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Benefits and toxicities of accelerated radiochemo- versus accelerated radiotherapy in advanced head and neck cancer - Results of a German randomized study

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Purpose: Concurrent chemo- and radiotherapy is proven highly effective in advanced head and neck cancer but associated with increased acute toxicities, especially mucositis. In a randomized phase III study the efficiency and toxicities of accelerated radiochemo- (RCT) versus accelerated radiotherapy (RT) were evaluated.

Materials and methods: This multicentric study opened in 7/1995 and closed patients accrual in 4/1999 with 263 randomized pts. with stage III+IV unresectable cacinomas of the oro- and hypopharynx without any pretreatment. Pts. were randomized either for RCT (2 cycles of 5-FU(600mg/sqm/d)/carboplatin (70mg/sqm), d1-5, 29-33, arm A) or RT only (arm B). Total RT-dose in both arms was 69.9Gy in 38d with a concomitant boost (weeks1-3: 1.8Gy/d, weeks 4-6. Bid RT with 1.8Gy/1.5Gy). In both arms, there was a second randomization for prophylactic G-CSF (263μg s.c.,d15-19) to test the effect on mucosal toxicity. Primary endpoint of the study was 1-year survival with local control (SLC).

Results: This analysis is based on 240 pts. (113 RCT-pts., 127 RT-pts., median FU 22.3 months),qualified for protocol and starting treatment. There were 178 oro- and 62 hypopharyngeal carcinomas, 96% in stage IV. The overall response rate (CR+PR) was 92.4% for RCT and 87.9% for RT (p=0.29). 1- and 2-year locoregional tumor control (LRC) was 69% and 51% after RCT versus 58% and 45% after RT (p=0.14). Median time of continuous LRC was 32 months after RCT versus only 14 months after RT with significant better 1y-SLC of 58% after RCT v 44% after RT (p=0.05). Oropharyngeal carcinomas showed highly better SLC after RCT (60% v 40%, p=0.01), the smaller group of hypopharyngeal carcinomas had no statistical benefit of RCT v RT (p=0.84). Regarding acute toxicities, RCT produced higher rates than RT, especially severe mucositis (68% v 52%, p=0.01). Patients with prophylactic G-CSF developed reduced mucosal toxicity (p=0.07), but also showed significantly reduced LRC (p=0.007), a completely unexpected result. Multivariate Cox regression analysis revealed intial hemoglobin level <13,5g/dl, G-CSF-application, and N2c-3- status as bad prognostic factors for SLC.

Conclusion: Accelerated RCT is more efficient than accelerated RT for patients with advanced oropharyngeal carcinomas. The increased acute toxicities are tolerabel. Prophylactic G-CSF may reduce mucosal toxicity but may result in significantly decreased locoregional tumor control.

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Radiotherapy with or without mitomycin C in the treatment of locally advanced head and neck cancer. Results from the IAEA multicentre randomised trial

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Single agent MMC has previously been shown to improve the outcome of radiotherapy in single institution trials without increasing the normal tissue toxicity. In 1996 the International Atomic Energy Agency (IAEA) initiated a two-armed randomised multicentre trial where head and neck cancer patients were treated with primary curative radiotherapy (66 Gy in 33 fractions with 5 fractions per week) with or without a single injection (15 mg/sqm) of MMC at the end of the first week of radiotherapy. A total of 558 patients were recruited in the trial from Feb 1996 to Dec 1999 from eight centres in Europe and Asia. Patients had stage III (n=264) or stage IV (n=294) squamous cell carcinoma of the oral cavity (n=255), oropharynx (n=170), hypopharynx (n=80) or larynx (n=53). Many of these patients had very advanced tumors. Prognostic factors like age, gender, site and stage were well balanced between the two arms. The first results six months after study closure showed that MMC was very well tolerated in combination with primary radiotherapy. Acute morbidity data were available from 393 patients. The haematological side effects of MMC were very modest (<5% grade 3-4) and did not require any specific interventions. Furthermore, MMC did not enhance the incidence or severity of acute or late radiation side effects. Confluent mucositis and dry skin desquamation was common, occurring in 56% and 65% of patients, respectively. Patient compliance to follow-up visit was a problem in many of participating centres from Asia. The overall 2-year locoregional tumor control, disease-specific and crude survival rates were 23%, 45% and 38%, respectively. Tumor stage and localization were significant parameters for loco-regional tumor control. There was no significant effect of MMC on locoregional control or survival. In conclusion, this large multicentre study did not show any influence of MMC on the outcome of primary radiotherapy in advanced head and neck cancer.

