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Chemoradiotherapy for stage IV, unmetastatic, head and neck cancer. Preliminary results of a prospective, single-institutional, phase II trial

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Background: By July 2000, we began a phase II prospective, single-institutional trial with chemo-radiation for locally advanced head and neck cancer (LA HNC).We present our preliminary results.

Matherial and methods: Treatment consisted of Radiation Therapy with the boost concomitant technique (72Gy/6w), and two cycles of concomitant cisplatin (20 mg/sqm/day, days 1-5 and 29-33). All patients received intravenous amifostine, 200 mg/m2 previously to the first fraction of irradiation, and their quality of life was also assessed before, during, and regularly after treatment. The endpoints of the study were overall survival, local control, and quality of life. There were 24 men and 1 woman, all stage IV of AJCC. Median age was 56 years (35-75 years). Primary sites were as follows: oropharynx, 7 patients(28%); nasopharynx, 2 (8%); hypopharynx, 7 (28%); larynx, 6 (24%); oral cavity, 1 (4%), and paranasal sinus, 2 (8%).

Results: According to the UICC criteria, twenty patients (80%) had complete response, two of these were found to have residual microscopic disease at neck dissection. One patient had partial response (4%), three patients did not response (12%), and one patient was not evaluated for response because he died while on therapy. 2-Year overall survival, disease free survival and local control (Kaplan-Meier) were 75%, 54%, and 67%, respectively. Acute toxicities were frequently severe. Ninety two per cent of patients had grade 3 or 4 mucositis. One patient died of treatment-related toxicity (sepsis and digestive hemorrhage. Five patients (20%) developed unexpected catheter-related venous thrombosis. Despite this acute toxicity, most patients completed their chemo-radiotherapy treatment at or near intended doses. This was facilitated by the administration of intensive supportive care. The quality of life scores reflect moderate limitations in global quality of life at the three assessment points, and in specific aspects in the second and third evaluations: insomnia, dry mouth, sticky saliva, coughing and sexuality. The other areas assessed reflect a good level.

Conclusions: This combined modality is a very active and toxic treatment for LAHNC. Nevertheless, it is probably that boost concomitant radiotherapy is not a good schema of irradiation for combining with chemotherapy in LAHNC, due to the elevated toxicity.

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Functional analysis of the larynx reconstructed with a vestibular fold flap after cordectomy

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Objectives: Several reports of techniques for larynx reconstruction after partial vertical laryngectomy are available in the literature, some of them using structures of the larynx itself such as the vestibular fold, but few have emphasized analysis of laryngeal function after reconstruction. Thus, the objective of the present study was to assess laryngeal function in patients submitted to cordectomy followed by reconstruction with a vestibular fold flap.

Study Design: Prospective.

Methods: Ten patients, nine males and one female aged 45 to 75 years (mean age: 64.5 years), with glottis carcinomas treated by cordectomy and reconstructed with a vestibular fold flap were submitted to videolaryngostroboscopy for assessment of laryngeal permeability, flap positioning, laryngeal closure, aritenoid movement, characteristics of the sound source for speech (vibratile or frictional) and, when the source was vibratile, location and structures of the sound source.

Results: There was no need to maintain a tracheostomy during the late postoperative period since the reconstructed laryngeal lumen remained pervious. A vibratile sound source was detected in 90% of cases and was located in the glottic region in seven patients. The vestibular fold flap participated in the composition of the vibratile sound source in all cases.

Conclusions: Laryngeal reconstruction with a vestibular fold flap after cordectomy was able to maintain laryngeal function, providing laryngeal permeability and maintaining the organ as the air flow pathway, with full coaptation of laryngeal structures in 30% of cases, with a vibratile sound source in the glottic region in 70% of cases and with participation of the flap as a vibratile structure in 90% of cases.

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Induction chemotherapy (CT) followed by hyperfractionated radiation therapy (HFRT) in unresectable squamous cell carcinoma of the head and neck. Experience with an institutional protocol.

