the patient. Improvement of salivary function after radiotherapy may lead to better swallowing function. In this study we focus on the correlation between prospectively measured parotid salivary output and quality of life items concerning xerostomia and swallowing based on the EORTC H&N questionnaire.
Materials and Methods: Since 1996 we prospectively perform measurements of stimulated parotid salivary output, using Lashley-cups, before and 6 weeks, 6 months and 1 year after radiotherapy. For 167 patients the relative parotid salivary output is correlated with the mean parotid dose and quality of life measurements using the EORTC H&N quality of life questionnaires. The tumour was located in the larynx, pharynx, oral cavity and other locations in 22%, 56%, 10% and 12%, resp. Advanced T-stage and positive nodes were noted in 31% and 50%, resp. Conventional RT, IMRT and Chemo (IMRT) RT was used in 91, 55 and 21 patients, resp. The mean dose of the parotid glands was 34 Gy. A parotid flow complication was defined as <25% of pre-RT flow. For analysis three groups were defined: both (A), one (B), or no parotid glands (C) with a flow complication.
Results: One year after radiotherapy the distribution of group A, B, and C was 27%, 34% and 39%, resp. At one year, on a scale of 1 (not at all) to 4 (severe) the distribution for complaints of dry mouth was 21%, 27%, 33% and 19%, and of sticky saliva 37%, 29%, 25% and 9%, respect. For the same scale, difficulty in swallowing solid food was seen in 50%, 27%, 13% and 11%, resp. Tube feeding was given in 5%, namely after chemoRT (18%). In univariate analysis, the grade of difficulty in swallowing solid food significantly correlated with therapy, tumor localization (grade 4 20% oropharynx, 0% larynx), N-stage, dry mouth and sticky saliva. After logistic regression three independent variables remained: treatment ($p = 0.006$), dry mouth symptom ($p = 0.001$), and, marginally, the number of parotid glands with a complication ($p = 0.04$).
Conclusion: One year after RT swallowing complaints strongly correlated with complaints of a dry mouth, however not with complaints of sticky saliva. Sparing one or both parotid glands was marginally related to swallowing complaints. Sparing one submandibular gland may further decrease dry mouth complaints, and is subject of on-going research.

8513 POSTER

Image guidance with bone matching alone is insufficient for conformal radiation of early glottic cancers − an analysis of laryngeal positional uncertainty based on daily cone beam CT

I. Mallick[1], S. Breen[2], J.N. Waldron[1]. *[1]Princess Margaret Hospital, Radiation Oncology, Toronto - Ontario, Canada; [2]Princess Margaret Hospital, Medical Physics, Toronto - Ontario, Canada*

Background: Highly conformal radiation therapy for early glottic cancers will require accurate daily image guidance to be safe and maximally spare voice and swallowing function. This study uses daily cone beam CT (CBCT) imaging to investigate the daily positional uncertainties of the glottis during a course of treatment and its relationship to the skeletal anatomy.
Methods: 160 CBCT image-sets of 8 patients with T1aN0M0 glottic cancer treated with intensity modulated radiation therapy (IMRT) with daily kilovoltage CBCT were used in this offline study. Daily setup variations were measured with the Elekta Synergy XVI 4 ® platform using an automatic bone match and a manual match of laryngeal soft-tissues by a radiation oncologist. Discrepancies between these matches were calculated to evaluate the extent of laryngeal displacement in relation to vertebral bodies. An internal target volume (ITV) was generated using the formula suggested by van Herk (2000).

