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Concomitant radiochemotherapy for advanced oropharyngeal cancer; tolerance and early results

A. Kawecki, A. Jarząbski, Z. Szutkowski, W. Rolski, E. Towpik. *Department of Head and Neck Cancer, Cancer Center, Warsaw, Poland*

Purpose: To estimate tolerance and effectiveness of the concomitant radiochemotherapy for advanced unresectable oropharyngeal cancer.

Method: Cisplatinum 20 mg/m^2/day d. 0–4, 5-Fu 450 mg/m^2/day d. 0–6; than every week (days 13, 20, 27 etc) 5-Fu 450 mg/m^2 one-day. Conventional fractionation 2 Gy daily starting day 1, total dose 66 Gy. In case of CR of the primary and only PR of lymph nodes – MRND 4. Inclusion criteria: unresectable squamous cell cancer (SCC) of the oropharynx T3–4 and/or N2–3, no distant secondaries, perf. status 0–1 WHO, age < 70.

Material: Fifty seven patients entered the study (52 M and 5 F, age 17 to 69 years). Stage: T2N2–3 – 10 pts, T3–4N0–1 – 12 pts, T3–4N2–3 – 35 pts. Patomorphology: SCC G2 – 26 pts, poorly differentiated SCC – 31 pts. Tolerance: skin and mucosal reactions EORTC/RTOG classification: G3 in 27 pts. Breaks in radiation in 23 pts (in 2 over 10 days). All completed radiotherapy in planned total dose. Neutropenia was observed in 18 pts.

Results: CR was obtained in 41/57 pts (72%). CR of the primary and PR of lymph nodes: in 6 pts. During the observation (from 6 to 41 months) 11 pts failed. Recurrence at the primary was observed in 3 pts. Recurrences at the primary site and in the lymph nodes – in 4 other. Four patients failed due to distant secondaries. At present 34/57 (60%) patients are alive with NED.

Conclusions: Tolerance of concomitant radiochemotherapy in patients with unresectable oropharyngeal cancer is acceptable. Early results suggest high activity of this regimen.

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Hiperfractionated vs. standard radiotherapy of advanced laryngeal cancer

V. Cernea[2], N. Todor[1], O. Coza[2], N. Ghilezan[2]. *[1]Oncological Institute "Ion Chiricuta", Radiotherapy II, Cluj-Napoca; [2]University of Medicine and Pharmacy, Oncology, Cluj-Napoca, Romania*

Objectives: We begun treating patients with advanced laryngeal cancer with hyperfractionated radiotherapy in 1987 and this study analyses the results and the optimal time dose ratio for this particular type of fractionation.

Material and Methods: between 1987 and 1993, 106 patients (pts.) with T3 and T4 larynx squamous cell carcinoma entered in a prospective non-randomised study comparing standard 2 Gy/day, 10 Gy/week (ST-group B), vs. hyperfractionated 2× 1.2 Gy/day, 12 Gy/week (HF-group A) radiotherapy. Total doses administered were: 70–72 Gy and 74–84 Gy for standard and hyperfractionated schedules respectively. Distribution of pts. accordind to T category: T3 – 14 pts. in group A and 21 in group B; T4 – 45 pts in group A and 26 in group. B.

Results: 5 year actuarial survival: 68% for T4 in group A (HF) and 28% in group B (ST), for T3: 75% in group A and 73% in group B. Local failure was the mos frequent (45% of failures) followed by loco-regional failures (12%). A logistic regression was performed for some fractionation parameters. Total dose (TD), overall treatment time (OTT) and the dose intensity (>1.7 Gy/day vs. <1.7 Gy/day) were found to be significant ($p < 0.02$) for local control at 3 years.

Conclusions: Hyperfractionated radiotherapy is a valid therapeutic option for the advanced laryngeal cancer. Significant survival diferences were for T4 tumours but not for T3. TD, OTT and dose intensity are therapeutic factors with significant prognostic value.

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A retrospective analysis and long term follow up on patients receiving radiation treatment for T1–T4 laryngeal carcinomas at Uppsala University during 1978–1987

M. Bergqvist[1], O. Brodin[1], A. Pouzon[1], A. Linder[2], P. Hesselius[1], E. Blomquist[1]. *[1]Inst. for Oncology/Radiology/Clin Immunology, Dep. of Oncology, Uppsala; [2]Inst. of surgery, Dep. of otorhinology, Uppsala, Sweden*

Laryngeal carcinoma affects approximately two hundred patients annually in Sweden. The treatment of choice is radiation treatment and if this treatment fails, the patient is admitted to surgery.

