500 mg/m^2 every 2 weeks, weekly cetuximab (400 mg/m^2 on day 1 then 250 mg/m^2 weekly), and combination with weekly cetuximab and docetaxel (35 mg/m^2 on day 1, 8 and 15 every 28 days) in 44%, 40% and 15% of pts.
ORR was 15%. Partial response, stable disease and progression rates were respectively PR = 15%, SD = 30% and PD = 55%. A toxic death occurred in one case related to an anaphylactic shock.
The median PFS was 9 weeks for all patients. The median PFS of patients treated with weekly cetuximab and cetuximab every 2 weeks was respectively: 12 weeks and 8 weeks. Median PFS of pts treated with cetuximab and taxotere combination was 6 weeks.
Conclusion: This monocentric retrospective study confirmed that cetuximab alone may confer clinical benefit as second-line or third-line treatment for pts with R/M SCCHN, with a 45% disease control rate, but median PFS remained shorter than three months.

8586 POSTER

Impact of Induction Chemotherapy on Local Control for Locally Advanced Nasopharyngeal Cancer

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Background: Concurrent chemoradiotherapy (CRT), with or without adjuvant chemotherapy, is a current standard of care for locally advanced nasopharyngeal carcinoma (NPC). However, prognosis of patients (pts) with stage IV or N2-N3 remains poor. Recently, induction chemotherapy (IC) followed by CRT demonstrated promising results in a randomized phase II trial (Hui EP et.al, JCO 2009). We retrospectively conducted a nonrandomized comparison between CRT alone and IC followed by CRT in NPC pts with stage IVA-IVB or N2−N3.
Method: Between Apr.1996 and Sep.2009, 54 consecutive pts were selected for this study: 32 were treated with CRT alone and 21 with IC followed by CRT. IC consisted of 1-hour infusion of docetaxel at 60 to 70 mg/m^2, 2-hour infusions of cisplatin at 60 to 70 mg/m^2/day on day 1 and of S-1 twice daily on days 1−14 at 60−80 mg/m^2/day, repeated every 3 or 4 weeks with a maximum of 3 cycles allowed (Tahara M et.al, Ann Oncol 2011). After completion of IC, pts received 66−70 Gy of radiotherapy concurrent with cisplatin. CRT alone consisted of 66−70 Gy of radiotherapy with platinum-based chemotherapy with or without adjuvant chemotherapy.
Results: No differences in sex, PS and median age in both groups were observed, but patients in the IC group had a more advanced stage (stage IVA-IVB: 76% vs. 63%, N2−3: 90% vs. 78%). During IC, the most common grade 3 or 4 hematological toxicities were neutropenia (76%) and febrile neutropenia (10%) while the most common grade 2 or 3 non-hematological toxicities were anorexia (42%), nausea (42%) and diarrhea (19%). During CRT, hematological and non-hematological toxicities were not increased in the IC group. After completion of IC, complete response was observed in one pt and partial response in 20 pts according to RECIST criteria. Median followed-up period was 29 months in the IC group and 42 months in the CRT group. 2-year progression free survival and overall survival were respectively 76% and 95% in the IC group and 71% and 83% in the CRT group. Recurrences of primary site were observed in one pt (5%) in the IC group and 8 pts (25%) in the CRT group.
Conclusion: IC was well tolerated and did not compromise sequent CRT. IC followed by CRT demonstrated better local control compared with CRT and further investigation is warranted.

8587 POSTER

A Phase II Analysis of Paclitaxel and Capecitabine in the Treatment of Recurrent or Disseminated, Squamous Cell Carcinoma of the Head and Neck Region − Results From an Extended Phase 2 Study

