671 PUBLICATION

## Effet of a pediatric form of granulocyte-colony stimulating factor (G-CSF) in radiotherapy-induced oral mucositis. A pilot study from the groupement de radiotherapie et d'oncologie de pyrenees (GROP)

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This pilot study investigates the role of G-CSF as reducing radiotherapy (RT) ± chemotherapy (CT) mucosal toxicity (mucositis) for patients (pts) treated for head and neck cancer. Sixteen consecutive pts (14 males), a median age of 57 years (36–74), tumors sites; nasopharyngeal (n = 1), tongue (n = 2), hypopharynx (n = 7), buccal (n = 4), tonsilar (n = 1), and non Hodgkin's lymphoma (n = 1), were enrolled in this study. Treatment was a daily fractionated RT (1.7–2.0 Gy) for 64 Gy as a median total dose (range 42–81 Gy). Six pts received concomitant platinum-based CT. G-CSF (13.4 × $10^6$ UI, Granocyte 13, LRPR) was administered in S.C. from day 10 to day 20 of the RT. Mucositis at 4 weeks and at the end of RT was:

| Grade (WHO) | 0 | 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|
| At 4 weeks | 4 | 2 | 8 | 2 | 0 |
| At the end of the treatment | 5 | 8 | 2 | 1 | 0 |

Main pts (14/16) were treated in outpatient department. There was only one case of parenteral nutrition. RT was delayed in 10 cases for 7 days as a median duration (2–10) but never stopped. Two pts presented more than 10% weight loss. Pediatric form of G-CSF (Granocyte 13) may decrease the severity of radiotherapy-induced oral mucositis in head and neck cancer pts.

672 PUBLICATION

## Alternating radio-chemotherapy with docetaxel/CDDP and involved field radiotherapy for recurrent, inoperable, and previously irradiated head & neck cancer

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**Purpose:** Prognosis of pat. with local-regional recurrence of head&neck cancer after operation and adjuvant irradiation or primary radio-(chemo-) therapy is poor. Median survival with symptomatic therapy is 4 months. Most pat. die of uncontrolled local tumor. High dose irradiation of recurrence cannot be delivered in pre-irradiated pat. due to insufficient normal tissue tolerance. Combined simultaneous radio-chemotherapy in phase I/II trials showed higher remission rates, but also higher toxicity compared to chemotherapy alone.

**Methods:** Twelve pat. with inoperable, and previously irradiated head & neck cancer, SCC, GII–III, median tumor diameter 3 cm (2–12 cm), underwent alternating radio-chemotherapy with docetaxel 60 mg/$m^2$ d1 + CDDP 15 mg/$m^2$ d2–5 in $1^{st}$, $4^{th}$, and $7^{th}$ week and involved field irradiation with 5 × 2 Gy in $2^{nd}$–$3^{rd}$ and $5^{th}$–$6^{th}$ week to 40 Gy total dose (ICRU50). Pat. characteristics: KI ≥ 70%, 8× nutritional deficiency, pretreatment: 4× primary radio-(chemo-) therapy 70.6 Gy, 8× adjuvant irradiation 60 Gy.

**Results:** All pat. received irradiation as intended. Planed docetaxel/CDDP chemotherapy was given in 22 of 36 courses, reduced chemotherapy in 7 courses, treatment was aborted twice due to WHO°II renal toxicity, and one docetaxel/Polysorbat80® hypersensitivity. Grade III–IV toxicity occurred in 9/12 pat.: 3/11 mucositis, 6/11 leukopenia (2/6 neutropenic fever), 1/12 hypersensitivity, 1/12 large bowel perforation (died at home 2 months later for unknown reason). Anemia WHO°II in 4/11 pat. required blood transfusion. Ten pat. were eligible for response: 5× CR, 4× PR, and 1× SD. Median time to local progression was 7 months, and median disease specific survival was 9 months. Three pat. died of progressive local tumor, 1 pat. due to cerebral filiae, 1 pat. lost of follow up 7 months after therapy with NED.

