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

severity of adverse events across the dose levels were noted. No dose-limiting toxicities were observed at any dose level.
Conclusion: The combination of cilengitide, cisplatin, 5 FU, and cetuximab was well tolerated. Cilengitide in combination with cetuximab and chemotherapy did not change the known safety profile of this standard treatment in SCCHN. Cilengitide 2000 mg was the recommended dose for the phase II study.

8518 POSTER

Prognostic value of the expression of SDF 1 and CXCR 4 in head and neck squamous cell carcinoma (HNSCC)

F. Clatot[1], S. Laberge-Le-Couteulx[2], J. Picquenot[2], M. Cornic[2], O. Choussy[3], A. François[4], D. Schultheis[5], E. Blot[1]. *[1]Centre Henri Becquerel, Medical Oncology, Rouen, France; [2]Centre Henri Becquerel, Pathology, Rouen, France; [3]CHU de Rouen, Head and neck surgery, Rouen, France; [4]CHU de Rouen, Pathology, Rouen, France; [5]Centre Henri Becquerel, Head and neck surgery, Rouen, France*

Background: HNSCC have a hardly predictable evolution, and new prognostic factors are warranted to guide treatment options. Using cell lines or immunohistochemistry data, SDF 1 and its receptor CXCR 4 has been involved in the metastatic spread of various tumors, including HNSCC. We focused on the expression of SDF1 and CXCR4 in HNSCC to assess its prognostic value.
Methods: Fifty-seven patients treated for HNSCC were retrospectively analyzed for SDF1 and CXCR 4 expression by real-time PCR (RT-PCR). Tissue samples were collected at the time of initial diagnosis. At least 50% of the sample was tumoral. Total RNA was reverse-transcribed with TaqMan quantitative RT-PCR (Applied Biosystems). Results were recorded as average threshold cycle, and relative expression was determined using Normalized Expressions method. Expression of SDF1 and CXCR 4 was related to survival after at least 1 year of follow-up.
Results: In the 57 patients, expression of SDF1 (mean value 3.54, median 1.75, range 0.02−32.32) and CXCR 4 (mean value 0.58, median 0.23, range 0−9.89) demonstrated a great variability between patients. After a median follow-up of 30 months (range 12−56), 37 patients were alive (group A) and 20 were dead because of cancer evolution (group D). In group A, median level of SDF1 was 2.5 whereas it was 1.6 in group D ($p = 0.01$). Median level of CXCR 4 was 0.84 in group D and 0.25 in group A ($p = 0.4$). In addition, patients with low level of SDF1 had a worse survival ($p = 0.004$) whereas level of CXCR 4 was not related to evolution. Among usual prognostic factors, only node involvement tend to be related with a worse survival ($p = 0.06$).
Conclusions: In this series, SDF1 expression seems to have significant prognostic value to predict survival of HNSCC patients which is in agreement with in vitro data suggesting a role for SDF1/CXCR4 signaling in the metastatic process. If confirmed in further studies, SDF1 expression may help in management decision for HNSCC patients.

8519 POSTER

A phase 2, randomized trial (CONCERT-1) of chemoradiotherapy with or without panitumumab in patients (pts) with unresected, locally advanced squamous cell carcinoma of the head and neck (SCCHN): Interim pooled safety analysis

A. Fortin[1], A. Cmelak[2], R. Mesía[3], H. Minn[4], A.T.C. Chan[5], A.C. Yunes[6], M.C. Merlano[7], S. Singh[8], M. Smitt[9], M. Henke[10]. *[1]L'Hotel-Dieu de Quebec, Departement de Radiotherapie, Quebec, Canada; [2]Vanderbilt University Medical Center, The Vanderbilt Clinic, Nashville, USA; [3]Institut Catala d'Oncologia (ICO) - L'Hospitalet, Medical Oncology Department, Barcelona, Spain; [4]Turku University Hospital, Department of Oncology and Radiotherapy, Turku, Finland; [5]State Key Laboratory in Oncology in South China The Chinese University of Hong Kong, The Sir YK Pao Centre for Cancer, Hong Kong, China; [6]Unidad de Oncología Servicios de Salud del Estado de Puebla, Servicio de Radioterapia, Puebla, Mexico; [7]A.S.O.S. Croce E Carle, Oncologia Medica, Cuneo, Italy; [8]Sunnybrook Odette Cancer Centre, Department of Medical Oncology, Toronto, Canada; [9]Amgen Inc, Oncology, Thousand Oaks, USA; [10]Universitätsklinikum, Klinik für Strahlenheilkunde, Freiburg, Germany*

