaxis of acute emesis	Prophylaxis of delayed emesis	High individual patient risk	Normal individual patient risk
High individual patient risk	5-HT3-Antagonist + dexamethasone + aprepitand	Subst. Benzamid oder 5-HT3-Antagonist + dexamethasone + aprepitand	5-HT3-Antagonist + dexamethasone	5-HT3-Antagonist
Moderate individual patient risk	5-HT3-Antagonist + dexamethasone	Dexamedthasone or 5-HT3-Antagonist	5-HT3-Antagonist	5-HT3-Antagonist eventually
Low	Dexamethasone	Dexamethasone	5-HT3-Antagonist rescue	5-HT3-Antagonist rescue

Figure 8: Antiemetic sites of action



5-HT_3: 5-hydroxytryptamine type 3; GI: gastrointestinal; Nk_1: neurokinin-1.

Figure 9: Mechanism of cytotoxic drug-induced emesis

- **Different mechanisms over time**
  - **Acute: induce release of serotonin and dopamine**
  - **Delayed: increased neuropeptide levels due to inhibition of catabolism**
  - **Late anticipatory: sensitization with formation of a 'memory protein'**
- **Although improved treatment, emesis still a problem following cytotoxic drugs**

P or neurokinin-1 receptor antagonistic drugs. New drugs blocking the substance P receptors, e.g. aprepitant, have shown good effects on cytotoxic drug-induced delayed emesis and are together with steroid drugs suggested as first-line treatment for cytotoxic drug-induced delayed emesis. For the clinical oncologist, the individualized prescription of antimetic drugs following cytotoxic drugs is recommended. The guidelines classify different cytotoxic drugs and drug regimens with respect to severity and duration to achieve optimized management.

The mechanisms of cytotoxic drug-induced nausea and vomiting, which differ from other causes of emesis, are still to be fully understood and properly used to develop drugs for more effective treatment.

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The elderly patient with cancer – Professor Per Hartvig-Honoré, PharmD, PhD

The physiological capacity of organ function reaches its maximum capacity at around 23 years of age. Thereafter, the capacity is slowly decreased in most organs by 1–2% per year, but at the end of life the rate is higher. Normally only a part of the capacity is used but at an older age the function may reach a level where symptoms similar to those in disease may arise. Though, it should be emphasized that 'Old age is not a disease'. Several general changes are shown as less capacity for digestion, more easily exhausted, circulation failures, slower healing rate, and for some drugs slower elimination or better effect, or more side effects. The capacity loss in different organ systems is very different from patient to patient and also over time. This might be obvious in cytotoxic drug treatment and special care is necessary for successful treatment.

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Interview

Where do you come from and where do you practise?
I was born in Sweden and worked as a scientist pharmacist at the University Hospital in Uppsala, Sweden, mostly in clinical pharmacology and clinical pharmacy tasks.

What do you think about the past, present and future of oncology and input of oncology pharmacy?
Oncology will cure more patients and give them a better quality and longer life. Oncology pharmacy can be important but must identify and implement its unique competences in the care team.

Where do you see yourself in the development of ESOP and clinical pharmacy practice?
I have just stepped down from ESOP, but will continue with quality, education and competence.

What are the highlights of your topic in oncology?
Support treatment: fatigue, pain, nausea.

CNS: central nervous system.

Side effects of anticancer drugs: neutropenia and diarrhoea

Neutropenia

Neutropenia is a serious disorder for cancer patients because of chemotherapy drugs. During the treatment process, the patient's normal bone marrow stem cells are killed along with the cancer cells. Because of this, chemotherapy often may adversely affect myelopoiesis.

Bogumila Julia Sobkowiak PharmD, PhD

Neutropenia is defined as a decrease in the number of neutrophils, which may lead to a low white blood count. The factors which contribute to the development of neutropenia include dosage and duration of chemotherapy. A higher dosage usually causes a lower neutrophil count.

Figure 1: Side effects of neutropenia

Risk of infection based on absolute neutrophil count (ANC)	
ANC greater than 1,500 cells/mm^3	No increased risk of infection
ANC 1,000–1,500	Slight increase in risk of infection
ANC 500–1,000	Moderate increase in risk of infection
ANC 100–500	High risk of infection
ANC less than 100	Extremely high risk of infection

ANC: Absolute neutrophil count.

Neutropenia and the integrity of gastrointestinal mucosa are the risk for invasive infection due to colonizing bacteria or fungi that can translocate across the intestinal mucosal surface. Neutropenia is also associated with radiation therapy that affects the bone marrow. The number of killed cells during radiation therapy depends on the dose and frequency of radiation, and how much of the body is irradiated.

Here below is a list of significant consequences of neutropenia:
- Increased risk of infections of organ systems
- The risk disorder proper course of treatment cancer (periodic interruption of radiotherapy)
- Reduction of computed tomography (CT) doses
- Delay in the next course of therapy

The best way to avoid these complications associated with neutropenia is to prevent its development with:
- regular blood tests, which can detect deficits and decreases in the number of leukocytes (WBC) on time
- use of granulocyte colony-stimulating factors (G-CSF): filgrastim, pegfilgrastim, lenograstim.

The aim of neutropenia treatment is to maintain the concentration of the neutrophils level that will protect the body against infections. It will allow optimal and effective cancer treatment.

Diarrhoea

Diarrhoea during the treatment of tumour disease is a complication that must be taken seriously. It occurs as a side effect of both radiotherapy and from certain cytotoxic drugs, particularly irinotecan and topotecan. In addition, tumour associated immunological or infectious processes must also be considered as causes. The reason for the diarrhoea is caused by the damage to the epithelial cells lining the intestine and impaired of secretion of enzymes. Chemotherapy also destroys bacterial flora, which has an impact on the bowel.

Diarrhoea in cancer patients may appear at any stage of disease or treatment, although it occurs less frequently than constipation. Patients are very exhausted both physically and mentally because diarrhoea contributes to deterioration of patients' nutritional status.