Table 1: Setup errors with different image match protocols

Axis	Manually verified soft-tissue match	Automatic Bone Match	Setup disparity between manual and bone match
ML			
Mean	0.7 mm	0.8 mm	0.7 mm
Range	0.0−2.3 mm	0.1−2.9 mm	−0.1 to +0.7 mm
SE	0.9 mm	1.0 mm	0.4 mm
SI			
Mean	1.1 mm	0.0 mm	2.5 mm
Range	0.1−3.9 mm	0.3−2.9 mm	−1.0 to +5.9 mm
SE	2.0 mm	1.7 mm	2.6 mm
AP			
Mean	0.3 mm	0.7 mm	1.0 mm
Range	0.1−2.0 mm	0.1−1.7 mm	−0.6 to +1.4 mm
SE	0.9 mm	0.9 mm	0.3 mm

SE: systematic error

Results: The mean translational setup errors in the mediolateral (ML), supero-inferior (SI) and antero-posterior (AP) directions for each type of match and the anatomical discrepancies are summarized in Table 1. Errors were most pronounced in the SI axis. There was an anatomical disparity in the bone-match compared to the manual soft-tissue match that was most pronounced in the SI axis (mean 2.5 mm, range −1.0 to +5.9 mm, SD = 2.6 mm) suggesting an independent daily positional variation of the laryngeal soft-tissues relative to the vertebral bodies. The calculated ITV margins for the larynx in relation to the bone match were 2, 8 and 2 mm in the ML, SI and AP axes.
Conclusions: There is a considerable daily variation in laryngeal position in relation to the vertebral anatomy. Image matching based on skeletal anatomy alone is inadequate and should not be regarded as a surrogate for laryngeal position. Image guidance and manual verification of soft-tissue setup errors is essential in order to proceed with highly conformal radiation therapy of early larynx cancer.

8514 POSTER

SPECTRUM, a phase III trial for patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck (SCCHN) receiving chemotherapy with or without panitumumab: interim pooled safety analysis

J. Stöhlmacher[1], I. Davidenko[2], E. Winquist[3], L. Licitra[4], K. Skladowski[5], T.E. Ciuleanu[6], R.R. Kumar[7], P. Foa[8], J. Gansert[9], J.B. Vermorken[10]. *[1]Universitätsklinikum Carl Gustav Carus, Onkologische Tagesklinik / Onkologisches Forschungslabor, Dresden, Germany; [2]Krasnodar Regional Oncology Dispensary, Krasnodar, Russian Federation; [3]London Health Sciences Centre, Dept. of Oncology, London Ontario, Canada; [4]Istituto Nazionale Tumori, Head and Neck Department, Milano, Italy; [5]Instytut im. M. Sklodowskiej-Curie, I Klinika Radioterapii, Gliwice, Poland; [6]Oncology Institute "Ion Chiricuta", Medical Oncology, Cluj Napoca, Romania; [7]Regional Cancer Centre Medical College Campus, Clinical Oncology, Trivandrum, India; [8]San Paolo Hospital, Department of Oncology, Milano, Italy; [9]Amgen Inc., Oncology Therapeutics, Thousand Oaks CA, USA; [10]Universitair Ziekenhuis Antwerpen, Department of Oncology, Edegem, Belgium*

Background: Panitumumab (pmab) is a fully human monoclonal antibody against the epidermal growth factor receptor (EGFR), a therapeutic target in patients (pts) with SCCHN. SPECTRUM is assessing the safety and efficacy of pmab + standard platinum-based chemotherapy (CT) in pts with recurrent and/or metastatic (R/M) disease (ClinicalTrials.gov ID: NCT00460265; sponsor: Amgen Inc).
Methods: This is a global, phase III, open-label study. As of March 2009, the trial has completed enrollment of 658 pts. Pts with R/M SCCHN were randomized (1:1) to receive cisplatin (100 mg/m^2) IV on day 1+5 FU (1000 mg/m^2) continuous IV daily on days 1−4 Q3W for up to 6 cycles ± pmab (9 mg/kg). Pts receiving pmab without disease progression after 6 cycles may continue pmab monotherapy until disease progression. Substitution of carboplatin (AUC 5) is allowed for specific toxicities. Primary endpoint is overall survival. Key secondary endpoints include progression-free survival, response rate, and safety. This trial is overseen by an independent Data Monitoring Committee (DMC).