In this study we have retrospectively analysed a consecutive material of patients with a histopathological confirmed diagnosis of laryngeal carcinoma. These patients have received radiation treatment at the Department of Oncology, University Hospital, Akademiska sjukhuset in Uppsala, Sweden during 1978–1987. The study focuses on the outcome of radiation treatment in terms of survival and local recurrence rates. The patients have been followed up to a maximum of nineteen years from start of radiation treatment. Approximately 150 patients have been included and analysed.

Local control rates at five years were approximately: T1:86%, T2: 87%, T3: 76% and T4: 62%

The percentage of patients that died due to laryngeal carcinoma at 5 and 15 years after radiation treatment is approximately:

T1. 5 years: 4.%, 15 years: 4.%
T2. 5 years: 15%, 15 years: 34%
T3. 5 years: 23%, 15 years: 27%
T4. 5 years: 50, 15 years: 50%

The results of this retrospective study is that radiation treatment produces high accuracy of cure for patients with laryngeal carcinomas in low stages and that the five year survival is maintained at ten and fifteen years follow up for all stages except for laryngeal carcinomas in stage T2.

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Low-dose gemcitabine with radiotherapy in advanced head and neck an thyroid tumors: A phase II study

I. Wildfang, M. Raub, S.A. Güner, J.H. Karstens. *Dpt. of Radiation Oncology, Medical School Hannover, D-30625 Hannover, Germany*

Objective: Gemcitabine (GEM) is a radiosensitizing agent Phase I studies combining RT and low-dose GEM have shown interesting activity in head and neck and pancreatic cancer, in part with severe side effects In order to evaluate the toxicity and efficacy of a combination of RT and low-dose GEM in locally advanced or recurrent head and neck and thyroid tumors, a phase II study was performed with GEM 200 mg/m^2 i.v. weekly during RT.

Methods: 26 patients with locally advanced and progressive head and neck (n = 22) and thyroid carcinomas (anaplastic 2, medullary, follicular 1), median age 60 yrs (range 36–71), male/female 21/5, were treated with 2–10 cycles GEM in combination with RT (mean 42 Gy, range 18–67), 14 untreated, 12 pts pre-irradiated (60 Gy, 40–80). 26/26 pts are evaluable for toxicity.

Results: The most common side effects were mucositis and erythema, in 8 pts toxicities > gr. 2; 6 pts mucositis gr. 3; 1 Pt skin gr. 3; 1 leucopenia gr. 3. Until now, previously reported late toxicities such as pharyngeal Stricture was not observed. 20/25 are evaluable for response: 3 CR (15%; first line 3, pre-irradiated 0), 9 PR (45%; first-line 4, pre-irradiated 5), 6 NC (30%), 3PD (10%). In untreated pts the response rate is 70% vs. 50% in pre-irradiated pts. Interestingly, thyroid carcinoma responded well (3/4 PR, 1 NC). After a median follow-up of 44 (3–83) weeks the median time of progression is 29 (3–83) weeks.

Conclusion: Low-dose GEM in combination with RT has a high radiosensitizing potential with durable response in first-line treatment of locally advanced head and neck and thyroid tumors, but is also effective in pre-irradiated pts, with low acute toxicity. While these preliminary data are encouraging, further assessment is required to define the optimal dosage for combinations of GEM and RT, especially with lower dosages in first-line treatment of head nad neck and thyroid tumors.

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Apoptosis in relation to topoisomerase IIa, p53, p21 and p27 in head and neck cancers

N. Kapranos, G.P. Stathopoulos, L. Manolopoulos, E. Kokka, C. Papadimitriou, G. Adamopoulos. *Amalia Fleming and Hippokration Hospitals, Athens, Greece*

Aims: The aim of the study was to estimate the apoptotic index (AI) in 65 cases of head and neck carcinomas and to correlate it with the clinicopathological characteristics of the cases, the expression of Topoisomerase, p53, p21 and p27 proteins and patients survival.

Material: Sixty five patients with head and neck cancer (38 from larynx, 8 from tongue and 19 from other sites were included in the study. The tissue specimens were taken at initial diagnosis.

Methods: Cells undergoing apoptosis were detected by the in situ end-labeling method on paraffin sections and the AI was estimated by measuring the percentages of apoptotic nuclei using the CAS 200 image analysis system. Topoisomerase IIa, p53, p21 and p27 proteins were detected by immunohistochemistry.

Results: Higher apoptotic index was found in tumors of advanced stage ($P = 0.03$) and in tumors with negative p53 expression ($P = 0.10$). Patients with