The side effects of chemotherapy depend on the type of the chemotherapy:
- Diarrhoea is a symptom, rather than a disease, often produced or induced in response to another condition or treatment, i.e. cancer treatments such as chemotherapy or radiation
- Diarrhoea associated mortality has been reported to be as high as 3.5% in clinical trials of irinotecan and bolus 5-fluorouracil in colorectal cancer

In conclusion, the key to the prevention of potential complications:
- Diarrhoea during the treatment of tumour disease is a complication that must be taken seriously
- The patient should be informed of side effects (diarrhoea) of both radiotherapy and chemotherapy, particularly irinotecan, topotecan
- An appropriate treatment of opioid-induced constipation, managed by laxatives

Interview

Where do you come from and where do you practise?

Nowadays, I work as Head of the Clinical Research Department in my hospital. Also, I work at the Medical University of Lublin giving lectures about side effects of anticancer drugs. Before this work, I had been the Director of Hospital Pharmacy at the Center of Oncology in Lublin, where I organized the first cytotoxic laboratory in the Lublin area.

How did you start this profession and why did you choose it?
I became interested in oncology pharmacy during my work at the hospital pharmacy at the Center of Oncology, and in particular when I attended the 1st Polish-German Oncology Pharmacy Conference 10 years ago. There, I met German pharmacists who impressed me with their professionalism. Since then I started to broaden my knowledge of oncology.

What do you think about the past, present and future of oncology pharmacy?
I think we have made huge progress in the field of oncology pharmacy in Europe and Poland in the last decade. At present, our challenge is to implement the QuapoS into practice, we have done it in some hospital pharmacies, but not at all hospitals where cancer patients are treated. Thanks to the use of QuapoS, the future will be safer for both patients and us pharmacists.

Where do you see yourself in the development of ESOP and clinical pharmacy practice?
I would like to contribute to the development of ESOP by giving lectures in clinical oncology and QuapoS to pharmacy students and hospital pharmacists in Poland.

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RESEARCH NEWS

Tumour markers not recommended for cancer detection

Stuttgart, Germany, January 2013 – doctors can assess the progress of cancer by laboratory tests of the cancer cells in blood, urine or OTHER body fluid measure molecules emitted. However, the usefulness of these tumour markers for cancer detection is low, says an expert in the journal *DMW German Medizinische Wochenschrift* (Georg Thieme Verlag, Stuttgart, 2013).

The best-known tumour marker is the prostate-specific antigen, in short PSA. It is the cancer of the prostate increasingly detectable in the blood. But since it is released in smaller quantities from healthy glandular cells that TEST is not reliable: Not all men with elevated PSA levels suffer from prostate cancer. On the other hand, a cancer cannot be excluded if the PSA level is only half of the generally accepted threshold, which is 4 nanograms to 1 milliliter of blood serum, has reached, said Professor Günther Wiedemann, Chief Physician at the Oberschwabenklinik in Ravensburg, Germany.

To confirm the diagnosis, the urologist must perform a biopsy. In this case, be removed from the gland and examined under the microscope with fine needle tissue samples. If any cancer cells are found, the patient is usually advised to remove the prostate by surgery. In the US, the introduction of PSA testing has led to a significant increase in operations. Professor Wiedemann said, the 'lifetime risk' of men diagnosed with prostate carcinoma has increased from nine per cent to 16 per cent.

The German expert questions the utility of PSA testing. Although the chance of death due to prostate cancer for men in the US has decreased significantly, however, the life expectancy has not increased. The reason being that prostate cancer occurs most often in older age and growth of the tumour is very slow. Most patients die after a relatively long life of a different cause. However, by removal of the prostate they suffer drawbacks: the complications of surgery, according to the internal include infection, bleeding, intestinal problems, thromboses, urinary incontinence, and erectile dysfunction.

Other tumour markers are not suitable for early detection. Professor Wiedemann called antigens CA-125, which occurs in ovarian cancer in the blood, CA 15–3, which is formed by breast cancer cells and the alpha-fetoprotein, which may indicate a liver cancer. All three markers were tested in clinical trials. No one could improve the early detection of cancer. Instead, the tests are often solved in patients out of fear. Tumour markers usually lead to over-diagnosis and over-treatment, laments the author.

The introduction of PSA tests has shown, however, that tumour marker tests for patients in the early detection can hardly be denied. The sense of security in not suffering from cancer is often stronger than the statistics, said Professor Wiedemann. He advises physicians to discuss individually with the relevant stakeholders the risk–benefit ratio of PSA screening. In the US internists have recognized the need for an open dialogue with the patient. With choosingwisely.org ('Smart Select') they would seek an open dialogue with the patient. On the Internet platform provides various professional associations about the sense and nonsense of diagnostic procedures and therapies available. Professor Gunther Wiedemann, together with his US counterparts, counts tumour markers are among the top five medical measures that are widely used, they are expensive and are not used in their effect.

This is only true for the early detection, unlike the situation in patients whose tumour is already known. Oncologists put the tumour markers after cancer therapy regularly for aftercare. An increase of the tumour marker may be the first indication of a recurrence, relapse of cancer suffering here.

This is a brief version in English based on the article published in German and the article was prepared based on the presentation (Sinn und unsinn von tumormarkern pros and cons) at the NZW 2014 Meeting, Hamburg, Germany, on 26 January 2014.

Wiedemann J Biomaker screening for early detection of cancer. DMW Deutsche Medizinische Wochenschrift. 2013;138(1-2):43-45.

Drug interactions with cytotoxic drugs

Drugs may interact with the vehicle or container, with food, herbal medicines and with other drugs. Some of these are absolute, such as physical interactions, whereas others are relative, with incidences from very high to almost none.

Known physical drug interactions for cytotoxic drugs, such as an incorrect pH, oxidizing or reductive substances in the solution, exposure to light and non-reversible adsorption on container walls or excipients should be well investigated before marketing.