AEs of Interest[a] (N = 446[b])

AE (MedDRA terms)	Any grade, n (%)	Grade 3/4, n (%)
Nausea	248 (56)	24 (5)
Skin and subcutaneous tissue SOC[c]	207 (46)	31 (7)
Neutropenia	206 (46)	141 (32)
Vomiting	177 (40)	23 (5)
Stomatitis/mucosal inflammation	172 (39)	40 (9)
Anemia	166 (37)	64 (14)
Diarrhea	143 (32)	15 (3)
Hypomagnesemia	122 (27)	27 (6)
Fatigue	111 (25)	18 (4)
Anorexia	110 (25)	16 (4)
Thrombocytopenia	91 (20)	29 (7)
Weight decreased	91 (20)	5 (1)
Leukopenia	65 (15)	34 (8)
Febrile neutropenia	29 (7)	27 (6)

[a]Treatment-related (CT ± pmab) grade 5 AEs included cardiac/vascular disorders (n = 8), febrile neutropenia/neutropenia-related complications (n = 4), multi-organ/hepatic or renal failure (n = 3), and 1 each of hemorrhagic diarrhea, tumor hemorrhage and aspiration pneumonia; [b]Excludes 5 pts who did not receive any protocol treatment; [c]SOC, System organ class

Results: Pooled data from this interim safety analysis includes the first 451 pts of 650 planned pts; 99% received any study treatment; 86% are male; median age is 58 years (range 26−84); ECOG PS 0/1 = 33%/67%. Median follow-up time is 17.1 weeks; 85% have ended CT. 18 pts (4%) had

a grade 5 adverse event (AE) considered to be treatment-related (CT ± pmab). Any AEs of interest occurring in ⩾20% of pts or those with grade ⩾3 in ⩾5% of pts are shown (Table).
Conclusions: After an interim analysis by the DMC of the first 451 pts, SPECTRUM continues per protocol. Enrollment is complete and the study is ongoing.

8515 POSTER

Patterns of failure after definitive intensity-modulated radiotherapy for head and neck squamous cell carcinoma

S. Rivera[1], M. Mounier[2], G. Créhange[1], J.P. Brenier[1], F. Bonnetain[2], G. Truc[1], S. Naudy[1], P. Maingon[1]. *[1]Centre Georges-François Leclerc, Radiation Oncology, Dijon, France; [2]Centre Georges-François Leclerc, Department of Statistics, Dijon, France*

Background: Our Purpose is to analyze patterns of failure in patients treated with definitive intensity-modulated radiotherapy (IMRT) for head-and-neck squamous cell carcinoma (HNSCC).
Methods and Materials: Between August 2001 and September 2007, 114 patients with histologically confirmed head-and-neck cancer were treated with IMRT for curative intent. Forty nine patients who received postoperative IMRT and 15 patients who had either previous irradiation or other histological type than HNSCC were excluded. Of the 50 remaining patients treated with definitive IMRT 12 (24%) were women and 38 (76%) men with a median age of 60 years (range 36−84). Sites included were oral cavity (16%), oropharynx (44%), hypopharynx (18%), and larynx (22%). Twenty four patients (48%) received neoadjuvant (12%) and/or concomitant (48%) chemotherapy. The mean prescribed dose was 70 Gy (range 69−75 Gy). The dosimetry plans for patients with failure were reviewed and fused over the computed tomography images corresponding with the location of failure.
Results: At a median follow-up of 22 months (range 6−65) 14 locoregional failures (persistent disease or relapse) were observed. Five were in-field, 5 were marginal, and 4 occurred out-field. Two of those marginal failures had received more than 95% of the prescribed dose on more than 95% of the failure gross tumor volume (GTVf). The 2-year overall survival, local disease-free survival and locoregional disease-free survival were 73%, 78%, and 72% respectively.
Conclusion: Despite high rate of locoregional and overall disease-free survival, target volume delineation and definition of margins should be analyzed with accuracy since local failure remains a major issue. Even if promising the implementation of IMRT in current practice requires standardized analysis of patterns of failure. A proposal for marginal failure definition is discussed. Such analyses with longer follow up are needed on ongoing and future randomized trials using IMRT.