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Introduction: Induction CT seems to increase survival in patients (pts) with unresectable squamous cell carcinoma of the head and neck up to 24% in 3-y overall survival. HfRT improves local control of disease in a 15%. This study evaluates the efficacy of our previous institutional protocol before introducing concurrent CT and RT as standard treatment in unresectable disease.

Material and Methods: We included all pts with unresectable disease from March/1994 to June/2002. Treatment schedule: CDDP 100mg/m^2 on day 1 + 5FU 1000 mg/m^2 c.i. on days 1 to 5 every 3 weeks for four courses followed by HfRT (1,2 Gy/fraction x 2 /day for a total dose of 76,8-79,2 Gy). A multidisciplinary committee undertook unresectability and response evaluation. Surgical neck dissection was planned for pts with persistent cervical nodes but complete primary tumour response.

Results: 99 pts were included. Median age: 55 [38-76]. All pts had stage IVM0 disease: T4 68%, N2-N3 89% and synchronic tumours 6%. 19% had previous tracheotomy. Tumour location: oropharynx 63%, hypopharynx 22%, oral cavity 8% and larynx 7%. Median interval between CT and HfRT: 29 days [0-113]. 41% presented grade 3-4 toxicity related to CT, mainly afebrile neutropenia and mucositis, but there were 5 pts (5%) with ischemic event. Grade 3-4 acute toxicity related to HfRT: 48% stomatitis (15% required enteral support), 21% epithelitis. Chronic toxicity related to HfRT: 6 emergency tracheotomy due to laryngeal edema, 5 pneumonia and 4-mucous/soft-tissue necrosis. There were 8 toxic deaths (2 CT, 6 HfRT). Final tumour response: Complete Response 54 pts, Partial Response 25 pts, Stable Disease 2 pts, Progressive Disease 9 pts and unevaluated 9 pts. Median follow-up: 28.3 months. From 54 pts with Complete Response, 22 are alive without disease, 19 pts have presented recurrence, 6 pts have died from non malignant reasons, 3 have died from second tumours and 4 pts were lost for follow-up without disease. The 3-year progression free survival was 36.2% [25.8 46.6] and the 3 and 5-year overall survival (OS) was 33.3% [23.4-43.2] and 23.6% [14.5-32.8] respectively.

Conclusion: Induction CT followed by HfRT increase OS rate in unresectable disease compared with those previously reported with RT alone or with Induction CT and conventional RT. However, the high acute toxicity rate needs a trained multidisciplinary support team. Chronic toxicity rate should be analysed by quality of life measurements in order to know if this benefit in survival is justified.

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Resectable thymoma: treatment outcome and prognostic factors in the late adolescent and adult age group

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Background: In this study we investigated the therapeutic outcome and prognostic factors in patients with resectable thymoma.

Procedure: Thirty-seven patients who underwent surgical resection for thymoma and referred to our clinic over the past decade were retrospectively analyzed. The median age was 41 years, ranging from 19 and 72 years. Myastenia gravis was observed in 28 patients (75.7%). The most frequent histologic subtype was epithelial (n: 21, 56.8%), followed by the lymphocytic type (n:6, 16.2%). Stage at presentation was distributed as stage I: 2 patients (5.4%), stage II: 19 patients (51.3%), stage III: 10 (27.0%) and stage IV: 4 patients (10.8%). The majority of the patients (n:33, 89.2%) had completely resectable disease, while 2 patients had microscopic and 2 more patients had macroscopic residual disease after surgery. Adjuvant radiotherapy was administered to 28 patients. One patient received adjuvant chemotherapy and 8 patients were followed with no adjuvant treatment.