Professor Per Hartvig-Honoré, PharmD, PhD

Food interactions can be divided into food–drug interactions and drug–food interactions. The interaction with food to lower or delay absorption is rare, and mostly occurs with metal-ion chelate complex drugs, such as tetracyclines, oxiquinolones and some cytotoxics. The second type of interaction occurs when long-term drug treatment induces physiologic and even pathophysiological changes that might be detrimental. Insulin-producing drugs, corticosteroids, antipsychotics and antidepressant drugs may increase appetite, causing weight gain, whereas drugs causing nausea, e.g. cytotoxics and opioids, have the opposite effect. Hyperglycaemia can be caused by opioids, antipsychotics, sulphonamides antiepileptic drugs and warfarin, and, in some cases, may develop into diabetes.

The interaction of herbal medicines with drugs is a huge issue, but little is known about the components of such medicines, their potency to induce or block metabolic enzymes, or how they interact with many drugs. The risks of combining herbal medicines with cytotoxic drugs may be cumbersome but rarely known. Some herbal medicines, such as St John's Wort, have known risks when combined with many drugs, but otherwise they pose risks that are unpredictable.

Drug–drug interactions are common. In standard reference books to support prescribing, they may amount to many thousands. The clinically relevant and significant drug–drug reactions are few. This is extremely important. Three main drug–drug interactions exist and their clinical context described below and in Table 1:

- The good: the therapeutically useful (agonist–antagonist). In many clinical situations, drugs interacting with each other are used to benefit the patient, such as antidotes in overdose, to combat heart effects, when reversing neuromuscular blockade by atropine after anaesthesia, and when giving leucovorin rescue after high methotrexate dose. Combination of cytotoxic drugs may enhance effect without worsening side effects.
- The awful: potentially harmful interactions, which should be remembered and spotted at an early stage.
- The ugly: most drug interactions are of no or little clinical significance and having low risk.

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Table 1: Type, significance and prevalence of interactions of anticancer drugs

Interaction with drugs	Drug interactions	Prevalence of drug interactions of anticancer drugs (%)*
In vitro interactions (incompatibility). These include drug reactions with the vehicle, container or degradation in solution. These are absolute.	Common	Glucocorticoids (42); aprepitant (27); sertrones (13)
In vivo interactions. These include drug–drug interactions in the body. These are relative.	Only few reach clinical significance	

*Data taken from lung cancer patients. Published with permission from L Knec, ECCO17, 2013.

Multi-professional case report summary

Case reports presented as abstract at the ESOP–ESO Advanced Oncology Masterclass 2013 highlight the integration of the oncology pharmacist within the multidisciplinary oncology team and individualization of therapeutic protocols.

Oncology pharmacists have increasingly become acknowledged as members of multidisciplinary oncology teams, and new opportunities have emerged in the integrated approach of chemotherapy-related side effects. The hospital pharmacy service can play a major role in developing highly individualized therapeutic protocols, as low-scale production of individually compounded formulations is one of the key competencies of the profession.

András Süle, PharmD, PhD

Three patients are presented in this case report. Two of them suffered moderate-to-severe, paravasation-related vascular damage, whereas the third patient presented with a substantially debilitating skin erosion as a result of post-operative rectovaginal fistula.

Patients 1 and 2: paravasation of cytotoxics

Patient 1 was a 72-year-old woman with colon cancer. She was admitted to hospital for her scheduled cycle of chemotherapy (FOLFOX-4 regimen) and subsequently discharged). Four days later, the patient was readmitted with severe signs of inflammation on the lower right arm extending from the wrist to the elbow. Diffuse haematoma and pain were observed in addition to the inflammation, swelling and oedema.

The clinical presentation was consistent with mild-to-moderate oxaliplatin extravasation.

The patient was presented to the oncology team, including an onco-dermatologist, a surgeon and a pharmacist. A consensus was reached that surgical measures were not needed. To stimulate the perfusion of the affected tissue, use of dry warmth was advised. As a new treatment approach, a set of two topical formulations were compounded.

Antiphlebitis-A ointment	Antiphlebitis-E ointment
• Lidocaine hydrochloride • Triamcinolon (steroid component) • Phenylbutazone (non-steroidal anti-inflammatory drug) • Monoxerutin (flavonol) • Heparin 25000 IU • Aluminium aceticotartaricum solution • Hydrophilic base cream	• Lidocaine hydrochloride • Mometasone (steroid component) • Monoxerutin (flavonol) • Heparin 25000 IU • Aluminum acetico-cotartaricum solution • Hydrophilic base cream

The 'Antiphlebitis-A' formulation was approved for inpatient application only, whereas the 'Antiphlebitis-E' ointment was prepared for outpatient use.

Patient 1 was treated with 'Antiphlebitis-A' ointment under careful observation. Her condition showed significant improvement after five days, and she was discharged from hospital. During her follow-up visits, a continuous improvement was observed with no remaining symptoms and visually detectable residual damage after 20 days.

Patient 2 was a 56-year-old man with colon cancer. He was admitted to hospital for his twelfth scheduled cycle of chemotherapy (FOLFOX-4 plus bevacizumab regimen) and discharged from hospital. Seven days later, the patient was readmitted to hospital showing severe vascular damage on the whole left arm. The patient also suffered from disabling pain.

The clinical presentation was suspected to be a side effect of long-term oxaliplatin exposure; however, the extent of tissue damage was unprecedented. The patient was referred to the oncology team, including an onco-dermatologist, a surgeon and a pharmacist. A consensus was reached that surgical measures were not feasible. As an individualized treatment approach, the use of the above-mentioned 'Antiphlebitis' ointments was indicated and dermatological advice was to use epithelial regenerative agents. A topical formulation was compounded containing vitamin A, vitamin D, Peru balsam, cod liver oil, and zinc oxide. After the patient's open wounds had healed, this formulation was applied to the affected area three times a day for the entire observation period.