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Radiation therapy in elderly patients with head and neck cancer: a G.R.O.G.* study on 394 pts.(*Geriatric Radiotherapy Oncology Group - Italy)

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Aim of the study: a prospective study on patients aged more than 70 yrs with HN cancer to address the following questions: a)how elderly HNC patients are treated in Italy b)is the choice of therapy justifiable? c)are toxicity and late effects of RT in elderly patients well quantified and identified?

Materials and Methods: in 1997 the GROG performed a study involving 22 Italian RT Dpts. 394 pts (M=305;F=89) aged between 70 and 92 (mean 76.6) were enrolled in the study. Data concerning the type of education,family life,site and stage of disease,type and RT dose, early and late complications and response to treatment, were collected. Response to treatment, PS and late effects were collected 2 mts after the end of therapy and then at 6, 12 and 24 mts.

Results: data showed that elderly pts with HNC observed in Italian RT Departments usually present with a good KPS (=70 in 79%), live with a family (82%), have a high grade co-morbidity in <25% and a weight loss >5 kg in only 12%.

303 pts with primary SCC were evaluable: 62 pts with recurrent disease and 30 with a histology different from carcinoma were excluded.

The site of neoplasm was: nasopharynx in 4%, oropharynx in 13%, hypopharynx in 6%, larynx in 47.5%, oral cavity in 21%, paranasal sinus in 5.5% and salivary glands in 3%.

Three pts were stage 0 (1%),91 stage I (3%),56 stage II (18%),59 stage III (19.5%) and 96 stage IV (31.5%). 35 cases underwent surgery alone,155 RT,92 adjuvant RT and 18 palliative RT.In 3 cases no therapy.

If cure was the aim, a median dose of 66 Gy was delivered to the primary tumour (T) and 58 Gy to neck nodes (N);a median dose of 60 Gy was administered to T and 54 Gy to N if RT was considered adjuvant.Early toxicity was evaluated 2 mts after the end of RT:grade 3-4 toxicity involving at least 1 site was observed in 22 pts.Of the 155 pts treated with RT for HNC, 64.5% reached a CR and 14.1% a PR 2 mts after the end of RT. After a median follow up of 23 mts, 39.6% are alive with NED and 23.8% died with disease.Of the 92 pts treated with adjuvant RT, 76% reached a CR and 5.5% a PR 2 mts after the end of RT. After a median follow up of 20.2 mts, 62% are alive with NED and 16.3% died with disease.

Conclusions: a) RT in elderly pts with HN-SCC plays a major role in the global therapeutic strategy, alone or as adjuvant treatment. b) a treatment schedule including RT is justifiable, feasible and well tolerated also in elderly pts. C) tolerance to RT seems well quantified and identified.

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Photodynamic therapy with Foscan® (temoporfin) in primary squamous cell carcinoma of the head and neck

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Aims: This prospective non-randomised Phase II study investigated the complete response (CR) rate to Foscan-mediated photodynamic therapy (Foscan PDT) in patients with primary head and neck cancers; duration of CR and survival time; and tolerability and safety of Foscan PDT.

Method: 114 patients with primary (Tis, T1, T2) squamous cell carcinoma (SCC) of the lip, oral cavity, oropharynx or hypopharynx and Karnofsky status =< 70 received Foscan (0.15 mg/kg IV), followed four days later by single non-thermal illumination of the tumour with red light (20 J/cm2,