**Conclusion:** The presented schedule of alternating radio-chemotherapy in inoperable, recurrent, and previously irradiated head&neck cancer resulted in a 90% overall response rate. However substantial systemic toxicity has been observed, requiring a dose reduction of chemotherapy.

673 PUBLICATION

## Paranasal sinus cancer; role of the external beam radiotherapy

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**Purpose:** the aim of this study is to estimate results of radiotherapy in patients with paranasal sinus cancer treated in Cancer Center in Warsaw.

Material and Method: between 1987 and 1993 fourty six pts have received radical radiotherapy mainly after surgery. The majority of these pts had primary T3–4 stages. Technique of treatment was modified in respect to tumor localization. Conventional fractionation (l.8–2.0 Gy per fraction) was used in all cases. Total doses ranged from 60 to 72 Gy.

**Results:** actuarial 5-years disease free survival is 43%. The main causes of failures were local reccurences. Treatment tolerance was acceptable. Serious late complications were not observed.

**Conclusions:** even in advanced T3–4 stages of paranasal sinus cancer combined treatment (surgery followed by radiotherapy) can produce long term disease free survival.

674 PUBLICATION

## p53, gp170 and K 19 as clinical prognostic factors for response in head and neck squamous cell carcinoma

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**Purpose:** There are several but poorly understood factors that influence chemo- and radio-resistance in head-neck squamous cell carcinoma (HNSCC). The aim of our investigation was to evaluate how p53, gp170 and the expression of K 19 could act to better predict the clinical response to chemoradiotherapy in locally advanced HNSCC.

**Methods:** Between October through September 1998, 29 (25 evaluable) previously untreated patients (18 male, 7 female), with biopsy proven Locally Advanced HNSCC, stage III (6/25) and IV (19/25) were immunohistochemistry evaluated on biopsies for p53 and gp170, and by serum RT-PCR essay for K 19, before starting combined neoadjuvant treatment with platinum-based chemotherapy and radiotherapy. Expression of each marker was correlated with response to chemoradiotherapy.

**Results:** 8/25 patients (32%) were positive and 17/25 (68%) negative for p53. 8/25 (32%) and 17/25 (68%) patients were positive and negative for gp170-expression respectively. 10/25 patients (40%) were K 19-positive and 15/25 (60%) negative. Both p53-mutation (6/7 = 86% of no-responders) and gp170-expression (5/7 = 72% of non-responders) were correlated with poor response to chemoradiotherapy. We also checked the non-association with K 19 (4/7 = 57% of non-responders). We didn't find correlation between biological markers and stage of disease. There was codependence between grade (G3) and p53 wild-type and gp170-negative.

**Conclusion:** The assessment of response to chemoradiotherapy by biological factors in HNSCC is today uncertain. Although we need further analysis, we propose the nuclear accumulation of both mutant p53 and gp170 expression as a possible marker of drugs- and radio-resistance. We didn't find clear correlation between cellular expression of K 19 and response.

675 PUBLICATION

## Quality of life (QoL) and patient's perspective for induction chemotherapy (CT) in advanced Head and Neck cancer (HNC)

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**Aims:** QoL could be an important criteria in the decision making process concerning treatment (T) of HNC patients (p). To investigate QoL at the beginning and at the end of CT and to compare clinical response with QoL and psychological changes.

**Methods:** P with HNC submitted for induction CT. CT: 3 cycles of CDDP (100 mg/$m^2$ d1) and 5FU (1000 mg/$m^2$/24 h c.i. d1–5) every 21d. Antiemetics: anti-HT3 and steroids. Portable pumps. P have been interviewed twice by a psychologist: before 1st and after 3rd cycles. Measures and variables:

WHO criteria for response and toxicity, EORTC-QLQ C30 for QoL, Specific Symptom List (SSL) for specific symptoms. HAD-scale for anxiety and depression.