Patient 2 showed significant improvement after 15 days. On day 30, only a slightly darker scarring was observed, which almost completely subsided by day 45.

Patients 3: skin erosion

Patient 3 was a 48-year-old woman with colorectal cancer and a serious case of recto-vaginal fistula after having a rectal tumour surgically resected. The abnormal connection between the rectum and the vagina resulted in a constant leakage of bowel contents. This constant irritation eventually lead to the severe inflammation and subsequent infection of the whole perineum, including a harsh vulvovaginitis.

The patient complained of intense pain (rated 8 on a 10-point scale) and consequential dramatic decrease in quality of life.

Surgical correction of the fistula was already scheduled; therefore, the main goal was to diminish pain while treating the underlying infections, enabling the affected area to heal. A topical for-

mulation was compounded containing lidocaine hydrochloride, mupirocin, fluocinolone acetonide, and sodium borate in a vaseline-based ointment, and applied to the affected area every 2–3 h.

The results were generally positive. The local anaesthetic lidocaine hydrochloride combined with orally administered tramadol hydrochloride kept the pain at acceptable levels. The antimicrobial and anti-inflammatory components proved useful in treating the inflammation, whereas the hydrophobic nature of the ointment protected the affected area from further irritation of the constant vaginal discharge. This combination therapy was maintained until the surgical reparation of the fistula.

Interview

Where do you come from and where do you practice? Can you introduce yourself briefly?
I am the Chief Pharmacist of the Péterfy Hospital and Trauma Centre in Budapest, Hungary. This hospital houses 1,650 beds and, apart from being a general hospital, it serves as a national trauma and toxicology centre. Our oncology ward has 40 beds and an outpatient clinic. As the head of pharmacy I oversee the whole workflow of oncology pharmacy in the hospital: procurement, handling, preparation, distribution, administration and disposal.

How did you start this profession and why did you choose it?
I have been involved in Oncology Pharmacy for over 5 years; prior to my current position, I was Supervisor of the Central Cytostatics Department of a large regional hospital in Hungary, with a substantial focus on preparation, handling and safety. I have also worked in collaboration with oncology wards and oncology teams. My main scientific interest has been the development of protocols for chemotherapy-related side effects and also the unique compounding of patient-tailored therapeutic formulations. I am also deeply interested in the pharmacoeconomic aspects of modern chemotherapy modalities.

What do you think about the past, present and future of oncology pharmacy?
Oncology therapy is experiencing a rapid evolution, as is oncology pharmacy. Although the preparative and dispensing aspects of our work still play a major role, other areas are quickly gaining importance too. Patient safety, environmental and exposure issues, therapeutic counselling and multidisciplinary decision-making are natural parts of our everyday practice now. Moreover, new roles for the oncology pharmacists are also emerging: nowadays, as an increasingly vital part of the medical team, oncology pharmacists are in frequent and much more direct contact with patients. Being involved in patient care in clinics, accompanying the medical team on rounds, and being an active participant of oncology teams all brings a sought-after visibility to our profession.

I do hope that, in the future, our in-depth understanding of pharmacotherapy and confident expertise in pharmacoeconomics will continue to bring our profession even closer to everyday practice in cancer care and, consequently, both patients and the oncology centres will experience the benefits of our continuous collaboration.

Where do you see yourself in the development of ESOP and clinical pharmacy practice?
In my opinion, the greatest strength of ESOP is synergy. As an organization bringing together several member countries and associates from all over the world, this shared knowledge and experience can really make a difference in forming the future of the European oncology pharmacy. As a committed member of ESOP, I have high hopes for our future cooperation and development. I would really like to contribute to initiatives such as the Yellow Hand, the Clean Work Trainings and QuapoS. I am determined that through our national organizations, and with the vision of 'Unity in diversity', we can inspire more and more young colleagues to contribute to our cause.

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Diagnosis and treatment: ovarian cancer

(please see the manuscript on page 6)

significantly improves OS in stage IVB, recurrent or persistent cervical carcinoma. Nearly four months improvement in OS was clinically significant. Bevacizumab also increased median progression-free survival (PFS). The current standard of care is cisplatin + paclitaxel, which do not underperform. A benefit was seen even when recurrent disease is in the irradiated pelvis. The incorporation of anti-VEGF therapy is a choice for primary treatment of locally advanced disease. Bevacizumab treatment is associated with a higher rate of adverse events (AEs) (3–8% of known Bevacizumab-related AEs).

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Case reports – examples from clinical practice


Beatrice Rieder, Pharmacist

In the tradition of ESOP's Masterclass in Oncology series, the Advanced Masterclass in Oncology was organized jointly, for the first time, by the European Society of Oncology Pharmacy (ESOP) and the European Society of Oncology (ESO). Set in the historical old town of Dresden, in the famous rebuilt Frauenkirche, the audience was experienced in many areas of internal oncology. The 20 participants came from around the world, from Estonia to Iceland, from Germany to Egypt, from hospitals and from community pharmacies with extensive experience in oncological patient care. Participants were all invited by the president of ESOP, Klaus Meier. They had to present two case reports from their own clinical practice. Over five days there was a broad spectrum of topics discussed by competent and celebrated specialists. The last day was reserved for 'Case Reports', patient documentation on the ward or in the pharmacy. The shared goal is to manage problems in medication or patient therapy and find solutions for patient benefit by using a structured approach.

Why is the structured approach needed now?

Due to the complexity of an (electronic) health report – with all the patient related diagnosis and problems on a ward – it is important to have a simple tool for assessment. The subjective, objective, assessment plan (SOAP) scheme is the tool of choice for treatment. Every symptom or problem discussed by the patient (subjective) is related to current diagnosis, imaging methods, results, medication or blood parameters (objective). The next step is an assessment according to up-to-date guidelines or common treatment rules of the healthcare professionals (analysis). In the case of queries or drug-related problems, pharmacists make plans for improved therapy.

