8511 POSTER DISCUSSION

Phase I Trial of Albumin-bound Paclitaxel (A), Cisplatin (P) and 5-Fluorouracil (F) as Induction Chemotherapy (IC) Followed by Concurrent Chemoradiotherapy (CRT) With Carboplatin (Cb) in Patients (pts) With Locally Advanced Squamous Cell Carcinoma of the Head and Neck (SCCHN)

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Background: Sequential therapy (IC followed by concurrent CRT) has been evaluated in the treatment of locally advanced SCCHN, with triplet IC containing docetaxel (T), P and F shown to be superior to the doublet PF regimen. A is a novel, biologically active, nanoparticle albumin-bound paclitaxel. Clinical studies of A in SCCHN are ongoing.

Methods: A phase I trial to assess the safety and efficacy of A, P and F as IC for 3 cycles, followed by concurrent Cb with radiation therapy (RT) (70 Gy/35), is conducted using the 3+3 design in patients with previously untreated, locally advanced SCCHN. Dose-limiting toxicities (DLT), consisting of standard hematologic and non-hematologic toxicity, as well as treatment delay, inability to complete $\geqslant$95% of RT, skin and mucosal toxicity related to RT, are assessed from day 1 of IC to 8 weeks after completion of CRT.

Results: To date, 7 pts have been enrolled in 2 dose levels. Demographics include: male:female = 6:1; median age = 58 yrs (range 51−64); ECOG 0:1 = 4:3; Oropharynx primary = 7; T1/2/3/4 = 1:1:2:3; N1/2a/2b/2c/3 = 0:0:3:4:0. Dose escalation is described in the table. Currently, dose level −1 is being expanded and so far only 1 DLT has been observed. Most common grade 3/4 treatment-related adverse events (AEs) were stomatitis (5 pts), neutropenia (4 pts), and dysphagia (3 pts). Seven pts have completed treatment so far, 5 remain disease-free, 1 pt relapsed and 1 pt died from unrelated myelodysplastic syndrome. Median follow-up is 13.1 months (4.1–26.5). Median progression-free survival has not been reached.

Conclusion: Accrual is ongoing to define the recommended phase II doses of APF in this sequential regimen.

Dose level	Sequential therapy regimen	No. of DLT/ No. of evaluable pts	DLT descriptions
1	A 75 mg/m^2 d1 + d8, P 100 mg/m^2 d1, F 1000 mg/m^2/d $\times$96 hours, Q3W $\times$3 cycles; then concurrent weekly Cb (AUC 1.5) $\times$7 with RT	1/3	1 pt with DLT: Febrile neutropenia; inability to receive 95% of RT; inability to receive at least 6/7 doses of Cb due to gr 3 stomatitis 2 pts without DLT: Both missed d8 of cycles 2 and 3 of IC due to intolerable gr 2 nausea, vomiting and fatigue.
−1	A 75 mg/m^2 d1 + d8, P 75 mg/m^2 d1, F 1000 mg/m^2/d $\times$96 hours, Q3W $\times$3 cycles; then concurrent weekly Cb (AUC 1.5) $\times$7 with RT	1/4 so far	1 pt with DLT: Inability to receive at least 6/7 doses of Cb due to gr 3 stomatitis

8512 POSTER DISCUSSION

A Three-Arm Randomized Trial Comparing Neo-Adjuvant or Concurrent Weekly Cisplatin to Radiotherapy Alone for Locally Advanced Head and Neck Squamous Cell Cancer (HNSCC)

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Background: Meta-analysis confirm the superiority of concurrent chemo-radiotherapy (CTRT) compared to loco-regional treatments (that include radiotherapy (RT) alone) for HNSCC, albeit with increased toxicity. This trial assessed the comparative efficacy of single agent cisplatin (CDDP) given in a doable weekly schedule either as neoadjuvant chemotherapy (NACT) or as CTRT to conventional RT in AJCC stages III/IV HNSCC where primary surgery was not an option.

