a platinum in some centers, based on UK trials. Therefore several options can be proposed as reference regimens: the doublets of a fluoropyrimidine (5-FU or capecitabine) plus cisplatin (or oxaliplatin) or triplets of DCF or ECF (or ECC or EOC). The median survival is however usually still in the range of 8−11 months in most modern trials. Recently, the benefit of second line chemotherapy has been also demonstrated with a modest, but clear impact of a second line regimen (irinotecan) compared to BSC.
Although gastric cancer is relatively chemosensitive (RR 30−40%), the outcome remains poor. The complete response rate is extremely low and the response duration is short. Moreover the combinations regimens are relatively 'heavy' for patients often in poor general condition. There is therefore a clear need for better treatment options. The research on targeted agents has been intensified recently. The doublet of 5FU/capecitabine and cisplatin serves often as a backbone for the combination with novel targeted agents. A significantly longer survival has been shown for the combination of a fluoropyrimidine/cisplatin plus trastuzumab in patients with a HER-2 positive gastric or gastro-esophageal junction adenocarcinoma compared to the cytotoxic doublet alone. Several other targeted agents are under investigation in combination with cytotoxics (angiogenesis inhibitors, epidermal growth factor inhibitors or other anti-HER2 inhibitors) or also as monotherapy (mTOR inhibitor everolimus) and offer the hope for an improved outcome.

305 INVITED

Integration of targeted therapies

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Gastric cancer (GC) is the second leading cause of cancer mortality in the world. Advanced GC patients have a poor prognosis. Palliative chemotherapy improves survival, as compared with best supportive care. Although oxaliplatin, docetaxel and capecitabine have demonstrated activity in recent phase III trials the median overall survival (mOS) remains poor [1−2], therefore novel treatment options are urgently needed. New biological therapies aim to inhibit different targets of signal transduction pathways that are thought to be functionally selective or overexpressed in certain tumor types. GC belongs to these tumor models with overexpressed signal transduction pathways that are potential targets of a number of new drugs that are currently being in clinical development (see Table).
Recognition of the vascular endothelial growth factor (VEGF) pathway as a key regulator of angiogenesis has led to the development of several VEGF-targeting agents. At present, available clinical data on the use of angiogenesis inhibitors are limited to nonrandomized phase II trials. The combination of bevacizumab and chemotherapy showed encouraging efficacy results: response rate (RR) ~65%, median time to progression (mTTP) ~8 months and mOS greater than 12 months [3−4]. However, the favorable efficacy results were counterbalanced by bevacizumab-related toxicities: gastric perforation, thromboembolic events and hemorrhage. An ongoing international phase III trial (AVAGAST) will elucidate the role of bevacizumab in the first-line setting. Sunitinib and sorafenib, two multi-tyrosine kinase inhibitors (TKIs), are being tested in the first- and second-line setting with promising preliminary results.
The epidermal growth factor receptor (EGFR) is a tyrosine kinase receptor that belongs to the ErbB family. EGFR is highly expressed in patients with advanced GC. Several phase II studies combining cetuximab with either irinotecan/5-fluorouracil(5-FU)- or oxaliplatin/5-FU-based chemotherapy have demonstrated encouraging activity: RR $\approx$ 50−65%, and mOS of 9.5−11.7 months [5−6]. Unfortunately, all these trials are limited by their nonrandomized design. An ongoing international phase III trial (EXPAND) will define the role of cetuximab in combination with capecitabine and cisplatin in the first-line setting. EGFR inhibitors are also being evaluated as second-line treatment in advanced GC. The human epidermal growth factor receptor 2 (HER2) is overexpressed in ~22% of GC patients. In an international phase III trial of patients with AGC the addition of trastuzumab to standard first-line chemotherapy showed a statistically significant improvement in the mOS of patients with HER2-positive GC. Trastuzumab in combination with chemotherapy (5-FU or capecitabine and cisplatin) has become a new standard option for the first-line treatment of HER2-positive GC patients.
Other potential targets, including other receptors (c-Met, IGF-1R), proteins involved in cell cycle regulation, proteasome, matrix metalloproteinases, histone deacetylases and chaperone proteins, have been demonstrated to be critical in the balance of the tightly regulated pathways that promote either cell survival or cell death. New drugs are being developed against those specific targets and preliminary clinical and clinical evaluation of these compounds is expected in the near future.