There is an interactive template on the ESOP website for publishing case reports:
www.esop.li/downloads/library/basecasereport.doc www.esop.li/downloads/library/basecasereport.pages

Case study examples

Here are selected examples from the presented cases.

1. Tumour lysis syndrome and its treatment

Author: Sherif Kamal, Director of Department of Pharmaceutical Devices, Children's Cancer Hospital Egypt, Cairo, Egypt

The case of a 64-year-old male patient with chronic lymphatic leukaemia (CLL) was reported. The patient was treated with bendamustin 100 mg/m² day 1 and 2, first circle. After the second administration, the patient complained of pain in the left flank, shortness of breath, dysuria, anorexia, but no cardiac symptoms.

Assessment

The tumour lysis syndrome (TLS) is a life-threatening complication corresponding to treatments of haematological disorders with a large tumour mass, such as lymphomas or lymphatic leukaemia. As a result of chemotherapy the number of intracellular particles, including electrolytes or proteins, increase in blood and overload the normal capacity of elimination. The key markers for TLS are hyperkalemia, hyperphosphatemia, hypocalcemia in consequence of binding calcium ions by phopsphates, and increased serum-creatinine (> 1.5 upper limit of normal) and uric acid (derived from protein metabolism), indicating an acute renal failure, in combination with seizures and arrhythmias. There are two classifications of TLS, depending on how the disorder is examined, either in laboratory or in the clinic. Without treatment the patient will probably die of acute organ failure.

Plan

The state of the art in treatment of TLS is managing the electrolyte abnormities by using sodium polystyrene sulphonate or IV glucose combined with fast acting insulin for hyperkalemia, hydration, diuresis, and oral phosphate binders against hyperphosphatemia, calcium gluconate only in the case of tetanic seizures, and allopurinol for preventing formation of uric acid. Haemodialysis is made in case of renal failure. But for reducing an acute high level of uric acid there is only rasburicase, which transforms the uric acid in soluble allantoin to avoid acute renal failure. Also, frequent cardiac monitoring is needed to protect from lethal arrhythmia caused by electrolyte disturbances.

What is the pharmacist's job?

Rasburicase (Fasturtec) is a genetically modified uratoxidase enzyme for the treatment of hyperuricemia. Before use it must be reconstituted strictly under aseptic conditions with sodium chloride solution. The normal dose is: 0.2 mg/kg BW once per day.

2. Treatment of NSCLC with tyrosine kinase inhibitor

Author: Charlotte Bornemisza, Pharmacie des hopitaux du nord Vaudois de la Broye, Switzerland

A 69-year-old female from Asia was diagnosed with non-small cell lung carcinoma (NSCLC) in October 2005. Although currently a non-smoker, she had smoked for 35 years, gave up in Spring 2003. Diagnosis was confirmed by imaging methods (CT – computed tomography, PET – positron emission tomography**),** the tumour lesion was in the right lung lobe, after resection (R0) and dissection of lymph nodes in the mediastinum the patient was free of symptoms. Annual CT-control was continued until 2011. During a control scan in August 2012, metastases were detected in the liver and spleen without any clinical symptoms, so that a new therapy with erlotinib (Tarceva) was started. Due to severe side effects the therapy was continued on a reduced dose.

Objective

A moderately differentiated lung adenocarcinoma, stage pT2 N0 M0, was diagnosed in the upper part of the right lung lobe. A superior right lobectomy (R0 – resection) with mediastinal lymph nodes dissection was performed. No additional chemotherapy, annual control with CT scan was continued until 2011. In August 2012, metastatic lesions were detected in the liver and spleen. A therapy with erlotinib was started after confirmation of genetic analysis of epidermal growth factor receptor (EGFR) – mutation in exon 19, normal dose is 150 mg absolute orally once per day on an empty stomach. First doxycycline and then minocycline were used because of acne eruptions on the face and chin along with a rash and xerosis. In addition, a cream with fusidic acid and betamethasone was given for external use, with loperamide for diarrhoea control.

By June 2013, there was no metastasis in the liver (according to CT scan).

Assessment/Plan

Lung cancer is the third most frequent malignant disease worldwide, increasing in women. The treatment depends on staging and histology (small-cell lung cancer [SCLC], NSCLC) and on genetic characteristics. NSCLC is divided into many different types of cancer corresponding to genetic variations. Depending on the result there are several therapeutic options: resection, radiation and/or (conventional) chemotherapy. The improvements made in genetics have led to progress in treatment, the 'targeted therapy' with EGFR - inhibitors seems to be more useful.

What is the advantage of small molecular tyrosine kinase inhibitors?

The advantage is that the patient is independent of a hospital or an acute day ward and can take their own pill at home.

The disadvantage is that there can be severe side effects in form of diarrhoea, skin reactions, rash, nail deformation, anorexia, weight lost, and the possibility of noncompliance.

Management of unexpected adverse events

1. Tetracyclines are preferable drugs in the treatment of acne form skin reactions, normal doses: 100 mg/d oral use, because of intolerance reactions (anorexia, weakness, diarrhoea) and interaction with CYP3A4 substrate erlotinib change to minocycline 100 mg/d oral use. No improvement of symptoms so that minocycline is stopped too.
2. Local therapy on skin with Fusidin acid + Betamethasone cream, moisturizing lotion for xerosis symptoms.
3. Diarrhoea: administration of loperamid, 4 mg loading dose, 2 mg for maintenance.
4. Erlotinib is CYP1A2 and CYP3A4 substrate, so there are many interactions to be expected. The elimination is delayed in a poor metabolizer in consequence to accumulation. Dose reduction of erlotinib (100 mg/d once per day) leads to an improvement of patient benefit with gain of weight, decrease of skin reactions and less frequent diarrhoea. At least therapy can be continued, the latest CT scan shows a disappearance of liver metastasis.
5. What can the pharmacist do?
   Before beginning erlotinib therapy the patient should be instructed with the correct use, once per day on an empty stomach, and be advised of the most important side effects especially on skin and intestine. Use information brochures if available. It is necessary to stop smoking because cigarette smoke reduces drug efficacy.

