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

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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

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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.

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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)

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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