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POSTER DISCUSSION 2 *

Concomitant association of CDDP-5Fu and radiotherapy for locally advanced laryngeal and pharyngeal squamous cell carcinomas (SCC). A phase II study

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Introduction: Despite combination of aggressive but mutilating surgery and radiotherapy (RT), loco-regional control and survival remain poor in locally advanced SCC of the larynx and pharynx. Recent meta-analysis have shown that the use of chemotherapy (CH) could increase survival, the largest benefit being when CH was given concomitantly to RT. The majority of these studies used single agent CH. As concomitant polyCH and RT might offer the best prospect for improving local treatment, the purpose of this study was to evaluate the toxicity, response rate and treatment outcome of a concomitant CDDP-5Fu regimen and RT.

Methods: Only patients with T3-T4/N0-3/M0 SCC of the larynx and pharynx eligible for curative but mutilating surgery were included. PolyCH consisted in CDDP (75 mg/m², d1) and 5 Fu (1 g/m², d1-5) given during the 1st and 5th week of RT (70 Gy, 2 Gy/fraction, 7 weeks). Neck dissection was planned after polyCH + RT in >N0 patients, as well as salvage surgery for patients with less than pathologic complete response (PCR) or loco-regional recurrence.

Results: Fifty three patients were included. Thirty eight patients were already evaluated. Grade 3 and 4 mucositis or pharyngitis occurred in 75% and 8%, respectively. The average weight loss reached 13%. A feeding tube was required in 50% of patients. Grade 3 and 4 skin toxicity occurred in 60% and 2%, respectively. Neutropenic fever requiring i.v. antibiotics (37%) occurred in patients experiencing both grade 3-4 neutropenia and grade 3-4 mucositis/pharyngitis. One toxic death occurred. PCR rates reached 92% and 59% for primary tumor and nodes, respectively. With a median follow-up of 14 months, the loco-regional disease-free survival, and overall survival reached 70% and 65% at 1.5 year, respectively. All survivors have a functional larynx and pharynx.

In conclusion, concomitant association of polyCH and RT is feasible but toxic. It is associated with a high rate of PCR and organ preservation. Higher accrual and longer follow-up are however required before validating this protocol in a phase III trial.

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Testing the hypothesis: Pretreatment oxygenation predicts radiation response in advanced head & neck squamous cell carcinoma

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Purpose: We have previously suggested that pretreatment tumor pO₂ measured by polarographic electrodes was predictive of locoregional control (LC) after primary RT as patients with hypoxic tumors had a significantly poorer LC probability ($p = 0.01$, $n = 35$). The present study was performed to test this hypothesis.

Methods: Between December 1995 and October 1998 pretreatment pO₂ assessments were done in 35 advanced HNSCC among whom 32 were eligible. As in the hypothesis generating study from 1996 all patients were treated by primary radiation alone according to the DAHANCA program. Total dose 66-68 Gy/2 Gy per fraction over 5 or 6 weeks. The endpoint was locoregional control and oxygenation was evaluated as in 1996 by the percentage of pO₂ values 2.5 mmHg (HF2.5). Also, we tested the hypothesis by using the same cut off (median HF2.5 = 15%). Results are reported as 3 year actuarial values and differences estimated by log-rank analysis.

Results: The original hypothesis generating study was updated and at 3 years LC probability was still significantly different with 63% in well oxygenated tumors vs. 18% in hypoxic tumors ($p = 0.05$). In the present study we confirmed the hypothesis as LC at 3 years was 91% among well oxygenated tumors and 49% in hypoxic group ($p = 0.04$). Finally, when pooling results of both data set ($n = 69$) the difference in LC at 3 years was significant 72% versus 26% ($p = 0.0015$).

* Poster Discussion 2 will be held on Wednesday 15 September 1999

Conclusion: This study confirmed that pretreatment tumor oxygenation status was predictive of locoregional tumor control after primary radiation alone in HNSCC.

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Hyperfractionated radiotherapy (Hfx RT) with or without concurrent low-dose daily cisplatin (CDDP) in locally advanced unresectable squamous cell carcinoma of the head and neck (SCC H&N). A prospective randomized trial

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Purpose: to investigate whether the addition of concurrent low-dose daily CDDP to Hfx RT offers an advantage over the same Hfx RT alone in locally advanced unresectable SCC H&N.

Material and Methods: 130 patients received either Hfx RT alone to a tumor dose of 77 Gy in 70 fractions in 35 treatment days over 7 weeks or the same Hfx RT and concurrent 6 mg/sqm of CDDP given on each day of RT.

Results: Patients treated with Hfx RT/CDDP had a significantly longer median survival time and a higher 5-year survival rate than those treated with Hfx RT alone (38 vs 23 months, respectively; 46% vs 25%, respectively; $p = 0.0075$). They also had a significantly longer median time to local recurrence and a higher 5-year local recurrence-free survival (LRFS) than those treated with Hfx RT alone (not attained yet vs 13 months, respectively; 58% vs 40%, respectively; $p = 0.018$). There was no difference in the regional recurrence-free survival, but patients treated with Hfx RT/CDDP had a significantly higher 5-year distant metastasis-free survival (DMFS) than those treated with Hfx RT alone (87% vs 57%, respectively; $p = 0.001$). There was no difference in either acute or late high-grade RT-induced toxicity.

Conclusion: Hfx RT/CDDP offered survival advantage over Hfx RT alone which was due to an improvement in LRFS and DMFS.

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Incidence of occult lymph node metastases in clinically and CT staged N0 neck in patients with oropharyngeal carcinoma

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Purpose: To quantify the false negative rate of clinically and CT staged N0 neck in patients with oropharyngeal carcinoma and to study the distribution of the involved lymph node groups.

Methods: The records of 42 patients with oropharyngeal carcinoma who had been staged clinically and radiologically (using CT scan) to have T1-4 N0 disease were reviewed. All patients were treated by surgical resection including neck dissection. Twenty-two patients (52%) had cancer of the tonsil and 17 patients (40%) had cancer of the base of tongue. One patient had cancer of the soft palate and 4 patients had unclassified extensive lesions originating in the oropharynx. T1, T2, T3 and T4 lesions were found in 1, 10, 9, and 22 patients, respectively.

Result: Fifteen patients (36%) had pathologically involved neck lymph nodes. Seven patients had more than 1 group of lymph nodes involved. The number of positive lymph nodes ranged from 1-19 with a median of 4. The number of excised lymph nodes ranged between 5-72 with a median of 20. Twelve of 15 patients (80%) had involvement of level II neck lymph nodes and 7/15 patients (46%) had involvement of level III neck lymph nodes. Lymph nodes of level I and V were involved in 1 and 2 patients, respectively. Lesions arising from the tonsil or the base of tongue had equal probability of clinically undetected lymph node involvement. Patients with T1, T2, T3, and T4 lesions had 0%, 20%, 36%, and 55% chance of pathological involvement of lymph nodes.

Conclusion: Negative clinical and CT examination of the neck in patients with oropharyngeal carcinoma is associated with a high false negative rate. T staging influenced the probability of clinically occult lymph node involvement. Clinically and radiologically undetected lymph node involvement was found in all lymph node levels, but was greatest at levels II and III.