$IR_{50}$and IR_{50A} groups received 50 Gy doses. The amifostine groups, C_A, $IR_{25A}$and IR_{50A}, were also incubated with 3 mg/mL amifostine for 15 minutes before irradiation. C group cells delivered neither radiation nor amifostine.
All groups were incubated in 37ºC and 5% CO_2 pressure for 12 hours. Prior to and 12 hours following the irradiation all samples were assessed in terms of total viable cell counts, colony numbers detected in mixed colony cultures and percentage of apoptosis by flow cytometry. The group means were compared for statistical analysis and significance level was set at $p < 0.05$.
Results: There was no statistical difference found for all assessments between control groups of C and C_A. Meanwhile, viable cell counts were detected higher in amifostine groups than those irradiated only ($0.9x10^9$/L, IR_{25} vs. 3.9 $x10^9$/L, IR_{25A}, $p<0.01$; 0.2 x 10^9/L, IR_{50} vs. 2.5×10^9/L, IR_{50A}, $p < 0.05$). In addition, the colony numbers were significantly higher in both dose levels (80, IR_{25A} vs. 20, IR_{25}, $p < 0.01$; 41, IR_{50A} vs. 12, IR_{50}, $p < 0.05$). The percentage of apoptosis was less in amifostine group but only for 25 Gy (46.0%, IR_{25A} vs. 29.7%, IR_{25}, $p < 0.05$).
Conclusions: Purging the malignant cells from stem cell grafts is done with several pharmacological agents and there are some data on amifostine preventing the normal bone marrow cells in procedure. Our study showed radiation may safely be administered in 25 Gy for the same purpose but with an amifostine like protector and further in vivo studies are required to test the feasibility.

Head and Neck Cancer

Oral presentations (Tue, 1 Nov, 13.45–15.45)
Head and neck cancer

994 ORAL

Paclitaxel and gemcitabine vs. paclitaxel and pegylated liposomal doxorubicin in advanced non–nasopharyngeal head and neck cancer. A phase III study conducted by the Hellenic Cooperative Oncology Group (HeCOG)

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Background: Advanced head and neck cancer (HNC) is an incurable disease and bears grave prognosis. Median survival with platinum-based chemotherapy does not exceed 6 months. In a series of phase II studies, we have shown that the combinations of paclitaxel (P) with gemcitabine (GEM) or with pegylated liposomal doxorubicin (PLD) have promising activity in patients with HNC. Median survival with these combinations, were 9 and 7.9 months respectively. The aim of the present study was to compare the efficacy of these two novel regimens with proven activity in phase II studies in patients with non-nasopharyngeal advanced HNC.
Patients and methods: From 15/9/1999 until 9/11/2004, 159 eligible patients entered the study. 5 patients presented with locally advanced and 154 with recurrent /metastatic disease. Patients randomized to Group A (n = 83) were treated with 6 cycles of P 175 mg/m^2 by 3-hour infusion on day 1 and GEM 1000 mg/m^2 on days 1, 8 of each cycle every 3 weeks. Patients randomized to Group B (n = 76) received 6 cycles of P, as in Group A, and PLD (Caelyx®) 40 mg/m^{2}every 4 weeks.
Results: There were 139 men and 20 women with a median age of 64 years and median PS of 1. Primary tumor site was larynx (48 vs. 46), hypopharynx (7 vs. 4), oropharynx (2 vs. 1), oral cavity (24 vs. 21), and other (2 vs. 4). 37 (45%) patients in Group A and 34 (45%) in Group B completed 6 cycles of chemotherapy. In 158 evaluable for response patients, the overall response rate was 20.5% vs. 29% (p = 0.215). After a median follow-up of 33.1 months, median time to progression was 4.4+ vs. 6.3+ months (p = 0.0568) and median overall survival (OS) 8.6 vs. 11.5+ months (p = 0.2784) in Group A and B, respectively.
Major (grade 3–4) toxicities included leukopenia (7.2% vs. 6.8%), anemia (0% vs. 3%), allergic reactions (1% vs. 7%, p = 0.02), peripheral neuropathy (1% vs. 0%), diarrhea (1% vs. 0%), infection (2% vs. 0%), fatigue (1% vs. 0%), skin (0% vs. 5.5%, p = 0.045), fever (2% vs. 1.4%), and hand and foot syndrome (0% vs. 3%). The incidence of neutropenia (12%), thrombocytopenia (1%) and pain (1%) was similar in the two groups. Alopecia was universal.
Conclusions: The present study has clearly demonstrated that there was no significant difference in OS between the two groups. Further, both regimens are accompanied with confirmed promising efficacy in advanced HNC and should be compared with the reference regimen of cisplatin and 5-day continuous infusion of fluorouracil.

