sorafenib, (pancreatic or hepatocellular carcinoma), reported by others, have indicated suppression of disease progression and increased survival times. Reasons for the different results are unknown but highlight the need for more studies.
Conclusions: A convincing biologic rationale for using antiangiogenic drugs to treat *early* stage microscopic metastatic disease has yet to be established. More intensive preclinical efforts to model adjuvant therapy (and compare the results to those obtained in metastatic models) in different disease indications are urgently needed, not just for antiangiogenic drugs but other therapeutic modalities as well.

References

Ebos & Kerbel "Antiangiogenic therapy: impact on invasion, disease progression, and metastasis." *Nat Rev Clin Oncol*. 8: 210–221, 2011.

76 INVITED
Biomarkers & Angiogenesis

Abstract not received

Scientific Symposium (Sat, 24 Sep, 16:00−18:00)
Probiotics, Calories and Cancer Care

77 INVITED
Probiotics and Colon Cancer Prevention

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While a myriad of healthful effects have been attributed to probiotic bacteria, a controversial one is that of anticancer activity. Reports in the literature, regarding the anti-coloncancer effects of lactic acid bacteria, fall into the following categories: *in vitro* studies and *in vivo* studies in laboratory animals; dietary intervention studies in human volunteers and epidemiological studies correlating colon cancer and certain dietary regimes. It must be emphasised that, to date, there is no direct experimental evidence for colon cancer suppression in humans as a result of consumption of lactic cultures in fermented or unfermented dairy products. However, there is a wealth of indirect evidence, based largely on laboratory studies, in the literature and this will be summarized in my presentation. At present, the results from the epidemiological studies do not appear to support the results from experimental studies. The reason for this is unclear but might be explained by differences in bacterial strains, with the strains being used in the experimental studies surviving better in the gastrointestinal tract than the strains present in fermented dairy products. It should also be emphasized that great care must be exercised in extrapolating the results of *in vitro* and animal studies to the human system. It must also be pointed out that the precise mechanisms by which probiotic bacteria may inhibit colon cancer are presently unknown and these will be discussed. However, even with these reservations in mind, the use of lactic cultures for human colon cancer suppression holds promise and deserves more scrutiny. The latter should involve carefully designed human dietary intervention studies to corroborate the wealth of experimental studies. I will report on such an intervention study that was recently completed as part of an EU funded project "Synbiotics and Cancer Prevention in Humans".

78 INVITED
Assessment and Management of Gastrointestinal Symptoms After Cancer Treatments

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Background: Chronic GI symptoms significantly impacting on quality of life after cancer therapy, affect more people annually than are diagnosed with Ulcerative Colitis **and** Crohn's disease together. Yet, whilst almost every hospital has one or more specialists in Inflammatory Bowel Disease, few patients with treatment related GI symptoms are referred to a gastroenterologist. When they do, most meet a professional who is not trained to manage their symptoms. As a result ineffective or dangerous treatments are frequently prescribed.
Results: The current priority of follow up after cancer is to detect disease recurrence. Patients will therefore often not tell their oncologists about symptoms if they do not feel they are due to cancer. Patients frequently believe that symptoms after treatment are inevitable, that little can be done and are embarrassed to seek help. Robust strategies to detect patients who need help are urgently required and every unit must develop reliable referral pathways to gastroenterologists who in turn need training to manage post treatment symptoms optimally.
The gastrointestinal tract is only able to respond to physical insults in a limited number of ways. Identical symptoms can arise from many different causes. The majority of patients with new onset gastrointestinal symptoms will have more than one cause for symptoms, surprisingly often not even related to their previous cancer therapy. Empirical treatment often fails to anticipate the true cause of symptoms and for this reason may be ineffective. A systematic, logical, physiological investigative approach will frequently allow straightforward, helpful and sometimes curative treatments to be prescribed.
Conclusions: It is no longer acceptable to ignore the GI morbidity of cancer therapies, which is the current norm for the vast majority of patients. A completely new approach to the management of chronic GI side effects of cancer treatment is required. Large numbers of patients are affected. Most patients can be helped or cured. Some problems are preventable.