8516 POSTER

A phase 2 randomized trial of radiotherapy (RT) plus panitumumab compared to chemoradiotherapy in patients with unresected, locally advanced squamous cell carcinoma of the head and neck (SCCHN): interim pooled safety analysis

J. Giralt[1], J.M. Trigo[2], S. Nuyts[3], M. Ozsahin[4], A.B. Markowitz[5], J. Daisne[6], K. Skladowski[7], C. Lonchay[8], P. Holeckova[9], M. Smitt[10]. *[1]Hospital Vall d'Hebron Passeig, Department of Radiotherapy, Barcelona, Spain; [2]Hospital Virgen de la Victoria, Medical Oncology, Málaga, Spain; [3]University Hospitals Gasthuisberg, Radiotherapy, Leuven, Belgium; [4]Centre Hospitalier Universitaire Vaudois, Service de Radio-Oncologie, Lausanne, Switzerland; [5]University of Texas Medical Branch, Comprehensive Cancer Center, Galveston Texas, USA; [6]Clinique Ste. Elisabeth, Radiotherapy, Namur, Belgium; [7]Centrum Onkologii Instytut M. Sklodowskiej-Curie, Radiation Oncology, Gliwice, Poland; [8]Grand Hôpital de Charleroi, Oncology Department, Charleroi, Belgium; [9]University Hospital Na Bulovce, Institut of Radiation Oncology, Prague 8, Czech Republic; [10]Amgen Inc., Oncology, Thousand Oaks CA, USA*

Background: Panitumumab (pmab), a fully human monoclonal antibody against the epidermal growth factor receptor (EGFR), is indicated as monotherapy for treatment of metastatic colorectal cancer. This ongoing study is designed to assess the efficacy and safety of pmab in combination with radiotherapy (PRT) compared to chemoradiotherapy (CRT) as initial treatment of unresected, locally advanced SCCHN (ClinicalTrials.gov Identifier: NCT00547157).
Methods: This is a phase 2, open-label, randomized, multicenter study. Eligible patients (pts) were randomized 2:3 to receive cisplatin 100 mg/m^2 on days 1 and 22 of RT or pmab 9.0 mg/kg on days 1, 22, and 43. Accelerated RT (70 to 72 Gy − delivered over 6 to 6.5 weeks) was planned for all pts and was delivered either by intensity-modulated radiation therapy (IMRT) modality or by three-dimensional conformal (3D-CRT) modality. The primary endpoint is local-regional control (LRC) rate at 2 years. Key secondary endpoints include PFS, OS, and safety. An external, independent data monitoring committee conducts planned safety and efficacy reviews during the course of the trial.
Results: Pooled data from this planned interim safety analysis includes the first 52 of the 150 planned pts; 44 (84.6%) are male; median (range) age is 57 (33−77) years; ECOG PS 0: 65%, PS 1: 35%; 20 (39%) pts received IMRT, and 32 (61%) pts received 3D-CRT. Fifty (96%) pts completed RT, and 50 pts received RT per protocol without a major deviation. The median (range) total RT dose administered was 72 (64−74) Gy. The most common grade ⩾ 3 adverse events graded using the CTCAE version 3.0 are shown (Table).
Conclusions: After the interim safety analysis, CONCERT-2 continues per protocol. Study enrollment is estimated to be completed by October 2009.