Results: After a median follow-up period of 39 months, 6 patients (16.2%)experienced recurrence. There was a significant correlation between recurrence and adjuvant radiation therapy (2-sided p=0.0001), as well as

stage (2-sided p=0.05). There were no objective responses to chemotherapy given to 4 patients for recurrent disesase. Overall (OS) and progression-free survival (PFS) was 79.8% and 74.6% at 5 years, respectively. Adjuvant radiotherapy had a significant association with both OS (p=0.006)and PFS (p=0.00001). Furthemore, recurrent disease was observed to have a significant negative impact on OS (p=0.006).

Conclusion: This study confirms the beneficial role of adjuvant radiotherapy in patients with resectable thymoma regardless of surgical margins.

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Cisplatin + irinotecan in recurrent/metastatic salivary gland malignancies

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The use of chemotherapy for recurrent Salivary Gland Malignancies (SGM) is under investigation. Fourteen pts (10 males, 4 females; median age = 55 yrs, range 20-70; median ECOG PS = 1) with recurrent SGM of major (9 pts) and minor (5 pts) SG origin (hystology: 1 adenocarcinoma, 10 adenoid cystic carcinoma, 2 undifferentiated carcinoma, 1 mucoepidermoid carcinoma) were treated with DDP 60 mg/m^2, on day 1 plus CPT11 60 mg/m^2 on day 1 and 8 (every 3 weeks for a minimum of 2cycles). All pts had been previously treated with surgery+radiotherapy and 6 with a DDP-based chemotherapy. One patient had a local lesion, 7 had loco-regional recurrences and metastases and 6 patients had metastases only. Responses were: PR in 1 patient (7%), lasting 4 months; 5 NC (36%) with a median duration of 3.5 months (2.5-6), and 8 PD (57%). The median survival time was 7 months. The major toxicity were neutropenia (grade 3-4 in 9/14 pts = 64%) and diarrhea (grade 3-4in 4/14 = 28%). In conclusion in our experience this combination appears less effective than DDP+vinorelbine (Cancer 91:541-547, 2001) and carboplatin+taxol (Anticancer Res. 20: 3781-3784, 2000) with a significant and unacceptable toxicity.

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Effect of radiation therapy fraction size on local control of T1 and T2 glottic carcinoma

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Purpose: Different radiotherapy fractionation schedules are used to treat patients with T1 and T2 carcinoma of the vocal cord in our institution. A retrospective analysis was performed to study the effect of fraction size (2.25Gy versus 2.5Gy) on local control in this group of patients.

Methods and materials: A total of 75 previously untreated patients with T1 and T2 invasive carcinoma of the true vocal cords were irradiated between July 1991 and Jan 2002. Five patients were censored due to missing information. All patients received irradiation (Cobalt 60 and 6MV), 56 patients (51 patients with T1 lesions and 5 patients with T2 lesions) received daily fractions of 2.5 Gy to a dose of 50 Gy and the remaining 14 patients (4 patients with T1 lesions and 10 patients with T2 lesions) received 65.25 Gy in 29 fractions of 2.25 Gy each.

Results: At a median follow-up of 30.5 months, the 5 year disease-free survival and overall survival were 81% and 98%, respectively. Local control at 5 years for patients treated with 2.5 Gy/fraction was 91% compared to 44% for those treated with 2.25Gy/fraction (p=0.0003). Among the prognostic factors tested, such as stage, anterior commissure involvement, smoking history, energy, field size, gender, age, duration of treatment and fraction size, the last three were significant predictors in univariate and multivariate analyses.

Conclusions: From the results of this retrospective review of patients treated with radiotherapy for T1 and T2 true vocal cord cancer and within the range of total doses and overall treatment times used in our patients, it was found that fractionation schedules using daily fraction size of 2.5 Gy, duration of treatment <=31 days and older age are associated with a better local control than delivering 2.25 Gy/fraction, a longer duration of treatment and younger age.

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Transoral CO2 laser surgery for organ preservation in hypopharynx carcinomas.