**Results:** 26 p has been included in the study. Most frequent primary tumors: Hypopharynx (7), Oropharynx (6). Mean score for EORTC-QLQ at baseline was 56 (0–100) and higher scored symptoms were: pain, appetite loss, sleep disturbance and constipation. For SSL (frequency/mean intensity): difficulty for speaking (85%/54), swallowing disturbances (73%/47), cough (54%/28), mouth pain or dryness (42%/21). Comparing 1st and 3rd EORTC-QLQ significant changes appeared for cognitive scale (improvement) and for physical scale (impairment). In SSL 7/9 symptoms were improved with $p < 0.05$ for speaking difficulty, swallowing disturbances and jaw movement. In HAD, 24% p showed high anxiety and 7.7% high depression levels.

**Conclusion:** HN p report an average score in QoL and its value is slightly modified by T. Cognitive domain improves and physical function decreases. Most symptoms show a tendency to improve with CT and no symptom have got significantly worse after CT. CT does not promote an increase of anxiety and depression levels. Difficulty for speaking, swallow disturbances, jaw movement and dyspnea are the symptoms significantly improved after induction CT. These results should be faced to the well known reduction in QoL after surgery or radiation therapy for HNC.

676 PUBLICATION

## High dose rate brachytherapy of the base of tongue

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**Purpose:** To demonstrate our radiotherapeutic treatment method applying different high dose rate /HDR/ after-loading techniques and to make the early results known in case of the cancer of the base of tongue.

**Method:** Between 1993 January and 1998 December nineteen patients with squamous cell carcinoma of the base of tongue were treated with HDR Ir-192 interstitial radioterapy. T stage was: 1 T1, 3 T2, 4 T3, 11 T4. N stage was: 9 N0, 6 N1, 4 N2. Nobody had distant metastasis. The implantation was carried out under general anaesthesia using rigid needles or plastic flexible tubes. There were two types of the indication of bracbytherapy: boost in definitive irradiation /15 patients/ after locoregional percutan therapy or postoperative interstitial treatment /4 patients/ without teletherapy by incomplete resection in case of T12, N0. The treatment planning was prepared by PLATO planning system. The mean dose was 21.8 Gy delivering generally with twice-a-day fractionation. Neck dissection was performed only in 7 patients.

**Results:** In case of definitive irradiation 66% complete remission and 33% partial remission occurred. At the mean follow-up period /29.9 months/ the local control is 32%. During this period from the 19 patients 6 /32%/ died in local recurrence. Among the living patients /68%/ 5 have recurrences and 2 have turnout progression. Late side effect /osteoradionecrosis, fistula/ did not occur.

**Conclusion:** The brachytherapy boost is a very effective treatment method in advanced base of tongue cancer, because it preserves the patients' quality of life and the results are the same as in the operated and postoperative irradiated cases.

677 PUBLICATION

## Radiotherapy and its results as concerns nasopharynx carcinoma at the National Institute of Oncology in Budapest

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**Purpose:** Rates of remission and the outcome were analysed in patients with cancer of nasopharynx treated with radiotherapy.

**Patients and Method:** Between January 1993 and December 1997, 65 patients with nasopharyngeal carcinoma were treated with primary external radiotherapy, in the vast majority of cases combined with brachytherapy.

Patients aged from 17 to 78 years (average 53 years). There were 41 men and 24 women. T stage distribution was 12 T1, 19 T2, 24 T3, 10 T4. 55 patients (85%) were initially seen with nodal metastasis. Primary treatment generally involved external radiotherapy to the primary tumor site and the whole length of the neck. The dose of external irradiation was between 60–72 Gy. 192-Ir brachytherapy boost was given for the residual or recurrent diseases in several (2–6) fractions with a total dose of 10–30 Gy.

**Results:** Complete remission was achived in 53 patients (82%). At a median follow-up of 32 months (range 12–60) 42 patients (65%) are alive without disease. 14 patients (21.5%) died, of which 9 in tumor progression and 5 tied of other causes.

**Conclusion:** The primary, radiotherapy of nasopharynx cancers produces excellent oncologic outcome. Further follow-up will be necessary to judge efficacy of radiotherapy.