Background: Panitumumab (pmab), a fully human monoclonal antibody against the epidermal growth factor receptor (EGFR), is indicated as monotherapy for the treatment of metastatic colorectal cancer. This ongoing study sponsored by Amgen is designed to estimate the difference in 2 year local regional control (LRC) rates in pts receiving chemoradiotherapy (CRT) alone or CRT plus panitumumab (PCRT) as first-line treatment of locally advanced SCCHN (ClinicalTrials.gov Identifier: NCT00500760).
Methods: This is a phase 2, open-label, randomized, international, multicenter study. Eligible pts were randomized 2:3 to CRT or PCRT. CRT included radiotherapy (RT) and cisplatin (100 mg/m^2 – days 1, 22, and 43 of RT). PCRT included RT and pmab (9.0 mg/kg Q3W) + cisplatin (75 mg/m^2 Q3W), both administered on days 1, 22, and 43 of RT. Standard fractionation RT (70 Gy delivered in 2 Gy fractions for 5 days/week $\times$7 weeks) was planned for all pts and was delivered by either the intensity-modulated (IMRT) modality or the three-dimensional conformal (3D-CRT) modality. The primary endpoint is LRC rate at 2 years. Key secondary endpoints include PFS, OS, and safety. An external, independent data monitoring committee (DMC) conducts planned safety and efficacy reviews during the course of the trial.
Results: Pooled data from this planned interim safety analysis includes the first 54 of 150 planned pts; 50 (93%) pts are male; median (range) age is 56 (37−74) years; ECOG PS 0: 69%, PS 1: 31%; 32 (59%) pts received IMRT, and 22 (41%) pts received 3D-CRT. Forty-eight (89%) pts completed all RT, and 48 pts received RT per protocol without a major deviation. The median (range) total RT dose administered was 70 (16, 70) Gy. The most common grade $\geqslant$ 3 adverse events (AEs) graded using the CTCAE version 3.0 are shown (Table).
Conclusions: After this interim safety analysis, the DMC recommended the CONCERT-1 study continue per protocol. Enrollment into the study completed (n = 153) on 26 March 2009. Updated pooled safety data for this group will be presented.

Table: Most common grade $\geqslant$ 3 adverse events[1] – safety analysis set (n = 53)

Adverse event	Any grade n (%)	Grade 3 n (%)	Grade 4 n (%)
Mucosal inflammation	35 (66)	21 (40)	0 (0)
Radiation-induced skin injury[2]	34 (64)	6 (11)	1 (2)
Dysphagia	31 (58)	14 (26)	0 (0)
Stomatitis	12 (23)	6 (11)	0 (0)
Hypokalemia	10 (19)	4 (8)	0 (0)
Dehydration	7 (13)	4 (8)	0 (0)
Infection	5 (9)	5 (9)	0 (0)

[1]There was one grade 5 treatment-related AE of syncope; [2]Any skin toxicities determined to be caused by radiation therapy.

8520 POSTER

Preliminary results of a pilot study with a modified induction docetaxel/cisplatin/5-FU (TPF) followed by concomitant chemoradiotherapy (CT/RT) in locally advanced head and neck cancer (LAHNC)

S. Serrano[1], J. Martinez-Trufero[2], S. Miguelsanz[3], A. Yubero[4], R. Lastra[5], E. Polo[6], J. Lambea[1], M.A. Segui[7], E. Pujol[8], D. Isla[1]. *[1]Hospital Clinico Lozano Blesa, Medical Oncology, Zaragoza, Spain; [2]Hospital Universitario Miguel Servet, Medical Oncology, Zaragoza, Spain; [3]Hospital Arnau de Villanova, Medical Oncology, Lerida, Spain; [4]Hospital Obispo Polanco, Medical Oncology, Teruel, Spain; [5]Hospital San Jorge, Medical Oncology, Huesca, Spain; [6]Hospital de Calatayud, Medical Oncology, Zaragoza, Spain; [7]Consorci Hospitalari Parc Tauli, Medical Oncology, Barcelona, Spain; [8]Hospital General de Soria, Medical Oncology, Soria, Spain*

Background: TPF induction CT followed by CT/RT has been evaluated in several trials showing high activity although associated with non-irrelevant toxicity. To aim the efficacy, toxicity profile and organ preservation of a modified neoadjuvant TPF to concurrent CT/RT in both resectable (R) and unresectable (UR) LAHNC.
Patient and Methods: One hundred seventy patients (p) with stage III-IV, PS ECOG 0−2, were included to receive 3 cycles of docetaxel 75 mg/m^2 iv day (d) 1, cisplatin (P) 75 mg/m^2 iv d2 and 5 FU 750 mg/m^2 iv continuous infusion d2−5, every 3 weeks with prophylactic ciprfloxacin 500 mg twice daily from d6−15 of each cycle and granulocyte colony-stimulating factor as secondary or primary setting, followed by P 100 mg/m^2 iv d1, 22, 43 concomitant with RT (66−70 Gy, conventional fractionation). Neck dissection was planned for p with stage N2−3 after induction CT or salvage surgery for resectable p with persistent disease at the end of treatment.
Results: Main p characteristics were: median age 58 years (39−77), male 89%, ECOG 0/1/2 47%/50.6%/2.4%, stage IV 62.7%, larynx/hipopharynx/oral cavity/oropharynx 45%/12%/17.3%/25.7% and R/UR 41.8%/58.2%. Median TPF/P cycles administered were 3/3. Neoadjuvant CT/total treatment overall response rate evaluation (R/UR): 70% (73%/68%)/86% (84%/88%). Neck dissection was performed in 16 p and salvage surgery in 6 p. Organ preservation was achieved in 90.8% of R p. Main G3−4 toxicity during TPF treatment was neutropenia 11.2%, febrile neutropenia 11.2%, mucositis 11.2%, and during CT/RT mucositis 16.5%, neutropenia 16.5%. Median time to progression was 19.5m (R:15.6,