79 INVITED
Continence Interventions − Bowel Problems

C. Taylor[1]. [1]*Kings College, Macmillan Education Unit, London, United Kingdom*

There is increasing evidence to indicate that cancer survivors have concerns and physical problems which are not being adequately addressed. One of the main difficultes which individuals diagnosed with colorectal cancer treatment can experience is an alteration in their bowel function. In particular, it is known that the majority of those recovering from rectal cancer surgery will have to cope with undesirable bowel symptoms; urgency, frequency, stool fragmentation and/or incomplete bowel emptying plus changes in levels of continence. Bowel continence embraces the ability to control flatus, liquid and stool.
This presentation will consider the particular effects for individuals suffering from anterior resection syndrome who following a low rectal resection may for example manage to remain continent to stool but when unable to control the release of flatus in public, feel acutely embarrassed. Another patient with this condition may manage to control their stool by day but then experience an urgent need to defecate at night which if not responded to in time may 'cause an accident to happen'. These bowel symptoms can be particularly problematic post stoma reversal and also for those post multimodal treatment i.e. after receving a combination of chemotherapy, radiotherapy and surgery. These symptoms have to date not been well articulated.
These symptoms may persist for a few weeks to months and although for many there will be improvement over time, there is unlikely to be a return to the same function relied upon pre-treatment. It seems that despite the potential for such symptoms to adversely affect quality of life, many individuals do not receive the help they need to manage them. It is suggested that without appropriate intervention these symptoms can become a late treatment effect which then impact on other health domains and disrupt normal daily functioning.
At present in the UK the nature of bowel assessment and frequency of monitoring during the follow-up period is subject to local service delivery models and variation exists. A more systematic approach to bowel assessment and management following such treatment is advocated. These is clear benefit in early intervention (Camelleri-Brennan 2002) but it is often not sought or offered. Work is underway within the National Cancer Survivorship Initiative within the UK to improve the after-care these patients receive, testing new models of assessment, integrating improved care planning and information exchange between care providers and the patient at the end of treatment. In line with these developments, this presentation will indicate ways we can ameliorate bowel continence problems, in order to enhance their cancer survivorship experience.

80 INVITED
The Experience of Living With a PEG

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Previous research has shown that appropriate nutritional interventions reduce the risk of surgical complications *(Bozzetti, 2001)* shorten the recovery time and the length of hospital stay *(Pirlich, 2006),* improves tolerance to treatment *(Braga, 2002)* and increase the chance of survival *(Stratton, 2007).* This improved awareness of the relevance of nutrition support in the treatment of diseases has contributed to a rapid increase in the use of percutaneous endoscopic gastrostomies (PEG) worldwide *(NCEPOD, 2004, Gauderer, 2002).*
For patients with preserved intestinal function but with inadequate or no independent oral food intake, enteral nutrition therapy with PEG is one of the preferred alternatives *(Kurien, 2010, ESPEN guidelines, NICE guidelines)* to nutrition support. The PEG is discrete and does not interfere with speech or swallowing *(Gomes, 2010)* but the social role with a meal

disappears with no pleasure on mealtime. The interference with family life seems to be of greater importance than PEG related problems of discomfort, leakage or blockage *(Rogers, 2007)*.
Since the insertion of the PEG is a minor surgical procedure, there is a common belief that it is harmless with a low impact on daily life. However, it transfers the treatment responsibility and activity to patients and their spouse to a large extent. Moreover, it moves treatment from inpatient settings to home with a need for care of by district nurses and general practitioners. Preliminary results from a study conducted in our group confirms that a majority of patients handle the PEG feeding by them selves, but those in need for assistance were mainly supported by their spouse and more seldom from district nurses. This might reflect that the patients' wants to live as normal a life as possible, and according to previous research, the nurses find this as a burdensome responsibility to fulfil *(Strandberg, 2003, Scott, 2005, Jordan 2006, Madigan 2007, Millard 2006, From, 2009, Bjuresäter, 2010)*. Studies on patients' experience of living with a PEG, is mostly qualitative with small sample sizes, but they all addresses the same problems of dependency, responsibility, time and skills shortages. Even though PEG is part of established practice there are obviously some flaws regarding the use of it. This highlights the need of an improved care chain for patients living with a PEG.

Scientific Symposium (Sat, 24 Sep, 16:00−18:00) **Head and Neck: What Next in Biologically Targeted Therapy?**

81 INVITED

Stem Cells in Head and Neck Cancer

D. Zips[1], M. Baumann[1], M. Krause[1]. [1]*TU Dresden OncoRay, Radiation Oncology UK Carl Gustav Carus, Dresden, Germany*

Despite improved management of patients with head and neck cancer, locoregional failure or distant metastases after high-dose radiotherapy or combined treatments occur in a substantial proportion of patients. Recent preclinical and clinical evidence suggests that among other radiobiological mechanisms the number of cancer stem cells (CSC) and their radiation sensitivity might contribute to treatment failures. Of particular interest and subject of intense research are putative CSC markers such as CD44 for prediction of response and CSC-related pathways of radiation response for novel approaches of molecular targeted drugs. It has been shown for breast cancer and glioma cells that radiation sensitivity in CSC-marker positive cells is governed by molecular pathways which might be distinct from CSC-marker negative cells. Such a differential response or direct targeting of CSC-marker molecules may offer new opportunities in molecular targeting. The CSC concept and recent data with relevance for radiation oncology will be discussed.