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Scientific Symposium (Thu, 24 Sep, 09:00−11:00)
Fertility and sexuality: the development of oncosexology

306 INVITED

Fertility: Understanding the options after cancer treatment

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Because most people with cancer are over age 50, fertility is mainly a concern for those diagnosed in childhood, adolescence, or young adulthood. It is interesting to compare the explosion of interest and research funding focused on fertility preservation, compared to the relatively small increase in attention to assessing or treating sexual dysfunction in men and women with cancer–problems that affect at least 50% of survivors, are profound, and do not improve over time without intervention.
However, cancer-related infertility also can cause profound emotional distress that does not disappear with time. In a recent survey of over 250 women diagnosed at age 40 or less, those who desired a child at the time of cancer diagnosis and were unable to have one were significantly more distressed at a mean of 10 years after cancer treatment than women whose childbearing was not interrupted. Smaller studies of men also have suggested long-term grief over infertility after cancer.
Fortunately, sperm banking is a practical option for 90% of men diagnosed with cancer. Although the choices for women are more expensive and less reliable, recent advances in vitrification of oocytes, use of immature oocytes matured in the laboratory, and banking/autotransplantation of ovarian tissue are gradually approaching the efficacy of ovarian stimulation with cryopreservation of embryos. Some cancer treatments have also been modified to spare fertility, for example less toxic chemotherapy for Hodgkin disease, ovarian transposition before pelvic irradiation, or conservative surgeries like trachelectomy or removal of only one ovary for low-stage ovarian cancer.
A major problem is that choices about preserving fertility must be made at the time of maximum stress, when a cancer diagnosis is recent and treatment planning is underway. It is difficult for younger patients to understand their disease and treatment plan, let alone to take the time to weigh the costs and benefits of options to store gametes or embryos for the future. Parents may also have to make decisions for their very young children that involve an additional minor surgery to collect tissue. Most settings do not have counselors with time to teach patients about their options much less to help them sort out their emotions.
After cancer treatment, some men and women will remain fertile or will recover fertility. They often have intense anxiety about whether their offspring will have special risks for cancer or will have a greater chance of a birth defect related to the parent's cancer treatment. Those relatively few who carry a mutation involved in a hereditary cancer syndrome now have the option of using prenatal diagnosis or preimplantation genetic diagnosis to avoid passing on their damaged gene. For women, another worry is whether pregnancy could provoke a cancer recurrence. Women are less aware of risks that subclinical cardiac or pulmonary impairment could become life-threatening during the stress of a pregnancy.
For those who remain infertile, adoption is not easy. International adoption countries may exclude cancer survivors, make them wait 5 years out, or want a letter from the oncologist. Domestic agencies and birth mothers also may be loathe to give a child to a couple when one spouse has had cancer. Adoption is also quite expensive in most Western countries. Third-party reproduction includes use of donated sperm, oocytes, or embryos, and/or a gestational carrier. Only a minority of cancer survivors are willing to consider these paths to parenthood.

307 INVITED

Talking about sex: identifying psycho-sexual concerns in the clinic

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Background: Multi-modal cancer therapy has led to significant improvements in disease control and survival. However this comes at a price in

relation to the number of people who experience treatment-related late effects months or years after cancer treatment is completed.
Sexual well-being is identified as a core element of quality of life for people affected by cancer, particularly those receiving treatment for malignancies involving the pelvic organs. Yet clinicians continue to experience significant difficulties talking to patients about the sexual consequences of cancer and its treatment. This paper presents selected data from two studies that explored the organisational, health professional and patient characteristics that act as barriers or enablers to the discussion of sexual concerns in the clinic.
Material & Methods: These two studies used participant observation of radiotherapy follow-up clinics and one surgical urology clinic plus interviews with health professionals, patients and partners to explore the context and content of discussions about male and female sexual morbidity after treatment. Participating patients were women treated for gynaecological or ano-rectal malignancy and men treated for prostate cancer.
Results: In the women's study consultations (n = 69) were led by medical staff and focused largely on disease surveillance, specific aspects of toxicity monitoring and managing active symptoms. Vaginal toxicity was discussed less frequently (42%) than bowel (81%) or bladder (70%) toxicity and sexual issues were discussed in only 25% of consultations. In the men's study (n = 60) content was also set by medical staff and disease and toxicity monitoring dominated discussions, yet men's sexual concerns were addressed in 53% of consultations.
In the urology clinic there was a proactive approach to the pharmacological management of erectile dysfunction that was considered a routine part of urological practice but this was not mirrored in the radiotherapy clinic. In both studies the broader aspects of male and female sexual expression that can be altered by cancer treatment such as desire, orgasm, sexual satisfaction or relationship impact were rarely discussed. Furthermore, partners were not actively involved in the consultation process even when present.
Health professionals felt inhibited discussing sexual concerns with couples, older patients, patients from an ethnic minority background, those with later stage disease, co-morbidities or a number of active problems. Service factors also adversely affected capacity to address the sexual recovery of patients and their partners. This was particularly the case with regard to time constraints, clinician's lack of knowledge regarding the availability of specialist resources and a lack of clear referral pathways both within and beyond the cancer centre.
Conclusions: If prompt and accurate identification of treatment related sexual concerns are to lead to appropriate clinical intervention or further referral these findings suggest change needs to take place at both an individual practitioner and service design level. Questions remain regarding the most appropriate time and context to raise sexual concerns within the constraints of conventional medical follow-up. These findings are important for the development of supportive care and cancer survivorship services and for the training of health professionals engaged in post-treatment toxicity assessment, patient information and support.

