

Therefore, recent concepts aim at designing frameworks that integrate individual contributions of health care providers into the entire treatment path. Moreover, the patient can play an active role in this process. The concept of pharmaceutical care (also called 'medication management') involves pharmacists as they have a central position concerning drug dispensing and utilization. Important components of pharmaceutical care are a complete medication review and patient education on expected adverse drug events and their management. A model project at the University of Bonn has shown that pharmaceutical care for patients with gynaecological malignancies leads to a significantly higher response to antiemetic prophylaxis, better maintenance of quality of life during chemotherapy and improved patient satisfaction. In conclusion, new drugs and guidelines for supportive care provide the basis for an effective management of adverse drug events. Multidisciplinary approaches have a large potential to improve safety of systemic cancer therapy as well as quality of life of cancer patients.

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INVITED

#### Identification and prevention of drug-drug interactions

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Drugs utilized in oncology are often characterized by narrow therapeutic ranges and are associated with major toxicities. Great effort is made to find the optimal dosage for an individual patient in order to achieve the maximum benefit. Drug-drug interactions may have a major impact on the antineoplastic therapy, as they can cause changes in the pharmacokinetics and/or -dynamics of the administered drugs, which can significantly alter the efficacy or toxicity. However, they are not regularly taken into account in the decision upon an individual therapeutic plan in clinical practice yet. This is often due to limited available knowledge about the clinical relevance of drug-drug interactions and suboptimal access to this knowledge for the prescribing physician.

Scientific literature addressing drug-drug interactions in oncology has mainly reviewing character. The different types of interactions are introduced in general with only limited practical advice. Tables of drug-drug interactions that provide a synopsis of the clinical consequences of individual drug-drug interactions along with a recommendation for measures to be taken have been generated. Moreover, various databases refer to drug-drug interactions with antineoplastic agents. All these sources of information on drug-drug interactions refer to the same studies and case reports. Valuable evidence is scarce and the clinical relevance is often arguable. The judgement on the categorisation in terms of severity differs substantially. In a general comparison of internationally recognized drug-drug interaction databases only nine out of 406 (2.2%) as major classified drug-drug interactions, were listed in all four tested databases. This reflects the lack of both: Standardisation of the used terminology and reliable scientific evidence.

Moreover, there is little evidence about the prevalence of drug-drug interactions in oncology patients. Riechelmann et al. (2007) investigated potential drug-drug interactions among cancer patients. In 109 of 405 cancer patients at least one potential drug-drug interaction was identified (27%; 95% confidence interval [CI] = 23% to 31%). Overall 276 potential drug-drug interactions were observed whereof the main part (87%) involved non-anticancer agents such as warfarin, antihypertensive drugs, corticosteroids, and anticonvulsants, but some (n=36, 13%) involved antineoplastic agents. Of these 36 drug-drug interactions only one was classified as major (resulting adverse effect can cause permanent damage or life risk) the others were classified moderate (resulting adverse effect can harm and treatment is required).

These findings indicate that drug-drug interactions need to be considered in the planning of individual cancer treatments. Apart from the antineoplastic agents, the screening needs to include the entire medication of the patient. In order to judge the clinical relevance of the potential drug-drug interaction and resolve upon the adequate measures, more scientific evidence needs to be established in significant clinical trials and a close collaboration among physicians and clinical pharmacists with expertise in oncology should be intended.

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#### How targeted are "targeted therapies"? Side effects of approved targeted agents

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The development of targeted therapies is one of the major ongoing efforts in the treatment of cancer. Targeted therapy refers to treatment strategies

directed against molecular targets (tumour microenvironment interactions, and proliferative, survival, and cell death pathways) considered to be involved in neoplastic transformation. Such molecularly targeted agents (MTAs) are currently investigated in all treatment settings and have already gained regulatory approval.

By design, targeted therapy is intended to have negligible side effects in comparison to classical cytotoxic chemotherapy.

Cancer-related morbidity and mortality have been reduced, and many new treatment paradigms are emerging in which newer MTAs are used singly or added to traditional concepts of cytotoxic chemotherapy.

Despite the theoretical concept of drug targeting, which seeks to avoid collateral adverse effects normally associated with classical chemotherapy, the molecular targets of MTAs are also expressed in normal cells resulting in disruption of normal cellular function often with the consequence of adverse events. Members of the health care team now encounter toxicities well beyond the scope of the side-effect profiles of cytotoxic chemotherapy. The toxicity profiles unique to MTAs have surfaced as some of the most challenging side effects for clinicians, and it is especially important to be familiar with their presentation and management. The side effects of selected approved MTAs which have emerged with the introduction of the new therapeutic concept of drug targeting, e.g. skin (rash), hair/nail changes, gastrointestinal toxicity, interstitial lung disease (Anti-EGFR therapies) cardiac toxicities/CHF (Anti-HER-2 therapies), venous thromboembolism, hypertension, proteinuria, bleeding, gastrointestinal perforation, posterior leukoencephalopathy syndrome/RPLS (Anti-VEGF therapies) and hand-foot syndrome/PPE, rash, hypothyroidism, hair depigmentation (multitargeted kinase inhibitors) are presented and reviewed herein.

Many of these toxicities are likely to become more pronounced as cancer patients are older and more likely to have comorbidity than the patient populations included in the registration trials.

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#### Prevention therapy of fatigue

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**Objectives:** Cancer-related fatigue is a significant and distressing suffering problem for patients with cancer negatively affecting their physical and psychosocial function and reducing their quality of life. Prominent symptoms are exhaustion and lack of physical energy and aggravated in presence of progressive disease, pain, nausea and by cytotoxic therapy. The biochemical mechanisms behind fatigue are largely unknown and there is no widely spread effective treatment strategy. In several studies simple physical exercise has been tried. The epidemiology of fatigue was investigated in patients with different cancer diagnoses receiving cytotoxic drugs in an outpatient clinic. A sub-group of the patients were randomised to simple exercise as a mean to combat the fatigue.

**Methods:** The fatigue was assessed using an international fatigue scale, Fatigue Symptom Index adapted to Swedish use. Patients were followed up to three treatment cycles.

**Setting:** Out-patient ward for cytotoxic drug administration in university hospitals in Sweden and Denmark

**Results:** The prevalence of fatigue was 90% during the week following chemotherapy and declined over the following weeks. Rated fatigue showed large inter-individual variations but patients were statistically more fatigued during treatment than before. Other side effects, particularly depressed mood showed a strong correlation to fatigue, but also untreated pain, nausea and insomnia contributed significantly. Simple exercise seemed faster to cure cytotoxic induced fatigue, although individualized information was demanded.

**Conclusions:** Fatigue is a common and distressing side effect in most patients treated with cytotoxic drugs. Effective treatment is still lacking but positive effects were shown following simple exercise.

#### Scientific Symposium (Thu, 24 Sep, 09:00–11:00) Multidisciplinary teams in cancer care

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#### Multidisciplinary teams: what are they, how do they work?

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Most solid tumors, if there are not very early and much highly localised, are associated at time of diagnosis/first treatment with a significant number