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Background: This study presents the results of an extended phase II study originally published in 2007 (HEAD & NECK jan. 2007), regarding the antitumour activity and toxicity of a non-platinum containing regime with paclitaxel and capecitabine for the treatment of recurrent or disseminated squamous cell carcinoma of the head and neck region. 50 patients were included in the original study and as the results were promising with respect to response (42%), overall survival (8 month's) and toxicity (very low), we decided to accrue another 100 patients in order to provide a more robust estimate of response and survival with this regime.
Materials and Methods: A total 183 patients with recurrent or disseminated squamous cell carcinoma were included in the study. There were 37 women and 146 men. Mean age was 56 years. Performance (WHO) was as follows: WHO 0: 31, WHO 1: 107 and WHO 2: 45 patients. The treatment consisted of paclitaxel 175 mg/m^2, once every third week and capecitabine 825 mg/m^2 p.o. b.i.d for 2 weeks.
Results: The overall response rate (CR and PR) according to the WHO criteria's was: 32.6%. (CR: 6%; PR: 26.6%; NC: 36.4%; PD: 20.7% NE: 8.2% and Not Known: 2.1%.) The mean survival time was 254 days or 8.5 month's for the entire population, but for patients in performance 0 and 1 only the mean survival time was 313 days or 10.4 month's. Toxicity was very moderate. Only 9% of 1131 delivered treatments had to be given in reduced dose. Apart from hairloss (50% had total hairloss) toxicity was low and grade 3 and 4 toxicity were uncommon. Two toxic deaths were registered though.
Conclusions: The response rate and overall survival for this low toxic regime are promising and comparable to the much recommended regime with Cisplatinum, 5Fu and Cetuximab (Vermorken regime).

8588 POSTER

Pilot Study of Target Therapy With EGFR Antibody (Nimotuzumab) in Patients With Unresectable Head and Neck Cancer

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Background: Nimotuzumab, a humanized anti-EGFR monoclonal antibody, has demonstrated well tolerate anti-cancer efficacy. Therefore, we designed this study to explore the efficacy of the combination of biological target therapy (utilize Nimotuzumab) and chemotherapy with unresectable neck and head carcinomas.
Material and Methods: 71 patients (54 men and 17 women, age 30−83 years, mean 60) were enrolled in this study. All patients had locally advanced oral-maxillofacial and head and neck tumours (no indication for surgery or radiotherapy) confirmed by histology and radiology, with indication for biochemotherapy. The chemotherapy regimen given was cisplatin 75 mg/m^2 day 1, paclitaxel 75 mg/m^2 day 1, fluorouracil 750 mg/m^2 days 1−5, and Nimotuzumab 200 mg/m^2 weekly.
Results: Patients completed 2−4 cycles of chemotherapy (mean 2.2). Nimotuzumab was given 2−8 times (mean 4.3). The prognosis was as follows: complete response in 4 patients, partial response in 39, stable disease in 18, and progressive disease in 3. 7 patients could not be evaluated. The total effective rate, calculated as complete plus partial responses, was 61%. 29 patients had surgery after biochemotherapy. No serious adverse reactions were noted during the course of the treatment, only one case of slight erythra infection.
Conclusions: Nimotuzumab was equally effective in the increase of chemosensitivity and good tolerability profiles.

8589 POSTER

COX-2 Inhibitor and Gefitinib in Recurrent And/or Metastatic Head & Neck Cancer

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Background: Metastatic and/or Recurrent Head & Neck Cancer patients following definitive therapy in the form of multi modality therapy, has dismal prognosis and options are extremely limited with only the combination of Cetuximab and Cisplatinum improving quality of life and overall survival.
Epidermal growth factor (EGFR) plays a role in tumorigenesis, stimulating cell proliferation, inhibiting apoptosis and promoting angiogenesis and metastasis. EGFR is over expressed in majority of Head & Neck cancer patients and is associated with poor prognosis and outcome.
Cylooxygenase-2 (COX-2) is also over expressed in Head & Neck cancer with poor outcome. Interaction of EGFR and COX-2 suggest that EGFR activates COX-2 in Head & Neck cancer.
Materials and Methods: Single institute study was done to find out safety and efficacy of combining Gefitinib and COX-2 inhibitor Eterocoxib. The study was done in 2 phases. Phase 1 was for dose finding and Phase 2 − a randomized pilot study comparing Gefitinib + Eterocoxib vs Methotrexate