678 PUBLICATION

## Alternating chemo-radiotherapy treatment of advanced head and neck cancer

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**Purpose:** combined (alternating/concurrent) chemo-radiotherapy is the most promising treatment for advanced, unresectable head and neck cancer. We have tried to test the feasiblity of one of the most effective combined treatments (Merlano and coll. J Natl Cancer Inst 1996; 88 (9): 583–9). In this multicenter trial however it was shown that there is a significant increase in the risk of death (34%) for patients treated outside the coordinating center (Annals of Oncology 8: 773–9, 1997). The results of our independent experience with the same treatment are reported below.

**Methods:** From Jan. 1994 to Oct. 1997 23 consecutive patients were enrolled. Treatment consisted of DDP 20 mg/m$^2$ + 5-Fu 200 mg/m$^2$ for 5 days, in weeks 1, 4, 7, 10 and of radiotherapy 2 Gy daily for 5 days/week in weeks 2–3, 5–6, 8–9. Patient's characteristics were similar to those reported in parenthesis in the randomized trial: M/F: 83%/17% (83%/17%), PS $\leq$ 1 98% (85%). Site: oropharynx 39% (37%), oral cavity 30% (30%), larynx 13% (7%), hypopharynx 17% (19%), Stage IV 57% (74%), III 43% (25%), unresectable 82% (91%).

**Results:** Our results were comparable to those reported in parenthesis by Merlano and coll: median overall survival 19.4 months (17 mo.), 2 and 3 years surv. 45% (40%) and 30% (37%) respectively; 2 and 3 years loco-regional relapse-free survival respectively 67% (65%) and 67% (62%) respectively; median progression free survival 12 months (10 mo.), 2 and 3 years 37% (28%) and 37% (34%) respectively. Grade III–IV hematologic and not hematologic toxicity were slightly superior: leukopenia 34% (21%), anemia 18% (6%), thrombocytopenia 15% (6%), mucositis 22% (6%), dermatitis 4% (3%). One septic toxic death was observed shortly after the end of treatment in a patient in CR.

**Conclusion:** We have confirmed that the alternating CT/RT treatment proposed by Merlano and coll. is feasible. The overall, loco-regional relapse-free and the progression free survival were similar. However, the toxicity we observed was slightly superior to that reported in the original article. The good results obtained outside a research setting confirm the value of this treatment for clinical practice.

679 PUBLICATION

## Phase II study paclitaxel (PTX) and cisplatin (Cis) in advanced and recurrent head&neck cancer

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**Purpose:** Paclitaxel is the most promising new drug in SCC-HN and has a response rate of 40%. Our study evaluated the activity, efficacy and toxicity of the combination PTX plus Cisplatin in advanced and recurrent H&N cancer.

**Methods:** 24 patients were enrolled from 2/97 to 2/99 (pts) 21 m and 3 f, median age 60 yrs, ECOG PS 0–2. All pts have histologically confirmed squamous cell carcinomas. Primary tumor sites: 13 oral cavity, 6 larynx, 3 nasopharynx, 2 hypopharynx. 16 pts were pretreated: 8 surgery + RT, 3 surgery, 2 RT, 3 RT + chemotherapy; 3 pts in advanced disease. Schedule was PTX 175 mg/sm in tree-hour i.v. day 1, Cis 75 mg/sm i.v. day 2, every 21 days. Up to date, 81 courses (range 1–9) were delivered.

**Results:** 23 pts are evaluable to activity, all to toxicity. Haematological toxicity was neutropenia (G2 12%, G3 21%) and anemia (G3 12%), non-haematological toxicity was alopecia (G3 79%), asthenia (G2 29%), myalgia (G2 25%), nausea and vomiting (G2 25%). Partial response was recorded in 9 pts (39.1%), stable disease in 8 pts (34.7%). Noteworthy, 7 pts in stable disease reported clinical benefit from this treatment.

**Conclusion:** PTX and Cis is an active and well tollerated combination in pts with H&N cancer. This regimen warrent further evaluation and in our opinion is a suitable alternative to consider for this disease.