Poster Session

Head and neck cancer and endocrine tumours

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Phase I study of cetuximab (C225)in combination with cisplatin or carboplatin and 5-fluorouracil (5-FU) in patients (pts) with recurrent and/or metastatic squamous cell carcinoma of the head and neck (R&M SCCHN)

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The background of this study is to investigate the safety of cetuximab, a chimeric anti EGFR monoclonal antibody in combination with platinum and different doses of 5-FU in pts with R&M SCCHN. Main eligibility criteria: KPS * 70, no prior palliative chemotherapy (CT), adequate biological functions and at least one measurable lesion. Cetuximab was given at a fixed dose: starting 400mg/m* and weekly 250mg/m*. The patients were randomised to receive either cisplatin 100mg/m* or carboplatin AUC5. Only 5-FU dosage was escalated through three dose levels, 600, 800 and 1000 mg/m*, continuous daily infusion x 5 days. CT cycles were repeated every three weeks. DLT were assessed during the first two cycles. So far, 53 pts have been enrolled, 28 in the cisplatin group and 25 in the carboplatin group. Median age was 56 years (36-70), median KPS 80 (70-100).

Results: 12 pts (6 carboplatin / 6 cisplatin) have been treated in the first dose level (5-FU 600 mg/m*). NCI-CTC Grade 3/4 drug related toxicity: vomiting (3pts), febrile neutropenia (1pt) conjunctivitis (1 pt). 2 DTLs occurred in the cisplatin group: Febrile neutropenia and elevated ALAT. 16 pts (10 cisplatin / 6 carboplatin) have been treated in the second dose level (5-FU 800 mg/m*). Grade 3/4 drug related toxicity: drug fever (1 pt), diarrhoea + vomiting (1 pt), vomiting (1pt), fatigue (1pt), thrombosis on catheter (1pt). One DLT occurred in the cisplatin group: Asthenia G 3. 13 pts have been enrolled in the third dose level (5-FU 1000mg/m*) (6 cisplatin / 7 carboplatin). Grade 3/4 drug related toxicity Catheter infection (1pt), Fanconi like syndrome (1 pt). Two DLTs occurred in the cisplatin group: Myocardial infarction (1pt with prior history of cardiac disease) and mucositis + febrile neutropenia (1pt). One DLT has been reported in the carboplatin group: Mucositis G3. For confirmation of tolerability 12 additional pts (6 cisplatin, 6 carboplatin) have been included at this third dose level. So far 2 DLTs have been reported in the cisplatin group: Nausea + vomiting G3 (1pt), mucositis + febrile neutropenia (1pt) and 1 DLT in the carboplatin group: Neurotoxicity G3. This group is still under DLT evaluation. Preliminary results of efficacy are available for 30 patients: 13 PR, 11 SD, 6 PD. Cetuximab can be safely combined with therapeutic doses of Cis-/ carboplatin plus 5FU. Updated data will be presented.

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Neoadjuvant chemotherapy plus radiotherapy versus radiotherapy alone and the quality of radiation therapy in the treatment of locally advanced nasopharyngeal carcinomas

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Background: To assess, in a retrospective study, if there is a long term benefit of adding neoadjuvant chemotherapy (CT) to standard radiotherapy (RT) for the primary treatment of locoregionally advanced nasopharyngeal carcinoma (NPC) patients (pts), taking also into account the quality of the RT: optimal RT (ORT) or poor quality RT (PRT), in terms of a lower total dose or prolonged overall treatment time.

Material and methods: Between 1/1990-12/1995, 185 locoregionally advanced NPC pts, UICC stage III (8 pts) and IV (177 pts), with histological WHO type II (34 pts) or III (151 pts), entered the study. M/F ratio was 124/61, median age 46 [8-78]. Combined CT+RT consisted in 3 cycles of neoadjuvant BEC (Bleomycin, Epirubicin, Cisplatin) or EC (Epirubicin, Cisplatin) followed by standard RT (70 Gy/ 7wks), versus the same RT alone.

Results: 175 pts were evaluable for long term follow-up, 81 pts had CT+RT (21 PRT) and 94 RT alone (28 PRT). *Response rate* (RR) at the end of the primary treatment was similar for CT+RT vs RT (89% vs 85%, p=.46). RR in the CT+RT arm was not influenced by ORT vs PRT (92% vs 81%, p=.35) but was different in the RT arm (ORT vs PRT: 92% vs 68%, p<.01). *Survival* (S) was not significantly influenced by the addition of neoadjuvant CT vs RT alone (5y S: 53% vs 44%, p=.16). Five-years S in the CT+RT arm was not influenced by ORT vs PRT (52% vs 56%, p=.81), but radiation quality decisively influenced S in the RT arm (ORT vs PRT: 56% vs 14%, p<.01). *Disease-free survival (DFS)* was similar for CT+RT vs RT alone (5y DFS 44% vs 40%, p=.3). DFS in the CT+RT arm was not influenced by the radiation quality (ORT vs PRT (45% vs 42%, p=.74), unlike the DFS in the RT arm (ORT vs PRT: 50% vs 19%, p<.01)*Freedom from local relapse* (FLR) was not different among CT+RT vs RT (5y FLR 62% vs 56%, p=.98). FLR in the CT+RT arm was the same for ORT vs PRT (63% vs 59%, p=.98), but difference was significant in the RT alone arm (ORT vs PRT: 67% vs 30%, p<.01).

Conclusions: Neoadjuvant CT+RT and RT alone results were similar in terms of RR, 5yS, DFS, FLR. In the RT alone arm, a poor quality RT gave significantly worse results for all these endpoints. In the combined modality arm, neoadjuvant CT efficiently compensated for the poor quality RT.

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Experience of the AJCC/UICC 5th edition nasopharyngeal cancer TNM in a single radiotherapy practice outside Southeast Asia

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Background: The 5th edition NPC TNM in 1997, based on Southeast Asian data, was a landmark change in classification for nasopharyngeeal carcinoma (NPC). Although heterogeneous populations exist in North America and Europe, no validation of the 5th edition exists for non-asian patients using a large patient cohort and several reports identify that ethnicity is important in predicting treatment response. This study was conducted to compare the 4th (1992) and 5th (1997) edition TNM classifications and to evaluate the potential effects of ethnicity, histology and TNM in a single institution outside of Southeast Asia.

Material and methods: The records of all 520 NPC cases (358:asian, 162:caucasian) treated at our institution from 1985-2002 were reviewed. Radical radiotherapy alone was used in 383, and 113 received induction or concurrent chemotherapy; the remainder were treated palliatively and contributed to the more advanced stage grouping. Stage distributions for both the 4th and 5th edition were determined. Percentage Variance Explained (PVE), a measure of variance in outcome prediction by each stage grouping scheme, and Balance (evenness of case distribution by groups) were calculated.

Results: The stage distribution for the 4th edition was I:27(5%); II:306.5%; III:56(11%); IV:407(78%) and for the 5th edition I:52(10%); II:137(26%); III:163(31%); IV:168(32%). Stage stratified 5-year cause-specific survival probabilities (4th edition) were: I:91%; II:96%; III:72%; IV:70% and (5th edition): I:93%; II:81%; III:75%; IV:56%. The stage distributions in both TNM editions were similar for asian and caucasians with no multivariate statistical outcome differences according to ethnicity or histological subtype. PVE was 2.1% (overall), 2.45% (asians) and 1.3% (caucasians) for the 4th