weekly. Totally 46 patients were studied. The effective combination dose of Gefitinib + Eterocoxib was Gefitinib 500 mg and Eterocoxib 400 mg.
Recurrent and metastatic disease patients who were not candidates for definitive loco regional therapy and had received platinum based chemotherapy.
Results: Out of 46 patients − 40 were accessible patients. There were 18 patients in Methotrexate (Arm A) and 22 patients in the combination Arm of Gefitinib + Eterocoxib (Arm B). The Response rates, Time to Progression, Median Survival time in Arm A and Arm B are as follows:
Arm A − 1 partial response and 2 stable diseases (clinical benefit seen in 16.67%) with a median time of survival around 94 days, and time to progression 36 days.
Arm B − 1 complete response, 4 partial responses and 6 stable diseases (clinical benefit seen in 50%) with median time to progression 60 days, median survival time 165 days.
The treatment was relatively well tolerated with predictable toxicity including skin rash, diarrhea and dyspepsia. Exploratory study of quality of life showed improvement in quality of life in the experimental arm. Exploratory study of pharmaco-economics suggests that it is cost effective.
Conclusions: Gefitinib combined with Eterocoxib shows better response rates, Median Survival time and Quality of Life, than Methotrexate weekly and historical Gefitinib data. It is worthwhile to combine the 2 oral drugs for a disease status which does not have very effective treatment. A randomized Phase III trial can answer this question.

8590 POSTER

Concomitant Radiochemotherapy With Weekly Cisplatin and Daily Capecitabine in Locally Advanced Head and Neck Cancer-Safety and Efficacy

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Loco-regionally advanced head and neck cancer is associated with a poor prognosis despite treatment with surgery or radiation or both. To improve the major end points of treatment we have focused on the used of concomitant radiochemotherapy. Cis and 5FU have been considered the standard for concomitant radiochemotherapy. The oral fluoropyrimidine, capecitabine was design to mimic continuous infusion 5FU. There is proved that oral capecitabine and 5FU continuous infusion have the same efficacy, therefore, our goal is to evaluate the efficacy and safety of concomitant chemoradiotherapy with cap and cis in locally advanced head and neck squamous cell carcinoma.
Method: Jan 2007–Jan 2009; 31 pts. with locally advanced head and neck squamous cell carcinoma, primary tumour sites: oral cavity − 6 pts, oropharynx − 10 pts, hypopharynx − 8 pts, nasopharynx − 6 pts, paranasal sinus − 1 pts, good performance status, good hepatic cardiac, renal and hematologic function.
Treatment: 70 Gy 3D-external beam RT (1.8−2 Gy/fr) concomitant with cap 660 mg/mp daily and cis 20 mg/mp weekly, entire period of RT.
Results: Follow up period − 2 years. CR − 24 pts. PR − 7 pts. PFS and OS rates at 2 years: 56% and 74% respectively. Toxicity grade 3−4 − neutropenia − 3 pts, digestive toxicity (vomiting, nausea) − 3 pts, mucositis − 5 pts. 4 pts needed to discontinuing the treatment due to toxicity. No death, no renal toxicity, no hand-foot sdr. were observed.
Conclusion: This modality of treatment was found to be well tolerated and effective in pts with locally advanced head and neck squamous cell carcinoma. This regimen can be regarded as an important chemoradiotherapy option for advanced head and neck squamous cell carcinoma and easily used in ambulatory patients. Long term follow-up is needed to evaluate (in larger trials) the late treatment failure and side effects.

8591 POSTER

Effects of Human Papillomavirus (HPV) and Other Potential Risk Factors on Survival in Patients With Oropharyngeal Cancer

