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.

311 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.

312 INVITED

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 de-pigmentation (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.

313 INVITED

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

314 INVITED

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

of circulating tumor cells/DNA, and at lower or higher risk to develop metastases. Furthermore, several tumors are locally advanced and either resectable only with loss of function like in the gastrointestinal region, trunk or extremities, or unresectable. Furthermore, several tumors have measurable metastases; however, sometimes associated with a biology allowing long term survival after surgical excision. Local treatment by surgery, radiation or both is the best option for the primary tumor; however, inadequate to have impact on micro- or macrometastases and therefore on survival. Combined modality approach follows this systemic character of obviously localised solid tumors, or the need to enable better surgery with loss of function. Several trials have shown that in many tumor types combined modality is the treatment of choice, and should substitute the traditional approach with primary surgical treatment and – probably – postoperative decision on the treatment of residual micro- or macroscopic mass or potential macrometastases by "adjuvant" measures. The complexity of this multidisciplinary approach requires a high expertise of the treating oncologists whatever nature (surgical or medical oncology based) to decide the optimal treatment strategy *and* perform the best treatment modality with the optimal and necessary expertise. Multidisciplinary teams are necessary to define the optimal treatment strategy and – sequence before the first treatment procedure is performed to allow the application of the best treatment at the time of the primary treatment. But also for relapse or metastatic disease the same principals apply. The best approach for a multidisciplinary strategy decision is the interdisciplinary meeting of experts (multidisciplinary team), either by teleconference or preferably by direct interaction after having seen the patient. However, the multidisciplinary approach per se is only of relevance if the involved specialists are experts in their fields and are aware of the most recent and optimal treatment strategy in their individual discipline. Member of a multidisciplinary team, even if not experienced in part, will train together to improve the quality of the treatment and the cooperation. The multidisciplinary approach is today an essential requirement of the management of patients with solid tumors.

315 INVITED

The impact of MDT meetings on cancer patient management

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Multidisciplinary team working has been implemented in cancer care systems throughout much of Europe, the USA and Australia, without a clear evidence base for its effectiveness. The introduction of multidisciplinary teams has been based upon the rationale that as the management of cancer becomes more complex it is important to involve all key professional groups in individual clinical decision making for patients. The widespread introduction of multidisciplinary teams meetings illustrates a recurring paradox in the modern healthcare systems: we demand an evidence base for individual clnical decisions, but not for overall organisational decisions. Based on a review of the current state of knowledge regarding the effectiveness of multidisciplinary team working in cancer, it appears that delivering cancer care in multidisciplinary teams leads to more rigorous decision-making processes, but not yet necessarily more patient-centred care. There is accumulating evidence that the introduction of multidisciplinary teams meetings has improved outcomes for patients with cancer, as well as their experience of care; some teams work more effectively than others; and participation in multidisciplinary teams meetings may increase team members' job satisfaction.
It is too late for randomised trials to further evaluate the effectiveness of multidisciplinary teams; they are so firmly woven into the fabric of clinical practice that is beyond unpicking. There is nevertheless a large and challenging research agenda to demonstrate their benefit for patient care. Evidence for the variation in the quality of cancer multidisciplinary teams is mostly anecdotal. We need to identify dysfunctional teams and using, the lessons from effective teams, improve their cohesion and performance. For this we need to determine the characteristics of high or low performing teams. Although there is relatively little firm evidence, we have an emerging clinical consensus about the key features. We need to develop approaches to measuring team functioning reliably in terms of the quality of clinical decision-making, patient's experience of care, clinical outcomes and the working lives of team members. We need to devise and implement packages that support and sustain all those who participate in multidisciplinary teams, including the different medical specialists, nurses and coordinators. Lessons learned from cancer may support the implementation of multidisciplinary teamworking in other disease areas.

Scientific Symposium (Thu, 24 Sep, 09:00−11:00)
Communication crisis in oncology

316 INVITED

Managing the family which demands that the patient not to be told

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Requests by family members to withhold information relating to the patients diagnosis or prognosis are very common. Data from the recent ESMO survey of oncologists' communication indicates that these requests are far more common than requests from the patient to limit information to the told to the family. Though these requests are more common in non Western cultures, they are universal. Oncologists demonstrate marked variability in the way in which they respond to such requests. Although most oncologists will try to convince the family members that it is in the patient interests that they receive information about their illness, many comply with these request without verifying the patients communication preferences. ESMO data indicate that local professional norms regarding appropriate physician behaviors is the strongest determinant of how physicians respond to these requests, and that the physicians likelihood of cooperating with a collusive request is also influenced by their training in breaking bad news, the country in which they work and the frequency with which they are barraged to requests to withold information. Strategies will be presented to help clinicians work with families, explore the information preferences of their patients and manage the delicate balance of dealing with stakeholders who may have different desires an expectations regarding what should or should not be explained. Cultural and ethical issues wwil be adressed. Common errors in will be discussed: particularly those related to cultural stereotyping and avoidance.

318 INVITED

Raising end of life issues in patients with advanced cancer

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Increasingly, patients themselves are expected to decide when and how they die. Respect for patients' autonomy and shared decision-making are seen as requisites for high-quality care at the end of life. Therefore patients need to be optimally informed, even when they are incurable or terminally ill and confronted with medical decisions at the end of life. Some counties have drafted laws to guarantee this right on information for the terminally ill.
The aim of this presentation is to explore firstly, *what kind of information* physicians should give to incurable patients and what kind of information these patients are expecting to receive? Secondly, *how and when* physicians should raise end-of life issues and what *problems* they might encounter. Finally, possible solutions are suggested to improve the informing the incurable patient.
For incurable cancer patients, truth-telling includes information about the potential futility of curative treatment, their impending death, possible clinical pathways to death, and the possible impact of end-of-life decisions on these pathways. Research on the information preferences of advanced cancer patients show that most patients want to be fully informed about their chances of cure and life expectancy. Fewer but still a majority are open to information about palliative care and end-of-life decisions.
For the physician, telling the whole truth and nothing but the truth to terminal patients is not an easy task. While most physicians inform advanced cancer patients about diagnosis and treatment options they do this less with regard to prognosis, and far less with regard to end of life issues. Specific problems are a lack of patient-centeredness and information that is not tailored to the patients' age, educational level, culture and social background.
Possible suggestions to deal with these problems are to 'dose the truth' by giving bad news step by step, to regularly check the patient specific information preferences. Physicians should however be aware that providing 'optimal' information on end of life issues is challenging. They also should be prepared to avoid some common pitfalls.
Conclusion: while there is consensus about giving information on diagnosis and treatment options, information on end of life issues is much more problematic. Therefore this topic should receive more attention in communication training of caregivers.