308 INVITED

Therapeutic approaches for sexual dysfunction in men treated for prostate cancer

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Prostate cancer (PCa) affects the lives of thousands of men across Europe and the USA, and is the most frequent non-skin male malignancy in Western countries. PCa incidence is greatly increasing because of the worldwide trend for increased longevity in the general population, and the routine prostate-specific antigen tests. Both external-beam radiotherapy (EBRT) and brachytherapy (BT) can be offered as curative options. Although it is commonly believed that the incidence of erectile dysfunction (ED) after radiotherapy is lower than after surgery, percentages reported in the literature vary from 6 to 84% after EBRT to 0−51% after BT. Ejaculation problems and a decrease in libido occur also frequently.
The etiology of ED after radiotherapy for PCa is multi-factorial. Vascular, neurogenic and psychogenic factors are equally important. The most likely mechanism is a damage of the vasculature of the neurovascular bundles and fibrosis of the penile bodies. The time elapsed between radiation therapy and evaluation of erectile function has to be considered; it takes at least 18−24 months before ED rates reach a maximum.
Before the introduction of oral drugs to treat ED, the only therapeutic modality for post-radiation ED was the use of intracavernosal injections that were effective in most of the patients. Two studies have investigated the use of PDE5 inhibitors for treatment of post-radiation ED. In the first study, 45% of the patients after sildenafil and 8% after placebo reported improved erections ($p < 0.001$). Successful intercourse was reported in 55% of the patients after sildenafil versus 18% after placebo ($p < 0.001$). In the second study, 67% of the patients after tadalafil and 20% after placebo reported improvement of erectile function with tadalafil ($p < 0.0001$). Successful intercourse was reported by 48% of patients after tadalafil versus 9% after placebo ($p < 0.0001$). Side effects for both studies were mild or moderate. Sexual dysfunction after radiotherapy for PCa has been often underestimated. Patients should be offered sexual counseling, and informed about effective oral drugs to treat ED.

309 INVITED

Education and training staff: how to develop and integrate oncosexology?

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Cancer and its treatment have extensive influence on sexuality and intimacy and as such seriously impair the quality of life of patient and partner.
In good cancer care 1. the topic of sexuality and intimacy is effectively addressed; 2. problems in these areas are taken seriously and handled well by the various oncology professionals, and 3. when necessary, patient or couple are referred to a sexology professional with enough relevant oncosexological expertise.
These three fields require an adapted set of knowledge. The first two fields require also a set of attitude and skills, that most oncology professionals do not have at their disposal. At the same time many professionals believe that they should possess such skills and attitude. This situation can constitute a major obstacle for changing the tradition of professional silence when intimacy and sexuality are at stake in the cancer population.
Oncology can learn from physical rehabilitation, where we developed extensive experience in the training the various professionals in matters of sexuality. Knowledge is a small part of what is needed. The majority of time is spent on training skills. This starts with 'talking sex' in role-playing and then with ones own patients. Attitude turns out to follow automatically during that training process.
An important part of change is developing the group-competence of discussing sexual topics in a professional way within the multidisciplinary team or unit.
Connected to this process the oncology group/unit should connect with sexology professionals who develop the necessary knowledge, skills and attitude to deal with cancer patients.

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Scientific Symposium (Thu, 24 Sep, 09:00−11:00)
Monitoring and management of adverse drug events

310 INVITED

Management of adverse drug events

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Systemic cancer therapy is associated with multiple risks for the patient. Most cancer patients under systemic treatment experience adverse drug events such as constipation/diarrhea, nausea/vomiting, fatigue, myelosuppression, skin reactions, anorexia, and mucositis. These adverse events are usually predictable by available clinical data and can often be prevented or ameliorated.
Nevertheless, the minimisation of toxic effects of anticancer therapy is a challenging task. During the last two decades, several new drugs have become available for supportive care, e.g. 5-HT_3 and neurokinin-1 receptor antagonists for the prevention of nausea and vomiting, or palifermin which reduces the incidence and severity of mucositis. In addition, evidence-based clinical practice guidelines have been developed and implemented, particularly for antiemetic prophylaxis and therapy. Several studies have shown a positive effect of these guidelines on both clinical and economic outcomes. Current research particularly aims at developing measures against other treatment-associated symptoms, e.g. the fatigue syndrome. As a consequence, adverse drug reactions are increasingly 'manageable' leading to a higher quality of life for the patient.
However, special efforts have to be undertaken in order to ensure that an individual patient benefits from this development. In terms of cancer many disciplines contribute to the care process. Thus, cross-profession and cross-sector cooperation is crucial in order to improve information flow and to exploit the specific knowledge of each profession.