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Background: Transoral CO2 laser surgery has been employed for organ preservation in early larynx carcinomas. We analysed the the follow-up and functional results of selected patients (pts) with hypopharynx carcinoma treated by means of CO2 laser and we compared retrospectively the results with our historical patients treated with neoadjuvant chemotherapy and external conventional surgery.

Material and methods: Selected patients with hypopharynx (stage I to IVA) carcinoma treated with curative intention. Tumors with preoperative invasion of thyroid cartilage, deep tumor growth into the cervical space, tumors involving the cervical esophagus or both arytenoids were excluded. Historical controls were treated with two courses of cisplatin, 120mg/m2 plus bleomycin, 20mg/m2 (day 1 to 5) iv. in continuous perfusion followed by conventional surgery. Postoperative neck radiation was added in both groups if there were intranodal metastasis in * 2 lymph nodes, node rupture at the histopathologic analysis, or the metastasis diameter was greater than 2 cm.

Results: 28 patients were included in the laser group, 27 were male and one female, with a mean age of 56.6±7.32 years. Stage distribution: 0% I; 21.4% II; 28.6% III; and 50% IVA. Complete tumor resection was achieved in 86%, and marginal resection in 14% of the patients. Postoperative radiation therapy was given in a 57% of the patients; 43% over the nodes and 14% over nodes and primary site. Functional outcome: larynx and function was achieved in 75% of the patients. In 21.4% a non functional larynx was preserved, and in 3.6% total laryngectomy was necessary. After a median follow-up of 40.5±12.2 months, 50% of the patients are alive and disease-free. Overall and disease-specific survival rates were 43.4% and 59.4% respectively. Patients were compared with a stage-matched control group of 25 patients treated with neoadjuvant chemotherapy plus conventional surgery at our institution. Preservation organ was achieved in two patients (8%), and there were no significant differences in overall and disease-specific survival rates comparing with the laser group. Conclusions: In selected patients with hypopharynx carcinomas, CO2 laser surgery is able to preserve larynx function without reduction in survival rates.

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Squamous cell carcinoma of the soft palate managed with primary radiation therapy: patterns of nodal failure.

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Background: Squamous cell carcinoma of the soft palate (SCSP) is a relatively rare tumour. The purpose of this report is to describe the patterns of nodal relapse for patients with SCSP treated with primary external beam radiation therapy (EBRT).

Materials and Methods: The clinical records of all patients treated with EBRT at our institution for SCSP between 1980 and 1996 were retrospectively reviewed. Data collected included patient demographics, tumour description, radiation details and clinical outcome. The location of recurrent neck disease was determined with respect to the irradiated volumes for each patient.

Results: During the period of review 133 patients with SCSP were treated with EBRT. There were 84 males and 49 females with a median age 60 years (range:43-93). T-categories were: Tis(9); T1(12); T2(60); T3(47); T4(5). Nodes were clinically involved in 37/133(28%) patients. N-categories were N0(96); N1(21); N2A(2); N2B(3); N2C(6); N3(5). The median radiation dose was 51 Gy in 20 once daily fractions (range 28-70 Gy) with 72% of cases receiving the median dose. Radiation was administered with bilateral techniques (parallel opposed pair) in 108(81%) and with an ipsilateral approach (wedge pair) in 24(19%). Posterior neck fields to include upper zone V (photons followed by direct lateral electrons) were used in 47(35%) and the lower neck (zone IV) was treated in 64(48%). The median follow up time was 3.6 years (range:0.4-17). Actuarial rates of overall and disease free survival at 5 years were 39% and 53%. 5 year local, nodal and distant relapse free rates were 65%, 70% and 65%. Local control by T-category was: Tis(86%); T1(57%); T2(77%); T3(51%); T4(0%). Nodal control by N category was: N0(80%); N1(48%); N2A(50%); N2B(0%); N2C(44%); N3(60%). Patterns of nodal failure indicated 5/24 (21%) patients treated