Material and Methods: Following an informed consent, between August 1995 and March 1999, 282 evaluable patients following randomization (table of random digits) received NACT followed by RT (n = 92); CTRT (n = 95) or RT alone (n = 95). NACT or CTRT consisted of CDDP 35 mg/m^2 weekly for 7 cycles, while RT doses were identical − 70 Gy/35fx/7weeks − using a conventional 3-field technique with telecobalt or a 6MV LA and electrons if required. Compliance and crude incidence of acute toxicity (RTOG) are reported using summary measures. The principal endpoint was overall survival (OS), computed with the Kaplan–Meier method and p values obtained with the log-rank test. Patients dying of any cause as well as those lost to follow up (LFU) with/without disease when last seen were considered as 'events' for computation of OS assuming the 'worst case scenario'.

Results: Data was analyzed as of March 2011. With a median follow up (range) of 157 (125–181) months (mo) of all patients alive (5%), data is presented for the NACT, CTRT and RT arms respectively. The mean age was 56, 54 and 56 years; proportion of males 83%, 87% and 80%; Karnofsky performance score $\geqslant$80 in 84%, 90% and 67% (p = 0.000); oral cavity primaries in 22%, 20% and 18% and AJCC stages IV in 68%, 73% and 73%. Median CDDP cycles were 7, 7 and Nil; median RT doses and median (10−90 percentile) of RT treatment days were 70 Gy/53 (36−60), 70 Gy/53 (39−62) and 70 Gy/54 (44−63). Grade II/III mucositis was evident in 78%, 96% and 76% (p = 0.001) while grade III leucocyte nadir seen in 1.2%, 7.4% and Nil. Complete response at 6 months of completion was seen in 39%, 54% and 36% (p = 0.03). With 95% events (51% dead, 32% LFU with disease and 12% LFU without disease when last seen) the median, 5 and 10 years OS was 8.8 mo, 12% and 5% *vs.* 18.3 mo, 23% and 13% *vs.* 7.6 mo, 14% and 5% respectively (p = 0.006).

Conclusions: In the context of resource constrained environments, for locally advanced HNSCC, CTRT as described is doable and is more efficacious than either NACT or RT alone.

8513 POSTER DISCUSSION

A Phase II Study of Neoadjuvant Bio-chemotherapy With Cetuximab, Paclitaxel, and Cisplatin (CPC) Followed by Cetuximab-based Concurrent Bio-radiotherapy in High-risk Locally Advanced Head and Neck Cancer − Representative of Head and Neck Cancer Study Group of Taiwan Cooperative Oncology Group

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Background: To evaluate the therapeutic efficacy of sequential regimen using cetuximab-based triplet neoadjuvant chemotherapy (NC) followed by concurrent bio-radiotherapy (BRT) in locally advanced head and neck cancer (HNC) patients.

Materials and Methods: Eligible criteria included treatment-naïve patients with histologically confirmed squamous cell carcinoma originated from oral cavity or oropharyngeal area, and the disease staging beyond N2b or T4. The CPC regimen for NC consisted of cetuximab 500 mg/m^2, paclitaxel 120 mg/m^2, cisplatin 50 mg/m^2, every two weeks for five courses. Patients without disease progression would receive cetuximab 500 mg/m^2 every two weeks concurrently with radiotherapy for total dose of 70 Gy.

Results: Since October 2009 to November 2010, 47 patients were recruited to the study. Of all patients, 93.6% had N2b, N2c or N3 disease. The mean age of the patients was 50.4 years old, and the Eastern Cooperative Oncology Group performance status 0 and 1 was in 31.9% and 68.1%, respectively. The primary lesion was located at oral cavity in 57.4%, and at oropharyngeal area in 42.6% of patients. On intention-to-treat analysis (ITT), the best overall response was partial response (PR) in 30 patients, complete response (CR) in 3, stable disease (SD) in 12. The overall response rate was 70.2%. The best response rate after NC was 48.9%, including PR in 22 and CR in 1. Two patients had progressive disease (PD) before BRT, and among the other 45 patients, two declined to have radiotherapy. Of the 43 patients receiving BRT, two patients discontinued treatment due to treatment-unrelated complication or suggestion of surgical intervention. In the remaining 41 patients, additional 10 and 2 patients achieved PR and CR, respectively. In addition, seven developed PD, and two were not evaluable due to early termination as a consequence of toxicity. The most common grade 3 or 4 adverse events in the NC were neutropenia, while mucositis, anorexia, and dermatits accounted for the major complications during the BRT.

Conclusions: The cetuximab-based sequential regimen showed to be efficient in high-risk locally advanced HNC. CPC regimen was feasible in