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

most patients. However, adequate supportive care is necessary for the toxicity during the period of cetuximab-based radiotherapy.
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Response of NC, BRT, and the best overall response

	NC	BRT	Overall
Evaluable patients (N)	47	39	ITT (Total N = 47)
CR	1	3	3
PR	22	26	30
SD	22	3	12
PD	2	7	2

8514 POSTER DISCUSSION

Should Elderly Patients With Locally Advanced Oropharyngeal Squamous Cell Carcinoma Be Offered the Same Curative Treatment Options as Younger Patients?

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Background: Elderly patients with head and neck cancer are less likely to receive aggressive anti-cancer therapy than younger patients due to concerns over their ability to tolerate such treatments. There is now increasing evidence suggesting that treatment decisions should not be based on chronological age alone. Most of these studies however are not site-specific. The aim of this report is to compare treatment compliance and outcome between the elderly (defined as 65 years and above) and younger patients with locally advanced oropharyngeal squamous cell carcinoma.
Materials and Methods: In our institution, treatment decisions for patients with locally advanced oropharyngeal squamous cell carcinoma are based on disease characteristics, performance status and co-morbidity score, not chronological age. Treatment protocol consists of 3 cycles of induction chemotherapy (IC) with cisplatin and 5-fluorouracil followed by radical radiotherapy (RT) with concomitant weekly carboplatin (CC). Patients with histologically confirmed AJCC stage III-IVB squamous cell carcinoma of the oropharynx who received non-surgical therapy with curative intent were identified from our electronic database and included in this study.
Results: 144 patients were identified, 113 males and 31 females. 50 patients were elderly. Median follow-up was 24 months. The following table shows the disease characteristics, compliance data on IC, RT and CC and treatment outcomes expressed as recurrence-free survival (RFS), disease-specific survival (DSS) and overall survival (OS).

	Younger	Elderly	p-value
Number of patients in the study	94 (65%)	50 (35%)	
Median age (years)	54	74	
Age range (years)	26–64	65–89	
AJCC stage			
III	18%	26%	
IVA	82%	64%	
IVB	0%	10%	
Disease subsite			
Tonsil	66%	64%	
Base of tongue	29%	24%	
Soft palate	2%	10%	
Posterior pharyngeal wall	3%	2%	
Planned IC cycles delivered	91%	89%	
Planned CC cycles delivered	79%	74%	
Completed radical RT with no prolongation of treatment duration by more than 2 days	96%	82%	
Did not complete radical RT	2%	8%	
Estimated 5-year RFS	79%	70%	0.213
Estimated 5-year DSS	82%	76%	0.160
Estimated 5-year OS	70%	53%	0.006

Conclusions: Treatment compliance of elderly patients is comparable to that of the younger cohort. There is no statistically significant difference in estimated 5-year RFS and DSS between the two groups. The difference in estimated 5-year OS is due to more non-cancer-related deaths among the elderly patients. Elderly patients with locally advanced oropharyngeal squamous cell carcinoma should be offered the same curative treatment options as their younger counterparts.

8515 POSTER DISCUSSION

A Dose Escalation Study With Intensity Modulated Radiation Therapy (IMRT) in Moderately Advanced (T2N0, T2N1, T3N0) Squamous Cell Carcinomas (SCC) of the Oropharynx, Larynx and Hypopharynx Using a Simultaneous Integrated Boost (SIB) Approach

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Background: The simultaneous integrated boost technique with dose per fraction slightly higher than 2 Gy offers the advantages of shortening the treatment time and increasing the biologically equivalent dose to the tumour. The aim of this study was to evaluate the feasibility of a dose-escalating radiotherapy treatment by using a SIB-IMRT approach in patients treated for moderately advanced head and neck cancers.
Materials and Methods: Between September 2004 and May 2008, 57 consecutive patients with T2N0, T2N1 or T3N0 pharyngo-laryngeal SCC were included. The therapeutic PTVs were treated according to three dose levels ie, 69 Gy in 30 fractions of 2.3 Gy (Level I), 72 Gy in 30 fractions of 2.4 Gy (Level II) and 75 Gy in 30 fractions of 2.5 Gy (Level III). The prophylactic PTVs received a dose of 55.5 Gy delivered in 30 fractions of 1.85 Gy. The overall treatment time was 6 weeks for all patients. The primary endpoint of the study was acute toxicity assessed during treatment and during the first 3 months following the completion of radiotherapy. The secondary endpoints included loco-regional control, disease-free survival, overall survival and late toxicity at 2 years of follow-up. The study design allowed patients to be enrolled in the second dose level group if no more than 10% of grade 4 acute toxicity was observed on the first dose level group within 3 months after the completion of IMRT, and so on for the third level group.
Results: Forty four men and 13 women with a median age of 61 were included in the trial. The majority of them presented with oropharyngeal cancer (53%) and laryngeal cancer (33%). Most patients had T2N0 (61%) staged tumours, followed by T2N1 (21%) and T3N0 (18%). Only 3 patients developed grade 4 acute mucositis during treatment, one in each dose level. Thirty two patients experienced grade 3 toxicity (56%) during IMRT, mostly dermatitis and mucositis, without any significant difference between the groups. Late grade 1 and 2 xerostomia was seen in 51% and 35% of patients respectively. Transient grade 4 late toxicity was observed in 12% of all patients and was equally distributed among the groups. The 2-year loco-regional control was 82% for all 3 groups, without any substantial difference between them (79% dose-level I, 88% dose level II, 79% dose-level III). The 2-year overall survival was 89% for dose-level I and II, and 95% for dose-level III.
Conclusions: This dose escalation SIB-IMRT protocol was safe and highly effective as the sole treatment of moderately advanced SCC of head and neck. No toxicity or outcome difference was observed between groups. A phase III trial should be initiated to assess a dose-response relationship on tumour control with such SIB technique.

8516 POSTER DISCUSSION

Predictive Factors of Critical Weight Loss During Radiotherapy of Head and Neck Cancer

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Background: Critical weight loss during radiotherapy (RT) is common in head and neck cancer (H&N). Despite of preventive strategies to maintain adequate protein and energy intake, weight loss in H&N undergoing RT is still a serious problem. PEG tube insertion has been reported to be associated with a mortality rate of a few percent, and minor complications in over 30%, which calls for strict selection criteria for appropriate nutritional interventions. We explored patient-specific and treatment-related factors that predicted weight loss and need for feeding tube during RT.
Methods: 490 consecutively irradiated H&N patients were investigated retrospectively. Standardized registrations of patient-specific data before and during primary RT as reported to the database of DAHANCA were obtained and correlated to nutritional observations. All patients had received individual institutional dietary counseling followed by weekly nutritional assessments. Patients with pretreatment feeding tubes were