82 INVITED

New Targeted Drugs − Biological Agents

K. Harrington[1]. [1]*Institute of Cancer Research, Targeted Therapy Laboratory, London, United Kingdom*

For head and neck cancers, the outcome of treatment is largely dominated by the success or failure of attempts to control the primary lesion and its locoregional extent. Radiotherapy (RT) is a key component of this treatment, but frequently fails to achieve locoregional control. By combining cisplatin chemotherapy with RT, we can improve tumour control probability (TCP) but this comes at the cost of increased toxicity from non-specific sensitisation of normal tissues. Indeed, it is widely accepted that most combination chemoradiation regimens are already delivered at or close to the limits of normal tissue tolerance and this limits further development of this strategy. The greatest opportunity for using RT more effectively in the future lies with the development of targeted drugs to achieve tumour-selective radiosensitisation. Promising strategies based on monoclonal antibodies or small molecules that act as inhibitors of EGFR, HSP90 or Chk1 will be discussed. In addition, the potential for rational patient selection (based on HPV status) for treatment intensification and de-intensification strategies will be discussed. These agents may also play an important role in palliative treatment of relapsed disease. In addition to these conventional agents, a range of novel biological therapies based on replication competent oncolytic viruses are now in phase I-III clinical trials. Data on our programme of work with oncolytic reovirus (Reolysin) and oncolytic herpes simplex virus (OncoVEX-GMCSF) will be also be presented.

83 INVITED

Management Based on Results of Functional Imaging

Abstract not received

84 INVITED

Targeted Agents in Salivary Gland Tumours

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The efficacy of molecularly targeted agents in recurrent or metastatic malignant salivary gland tumours (MSGT) has been modest but the momentum to mount clinical trials in these rare tumours warrants continued support. Typically, due to the histological heterogeneity of this diagnosis, most MSGT studies divide patients into adenoid cystic carcinoma (ACC) versus non-ACC cohorts. Molecularly targeted agents such as the epidermal growth factor receptor (EGFR) inhibitors, HER-2 targeting agents and multi-kinase antiangiogenic inhibitors have been evaluated in single-arm phase II trials of advanced MSGT, with limited evidence of tumour shrinkage and variable degrees of disease stabilization. As agents with novel mechanisms of action (e.g. agents modulating cancer stem cells, apoptosis, DNA repair, cellular adhesion, etc) enter preclinical and clinical development, there needs to be an efficient approach to determine their activity in MSGT. Clinical trials of combinations of molecularly targeted agents to overcome resistance via compensatory pathways are also emerging in the field of experimental therapeutics. Preclinical models that can reliably predict efficacy of new agents alone, in combination with other agents or with radiation, are lacking. The design of early phase clinical trials in MSGT needs to be reinvigorated to proficiently screen out inactive agents while selecting the precious few that justify late phase assessment. Through targeted and next-generation sequencing of the cancer genome, specific somatic mutations and other genetic aberrations that drive many human malignancies are increasingly being identified. This rapidly growing knowledge and technology in cancer genomics has brought promise to a new era of personalized medicine that may ultimately benefit the selection of therapies in MSGT.

Scientific Symposium (Sat, 24 Sep, 16:00−18:00) **Clinical Trial Methodology**

85 INVITED

How to Optimise the Preclinical to Phase I Transition?

Abstract not received

86 INVITED

Novel Designs and Alternate Endpoints for New Drug Studies

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The rate of novel antitumour agents failing at phase III is high in comparison to other therapeutic areas, resulting in registration of less than 10% only. In the era of targeted therapies, the proof of mechanism of action (MoA) on the base of a qualified assay became part of the phase I and may even be anticipated by so-called phase 0 trials, assessing pharmacodynamic responses up-front. Phase I cohorts should be enriched for the target population to allow the detection of the underlying MoA, but should not be limited to it. Biomarker studies have to be integrated into the phase I process for patient selection and assessment of the MoA. Once, the recommended dose for phase II has been reached, enriched expansion cohorts are to be set up to assess antitumour activity already early in the development as demonstrated for hedgehog inhibitors in basal cell carcinoma (Von Hoff et al, NEJM 2009). The optimal time point and methods of patient enrichment are debatable. The ultimate goal of the phase I trial procedure is to guarantee that the number of patients treated at sub- and/or supra-therapeutic doses is minimized. Whereas the accelerated titration design, which successfully avoids unnecessary toxicity, is widely used, the more individualizing continual reassessment method has not found wide acceptance so far due to its immanent complexity necessitating biomathematical support on-site. Whereas the goal of classical non-randomized phase II trials was to gain an estimate of response and safety, new phase II trial methodology aims at the evaluation of the therapeutic activity and toxicity in the context of the target modulation. Examples are the development of vandetanib in *RET*-mutated medullary thyroid carcinoma (Wells et al, JCO 2010) and that of crizotinib in *EML4-ALK* gene fusion positive NSCLC (Bang et al, Proc ASCO 2010). Adaptive trial designs in the phase II as exemplified by the BATTLE trial, coupling real-time molecular interrogation of cancer specimens with an adaptive Bayesian clinical trial design, merit systematic integration(Kim et al, Cancer Discovery 2010). For cytostatic antineoplastic compounds with PFS as endpoint, the use of the randomized discontinuation design during phase II