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Background: Oropharyngeal carcinomas are associated with HPV or with tobacco smoking and alcohol. HPV associated carcinomas arise most frequently in the tonsils and have a more favorable prognosis in contrast to tobacco smoking and alcohol induced carcinomas. Here we report on frequency and outcome of HPV associated oropharyngeal carcinomas (tonsils and base of tongue) in a Berlin cohort with high prevalence of smoking.
Methods: Between 2005 and 2009 114 patients with oropharyngeal squamous cell carcinomas were diagnosed in a city hospital, 60 arising from tonsils and 54 from the base of tongue. Patients received surgery, chemoradiation or radiotherapy according to stage of disease. Complete follow-up information was obtained in fall of 2010. Histologic slides were retrieved and stained for p16 as indicator of HPV associated disease. Proportional-hazard models and log-rank tests were used to compare the risk of progression and death among patient subgroups.
Results: Of all 114 patients, 81% were smokers and 64% tumours stained positive for p16 (tonsils 73%, base of tongue 54%). With a median follow-up of 28 months 31 patients had disease progression and 39 patients had died. 3-year PFS rates were 79% and 52% in patients with p16+ vs. p16- tumours ($p = 0.001$ by log-rank test) and 3-year OS rates were 78% and 39% in patients with p16+ vs. p16- tumours ($p < 0.001$ by log-rank test). In cox regression analysis, only stage and p16 were independant prognostic factors. For PFS p16 had a hazard ratio (HR) of 0.44% (95% CI, 0.25 to 0.78) and also for OS a HR of 0.44% (95% CI, 0.24 to 0.78).
Conclusions: Even in a European population with high prevalence of tobacco smoking, p16 positivity remains a strong favorable and independant risk factor, as has previously been shown in US cohorts with far lower smoking prevalence.

8592 POSTER

Long Term Quality of Life, Physical and Psychological Functioning in Patients Affected by Relapsed Head and Neck Cancer

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Background: Primary head and neck squamous cell carcinomas (HNSCC) and their recurrences can heavily affect patient's quality of life (QoL). Aim of our study was the evaluation of the impact of treatment on QoL, physical and psychological functioning of patients affected by recurrent HNSCC.
Material and Methods: The sample was composed by 34 patients affected by recurrent HNSCC. Primary tumour treatment was as follows: exclusive RT (radiotherapy) 18%, S+RT 55%, RT + chemotherapy (CT) 27%. In order to evaluate the late effects of RT we used the RTOG–EORTC late radiation morbidity score plus the DISCHE morbidity recording scheme.
Psycho-oncological assessment included: HADS, MADRS, MINI MAC, EORTC QoL HN 35.
Results: Among this population, 55% of pts relapsed on T, 15% on N, 21% on T+N and 9% on M. Recurrences were treated with S+CT 6%, RT+CT 21% and CT alone 73%. The late toxicity evaluation demonstrates that skin alterations, salivary glands impairement, subcutaneous fibrosis and mucous membrane alterations are the most relevant and severe damages. After a median follow-up of 60±26 months, analysing RTOG-EORTC scale, high scores of skin and mucous membrane alterations are related ($p < 0.05$) with higher levels of anxiety and depression, negative coping styles (reduction of fighting spirit, anxiety and depression) are increased by salivary and mucous membrane dysfunctions ($p < 0.05$), moreover lower levels of QoL, in particular physical and social functioning, are correlated with higher levels of mucous membrane damages ($p < 0.05$); all the mentioned above symptoms increase negative thoughts ($p < 0.05$). DISCHE findings are superimposeable.
Conclusions- Treatment of relapsed HNSCC added to surgery and or RT and or CHT on the primary tumour could result in a heavy addictive effect on mucous membrane, skin, subcutaneous tissues and salivary glands referred symptoms. Negative coping styles and thoughts, increased anxiety and depression and lower levels of QoL are strongly associated to high scores of such symptoms.

8593 POSTER

VEGF and Oral Cancer − ex Vivo and in Vitro Studies

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Introduction: Scotland has the highest occurrence of oral cancers in both men and women across the UK (CR-UK, 2006) and the incidence is on the rise. The frequency in Scottish males is 18.4 per 100,000 (UK average is 11.9) and in Scottish women is 7.4 per 100,000 (UK average is 5.8). The aim of this study was to investigate the VEGF family as markers of tumour progression and to investigate how VEGF affects cell migration and signalling pathways, in vitro.
Materials and Methods: Tissue was collected from a cohort of 64 patients with oral cancer and 22 patients with dysplastic lesions. The tissue was analysed for expression of VEGF-A and VEGF-C by immunohistochemistry and then semi-quantitatively assessed. A cohort of serum samples was