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Epidemiology of carcinogenic factors influencing cancer development

(please see the manuscript on page 4)

What are the highlights of your topic?

We still have a lot to learn about carcinogenesis. It is estimated that in 10 years one person per four will get cancer. So we should try to do everything (eat healthy, exercise, perform screening tests) not to be that one person in four.

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Impressions of participants of the Advanced Masterclass, Dresden, Germany, 21–26 October 2013

Dorota Eppel, Poland
You may have wondered how to describe the Advanced Masterclass in Oncology Pharmacy, and I have found a few simple words! Excellent lectures, excellent participants and a great impression. Practical benefits from theoretical presentations.

Anita Molenda, Poland
In my opinion, the level of our lectures was accurate for the Advanced Masterclass. The organization was very good and the atmosphere even better. I had a great time and I am full of 'take home' messages from the excellent presentations of the great speakers. Thank you!

Sherif Kamal, Egypt
Very great staff and participants on this state-of-art course. A new perspective on learning about cancer.

Beatrice Rieder, Germany
Impressions of the Advanced Masterclass in Oncology Pharmacy from the point of view of a community pharmacist:
- Very specific topics; the speakers were all specialists in their subjects.
- The class had 20 participants, and intensive discussion and exchange took place among them; contact with the speaker was close.
- Extended sessions, approximately 10 hours long.
- Some topics such as surgery of entities are less interesting to a pharmacist, especially a community pharmacist.
- In conclusion, very intensive lessons providing an overview of internal oncology. Detailed discussions on the impact of treatment on several kinds of cancer. Hotel provided meals and coffee breaks. It is worth taking part!

Velina Grigorova, Bulgaria
I am very happy with the Advanced Masterclass. Of course, some of lectures were better than others. But, generally speaking, it was really useful. I would like to receive the lectures that are not in our materials.

Marta Trojniak, Italy
I am really impressed with the content of the first advanced level Masterclass. I found practically all the lectures very interesting and extremely useful for my professional activity. My clinical knowledge of different tumours especially has increased significantly. I want to thank the organizers for this magnificent and high quality update in oncology pharmacy.

Marika Saar, Estonia
Great Masterclass with good lecturers from top specialists in their field. The schedule was very tight (long days), but it allowed many interesting topics to be covered, so no complaints. Many thanks to ESOP for organizing the Advanced Masterclass.

Thorunn Kristin Gudmundsdot, Iceland
All lecturers are extraordinarily great, easy to understand and practical. Lecture days are long, but worth it. Lung cancer Professor Dr E Laack was my favourite. More time for supportive care with cases needed. It would be better to have handouts electronically (or choice to have) to avoid heavy luggage!

Teresa Lopez, Portugal
Great presentations, great participants. New data were presented. I had the opportunity to learn more and acquire knowledge that will greatly contribute to my daily activity, and I will integrate new ideas into my practice.

Andras Süle, Hungary
This has been an absolutely inspiring and encouraging week for me. I think that the oncology pharmacy service could really benefit from the largely medical viewpoints that I have had the chance to experience during the past couple of days. The same goes for our role as oncology pharmacists; we should always remember that our profession is interdisciplinary and multiprofessional. As for the courses and workshop, I was largely satisfied with both the concept and content presented. The medical doctors, professors and practicing surgeons were very interesting, they presented relevant discussions on treatment plans, disease aetiologies and pathological aspects. In summary, the past couple of


Starke and Hoeckel lecture


Dresden by night


ESOP-ESO Advanced Masterclass 2013

days have been extremely useful for me and I do hope that ESOP carries on this tradition of continuing high level education.

Ozlem Goksen, Turkey
It was a great experience to take part in such a great Masterclass as a student, and it was a great opportunity to meet with the precious professors.

Bogumila Julia Sobkowiak, Poland
I remain deeply impressed by the high level of the scientific course of the first ESOP–ESO Advanced Masterclass in Oncology Pharmacy. Receipt of the certificate granted by the European Society of Oncology Pharmacy on completion of this course is a huge motivation for my further hard work and scientific development.

Anonymous
Good speakers, good topics, good food, and good organization. Wish to have the printed handouts before the course and to have a USB memory stick containing the presentations. Each doctor should also talk about how he collaborates with his pharmacist, what he expects from his pharmacist, and give one clinical case with a drug issue, e.g. ZALTRAP for colorectal cancer.


Participants of the Advanced Masterclass 2013

Interview with speaker of the Advanced Masterclass in Oncology Pharmacy 2013 Meeting

Interview

Can you introduce yourself briefly?
I live in Kassel in the middle of Germany, well known as the city of documents and the world famous exhibition of modern art. I am Head of Pharmacy at Hospital Kassel of Gesundheit Nordhessen Holding AG. We provide our service to eight hospitals.


Michael Hoeckel

How did you start this profession and why did you choose it?
After vocational education as a policeman and male nurse, and a second educational chance, I studied pharmacy at the University of Marburg. I was interested in natural science and during my practical year at the community pharmacy, I discovered pharmaceutical care to patients as being a challenge.

What do you think about the past, present and future of oncology and input of oncology pharmacy?
In Europe, one can find different ways of patient-oriented work. In Germany today, we are on the way to pharmaceutical care for in- and outpatients. In my opinion, it is the only way for a pharmacist to realize his/her benefit for people or patients. This applies especially to oncology in- and outpatient. Our professional work for patients as pharmacist by no means ends in logistics and drug delivery. In Germany, we as hospital pharmacists look to the UK and the US where pharmacists work closer to patients. For myself, as a hospital pharmacist, I prefer patient-oriented work and service, and it seems very important for our future as professionals in multidisciplinary teams.

