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

L. Siu[1]. [1]*Princess Margaret Hospital, Division of Medical Oncology and Haematology, Toronto, Canada*

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

C. Dittrich[1]. [1]*LBI-ACR Vienna and ACR-ITR Vienna, KFJ-Spital/3rd Medical Department Centre for Oncology and Haematology, Vienna, Austria*

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