Table: Most common grade ⩾ 3 adverse events[1] – safety analysis set (n = 51)

Adverse Event	Any Grade n (%)	Grade 3 n (%)	Grade 4 n (%)
Dysphagia	36 (71)	16 (31)	3 (6)
Mucosal inflammation	35 (69)	20 (39)	3 (6)
Odynophagia	21 (41)	9 (18)	0 (0)
Radiation-induced skin injury[2]	18 (35)	9 (18)	1 (2)
Stomatitis	10 (20)	5 (10)	0 (0)
Anorexia	7 (14)	2 (4)	0 (0)
Febrile neutropenia	5 (10)	3 (6)	2 (4)

[1]Three patients experienced any grade 5 AE: 1 cardiac arrest; 1 death; 1 sudden death.
[2]Any skin toxicities determined to be caused by radiation therapy.

8517 POSTER

Phase I results from an open-label, randomized, controlled, phase I/II study (ADVANTAGE) to evaluate the combination of different cilengitide regimens with cisplatin, 5-FU, and cetuximab in patients with recurrent/metastatic squamous cell cancer of the head and neck (SCCHN)

T. Brümmendorf[1], J. Guigay[2], R. Mesía[3], J. Trigo[4], U. Keilholz[5], C. Dittrich[6], A. Kerber[7], M. Picard[7], J. Vermorken[8]. *[1]University Cancer Center Hamburg (UCCH) University Medical Center Eppendorf, Dept. of Oncology and Hematology, Hamburg, Germany; [2]Institut Gustave Roussy, Medicine, Villejuif, France; [3]Institut català d'Oncologia − L'Hospitalet, Medical Oncology, Barcelona, Spain; [4]Hospital Universitario Virgen de la Victoria, Medical Oncology, Malaga, Spain; [5]Charité, Hematology and Medical Oncology CBF, Berlin, Germany; [6]ACR-ITR VIEnna and LBI-ACR VIEnna, Kaiser Franz Josef (KFJ)-Spital, Vienna, Austria; [7]Merck KGaA, Global Clinical Development Unit, Darmstadt, Germany; [8]University Hospital Antwerpen, Oncology, Edegem, Belgium*

Background: Cilengitide (EMD 121974) is the most advanced compound in clinical development in oncology of a new class of agents, the integrin inhibitors. Integrins (heterodimeric transmembrane receptors) play key roles in cell interactions. Cilengitide selectively inhibits the cell-surface integrins $\alpha V\beta 3$ and $\alpha V\beta 5$ on activated endothelial cells during angiogenesis and on tumor cells. The rationale for this study is that SCCHN is a highly vascularized tumor expressing integrins and cilengitide plus cetuximab have shown additive effects in rodent xenograft tumor models.
Methods: ADVANTAGE (EudraCT-Number 2008−000615−15; sponsor Merck KGaA) is an ongoing, phase I/II study to determine the safety and tolerability of the combination of cilengitide with cisplatin, 5 FU, and cetuximab in SCCHN. Patients received cisplatin (100 mg/m^2 i.v. day 1), 5 FU (1000 mg/m^2/day continuous i.v. days 1−4) every 3 weeks, and cetuximab once weekly (first dose 400 mg/m^2, subsequent doses 250 mg/m^2). Cilengitide was administered by 60min i.v. infusion on days 1 and 4 each week; cohort 1: 500 mg; cohort 2: 1000 mg; and cohort 3: 2000 mg.
Results: Ten patients (median age 56 years; ECOG PS 0/1; 9 male) were included in the phase I study: cohorts 1 and 2 n = 3, cohort 3 n = 4. Six patients (60%) experienced an adverse event assessed as related to cilengitide by the investigator. The most common were nausea (n = 4), vomiting (n = 3), asthenia (n = 3), and mucosal inflammation (n = 3). No adverse events of CTC grade 4 were assessed as related to cilengitide by the investigator in any cohort. Two patients (20%) in cohort 2 experienced four adverse events (mucosal inflammation, asthenia, nausea, and vomiting) of CTC grade 3 assessed as related to cilengitide. Overall the observed adverse events are in line with the patients' underlying cancer disease or reflect the known toxicities of cetuximab and/or the concomitant chemotherapies. No relevant differences with regard to the frequency and