Where do you see yourself in the development of ESOP and oncology pharmacy?
For me, ESOP is a very important society for oncology pharmacists to be a part of. Especially as the community of oncology pharmacists in Europe, and as a forum to exchange experiences.

What are the highlights of your topic?
To exchange experiences and discuss with colleagues on how they work in their work environment in different countries and how they respect quality standards.

Interviewee

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High standards of oncology pharmacy in practice and research

ESOP Delegate Assembly

Introduction

Oncology pharmacy deals with the expertise in supply, preparation, handling, and safe distribution of cytotoxic drugs to cancer patients, including support, treatment, information, education and research for high quality and safe treatment.

Typical features of oncological drug therapy are a tight range of dose and effect, and a highly complex treatment regime. Frequently, patients are immune deficient, either because of their underlying condition or due to the therapy, or they suffer from co-morbidities. Intensive chemotherapies based on conventional cytostatics, but also new treatment options with typical side effects, call for supportive measures and specialist supervision which comply with guidelines. Cancer outpatients need broad management and counselling in how to use their medication and how to respond to any product-related problems.

Ensuring the quality essential to safe oncological drug therapy requires pharmaceutical expertise. The oncology pharmacist is indispensable as an integrated member of the clinical oncology team. Thanks to the initial and further training they receive, and to continuing professional development, oncology pharmacists acquire the best possible expertise for ensuring a safe oncological drug therapy of impeccable quality.

Product procurement

Purchasing the products used in oncology therapies calls for an expert appraisal of the economic benefits in the light of the quality and safety of a drug therapy. Any risks associated with counterfeit goods, inappropriate handling or failed delivery must be minimized as much as possible. Products must be recalled immediately if any defects in quality are identified. Any gaps in delivery must be bridged as well as possible in consultation with the physician in charge of the case. If it proves necessary to draw on imported goods, the pharmacist is responsible for making sure that reliable sources are chosen. It is vital to avoid the use of risky drugs for the sake of saving (possibly not much) money, but optimum use must be made of resources. The use of drugs must always be considered in the light of the treatment process, the suitability of the drug and the period for which it is administered, the nature and frequency of the application and many other factors, and these must all play a part in an overall pharmacoeconomic assessment.

Preparation

Cytostatic preparations which are wrongly selected, wrongly labelled, not properly stored or subject to microbiological contamination could mean that the therapy will fail or that the patient will be harmed. The organization of the entire process chain is the duty of the oncology pharmacy practitioner; this includes standardization of the prescription, plausibility testing, procurement, selecting adjuvants, monitoring the preparation environment, the preparation itself, labelling, transportation, and storage. Cancer drug dosage can vary considerably depending on the diagnosis. The plausibility check carried out on the prescription by the oncology pharmacist, taking into account all relevant clinical parameters and the patient diagnosis, therefore plays a major role in safe medical treatment. If anything is unclear, this is immediately discussed with the physician who issued the prescription. If a need for consultation arises following prescription, the prescriber and/or patient is given enough relevant information in a comprehensible form to ensure safe use of the drug. The aseptic preparation of infusions, in particular, is essential in order to keep the product germ-free as there is no final sterilization. The oncology pharmacist has the task of ensuring that a preparation of impeccable quality is available at the right point in time.

Releasing the drug

An oncology pharmacist makes sure that the required data and labelling are provided when the drug is released. If the drug needs transporting, the pharmacist will take care that the quality and integrity of the drug are not impaired during this period.

Information and advice

The demands made of the pharmacy service during cytostatic therapy are not confined to instructions on correct administration or application. Information must also take account of any possible interaction with other drugs or supportive medication, even those acquired by patients themselves, and of the influence of diet. Given that such products, and any product-related problems or adverse side effects, can have a substantial impact on treatment and on the success of oncological therapies, the provision of detailed information and pharmaceutical support to patients is an important factor in therapeutic success. Competent advice, in which physicians and pharmacists concur, conveys a sense of therapeutic security, which is in the interest of the oncology patient. Boosting adherence by

optimizing the multi-professional management of medication, with the involvement of the pharmacist, plays a crucial part in this.

Applying IT solutions

The use of IT solutions in logistics, ordering, prescription, testing, preparation, documentation and invoicing can help to enhance therapeutic security. One factor of particular importance is the choice of the right software in the light of local requirements, processes and objectives. Because oncological pharmacists play a key role in the process and have competence in the use of drugs, they work in conjunction with clinical departments and administrative managers to ensure that appropriate, secure, user-friendly software is implemented.

Quality assurance and guidelines

Evidence-based algorithms and guidelines are an essential feature of quality assurance when using drugs in tumour and supportive therapies. Oncology pharmacists contribute specialist expertise to the inter-professional drafting of guidelines for the physicians and hospitals they supply. Their participation in therapeutic teams includes attending tumour conferences and working in specialist teams and quality task forces. They also conduct individual patient monitoring and pharmaceutical interventions in a context of collaboration between health professionals (e.g. ward visits and reviews of patient documents). Oncology pharmacists are furthermore also involved in implementing, regularly reviewing and further developing quality management systems in their own work environment.

Provision of courses

Coordinated information and education strategies are crucial to the correct, quality-assured use of drugs. The safety of patients and care staff dealing with potentially harmful medication is as much a part of this as the right use of the right drug for the right patient at the right time. As specialists in the administration of drugs, oncology pharmacists are committed to devising and offering courses for patients in the correct use of medication and appropriate conduct, and also courses for physicians and nurses.

Further training and continuous professional development

Further training and continuing professional development (CPD), like specialization in specific fields, lay the foundations for the services provided by oncology pharmacy practitioners. Just as important as regular further training for oncology pharmacists is further training for the health professionals they work with, such as pharmacy technicians. Suitable further training and CPD schemes are regularly provided and taken up.

Research and science

Data compiled in the course of the work of the oncology pharmacist can be used to generate observations about applications, to enhance processes and to analyse the optimum use of drugs. In this way, oncology pharmacists can make an active contribution to health services research.