995 ORAL

A phase II trial of BAY 43–9006 in patients with recurrent and/or metastatic head and neck squamous cell carcinoma (HNSCC). A Southwest Oncology Group (SWOG) trial

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Background: BAY 43–9006 is a potent raf kinase inhibitor of kinases of Raf-1 and B-Raf of the RAS/RAF/MEK/ERK pathway. The compound also inhibits protein tyrosine kinases associated with VEGFR-2 and 3 as well as PDGFR-B. We conducted a phase II trial to evaluate the efficacy of BAY 43–9006 in chemotherapy naive patients with metastatic or recurrent HNSCC.
Methods: Chemotherapy naïve patients with histologically proven squamous cell carcinoma of the head and neck either metastatic, persisted or recurred following definitive surgery and/or radiation therapy, and not amenable to salvage surgical resection with measurable disease were eligible. Patients must not have received any previous chemotherapy for the recurrent or metastatic disease. Patients who have received induction or adjuvant chemotherapy are eligible, provided that at least six months have elapsed since the last course of chemotherapy was administered. Patients may have received only one induction or adjuvant regimen. Patients must have adequate cardiac, hematologic, renal and hepatic function and a Zubrod Performance Status of 0 or 1. We obtained specimens from either archival or fresh pre-treatment biopsies and planned to obtain a second tissue specimen at the time of progression of disease for biologic correlative studies. BAY 43–9006 was administered orally at 400 mg BID on a continuous basis, in 28-day cycles. Respnses were evaluated every 8 weeks according to RESIST criteria.
Results: Twenty-two patients (17 males, 5 females, median age 65 years) have been enrolled to date. Fourteen patients are evaluable for toxicity. The drug was generally well tolerated. The grade 3 toxicities included one patient with hand/foot syndrome and another with stomatitis. The most common grade 2 toxicity was fatigue (3 pts.), and anorexia (3 pts.), nausea (1 pt), weight loss (1 pt), lymphopenia(1 pt), AST/ALT elevation(1 pt), and stomatitis (1 pt). The trial was temporarily closed on April 1, 2005 after reaching its first stage accrual goal and will reopen if any responses are documented.
Conclusion: BAY 43–9006 is well tolerated. Updated toxicity data will be reported. Response, time to progression and survival data will be presented, if the trial has met its final accrual goal and has permanently closed. If any response is noted the trial will re-open to accrue an additional 20 patients.

996 ORAL

Randomized phase III study in squamous cell carcinoma of the head & neck (SCCHN) using Lipoplatin: First safety results of a multicenter trial

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Background: Based on a metanalysis of >10.000 patients, cisplatin emerges as an essential chemotherapy drug for the treatment of advanced SCCHN. However, its clinical use is impeded by its severe adverse reactions, especially renal toxicity, peripheral neuropathy, and ototoxicity. In a randomized, multicenter phase III trial, we replaced conventional cisplatin by a liposomal formulation of cisplatin (lipoplatin), and compared the safety profiles of patients in the two treatment arms.
Material and methods: Main inclusion criteria selected patients with histologically confirmed SCCHN (primary metastatic or patients with relapsed/progressive disease) between 18–75 years of age with sufficient renal function defined as creatinine clearance >50 ml/min. After stratification (criteria: primary metastatic disease, recurrent or progressive SCCHN, prior chemotherapy, no prior chemotherapy, prior cisplatin-based chemotherapy, prior non-cisplatin based chemotherapy and center), patients were randomized between the following arms: Arm A: 100 mg/m^2/d lipoplatin (d 1, 8, 15) plus 1000 mg/m^2/d 5-FU (d 1–5) q3w for 6 cycles; arm B: 100 mg/m^2/d cisplatin (d 1) plus 1000 mg/m^2/d 5-FU (day 1–5) q3w for 6 cycles. Main endpoints for this interims analysis were hemato-, neuro- and nephrotoxicity. We tested for non-inferiority.