Abstracted Scientific Content

Generics and off-patent biologicals for cancer treatment in developing countries

Cancer represents a significant, and growing, burden on healthcare systems around the world. Population growth and ageing will increase the number of new cancer cases in the coming years [1].

Furthermore, cancer is becoming a more widely recognized health issue in developing countries. The understandable focus on infectious diseases, such as human immunodeficiency virus (HIV), tuberculosis (TB) and malaria, has meant that an increasing burden of non-communicable diseases (NCDs), notably cancer, now needs urgent attention [2]. Generics and off-patent biologicals offer a lower-cost approach to treatment, but these drugs raise challenges of their own.

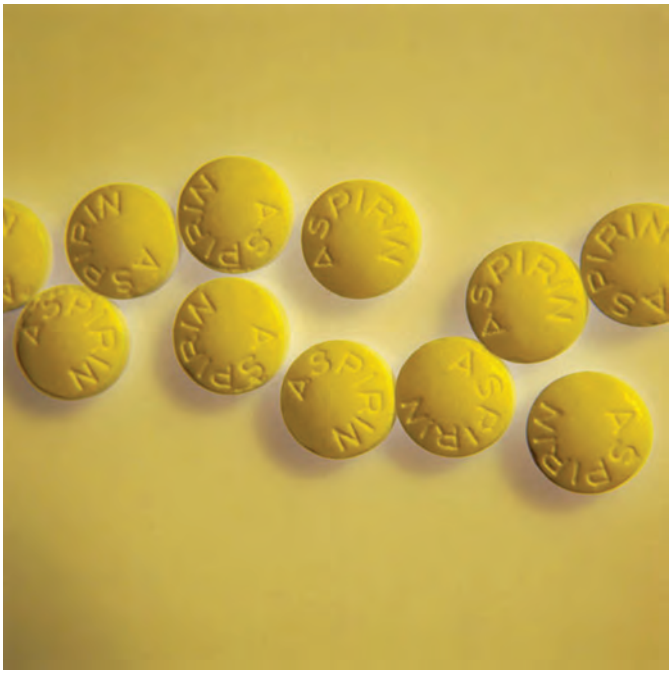
Cancer is a growing problem across Africa and other low-income regions, where resources for treatment and prevention can be pitiful and sometimes non-existent. A United Nations high-level summit on NCDs was held in New York, USA, in 2011 [3] to address the issues. As a result, it became clear that the complexities of cancer care require more focused and dedicated attention if progress is to be achieved quickly, especially in low-income regions such as Africa.

From the outset, there are problems with the collection of data – in countries preoccupied with the challenges presented by HIV, TB and malaria, there may be no cancer registries, few treatment facilities, a lack of cancer awareness and a lack of screening and diagnostic facilities.

Aside from this issue of scant information on the challenge ahead, the issue of cost plays a significant role in cancer care in developing countries. The cost of medicines can be a barrier to effective treatment in countries where patients with little money often have to pay for their own cancer care. Generics and off-patent biologicals could offer a sizeable reduction in cost, but these drugs are hit by many of the same issues as cancer treatment overall.

Regulation of all medicines, including generics and off-patent biologicals, is variable across developing countries. Sometimes medicines are not regulated at all. This is particularly dangerous in the case of generics and off-patent biologicals, where patients and prescribers need assurance that these products are equivalent to the more expensive brand-name drugs [4].

Dr Alex Dodoo at the University of Ghana Medical School in Accra, Ghana, and co-authors have examined the role of



generics and off-patent biologicals in low-income countries using Ghana as an example. Dodoo et al. discuss the options available to developing countries and healthcare facilities, and make recommendations for proper regulation of generic and off-patent biological oncology medicines while calling for special quality and safety monitoring of these products and a rigorous examination of their effectiveness in real-life settings. There is very little safety monitoring of generic oncology medicines. The temperature that medicines may be stored at in tropical countries is a particular – but often overlooked – concern.

The average cost of the most common generics used in Ghana is several times lower than that of branded products. Some branded products are six or more times the cost of generics. The cost comparison for Ghana applies equally to most of sub-Saharan Africa. The situation is even worse in countries where the supply chain is weaker. In fact, Ghana is, according to Dodoo et al., widely held to be among the 'better performing' countries. Only South Africa fares better, with its improved human, technical and financial resources [5, 6]. Other countries are far worse. With huge differences in price between branded and generic drugs the case for generics is clear. The case for off-patent biologicals in developing countries is less clear, since these products are more expensive and demand is low.

The downsides of generics and off-patent biologicals in developing countries are related to quality control. Where there is any question over the integrity of the product or the circulation of counterfeit or substandard products, the branded product obviously looks like a far safer option. There are many generics manufacturers, so faking oncology products is a growing problem. There are an estimated 1,000 manufacturers in generic oncology medicines in India alone, with only slightly lower numbers in China.

Importantly, argue Dodoo et al., there are not yet any World Health Organization (WHO) prequalified products for oncology medicines. It is left to national agencies or individual hospitals and pharmacies to source oncology medicines. For this reason, there is no impetus for generics manufacturers to seek WHO prequalification.

The authors agree that generic and off-patent biological medicines in developing countries, appropriately priced and quality controlled, have an obvious role to play in the management of established cancer. The availability of these medicines must be widely publicized, with a particular focus on potentially curable cancers [7].

There is also a need for the development of treatment guidelines for low-income countries [7]. Most countries still use cancer treatment guidelines drawn up by the major professional societies, which recommend therapy with what the authors call 'very expensive branded medicines which are stratospherically out of the reach of cancer patients in low-income countries.'

Dodoo et al. argue that now is the time to establish therapeutic guidelines developed by and aimed at cancer health professionals and their patients, to provide cost-effective solutions for cancer care in low-income countries. They also call on WHO to consider generic and off-patent biologicals medicines in its medicines prequalification scheme.

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