model. The dose lost with the prolongation of OTT (decrease of dose per fraction) was lambda/alpha = 0.36 Gy/day, during the gap the proliferation is equivalent to lambda/alpha + delta/alpha = 0.67 Gy.

Conclusion: The repopulation of tumour cells is faster during the gap than during the normal days of irradiation.

600 ORAL

Continuous hyperfractionated accelerated radiotherapy with/without mitomycin C in cancers of the head and neck region

W. Dobrowsky[1], J. Widder[1], J. Naudé[1]. [1]*Allgemeines Krankenhaus der Stadt Wein, Dept. Radiotheraphy and Radiobiology, Vienna, Austria*

Purpose: To evaluate the effect of a very accelerated fractionation regime with and without chemotherapy (Mitomycin C) an advanced head and neck cancers a randomised trial was initiated following approval be the Ethics Committee of the Univeristy of Vienna.

Patients and Methods: From 10/1990 to 12/1997 a total of 229 patients (193 male, 36 female, median age 56 years, range 31–75 years) with squamous cell cancer of the head and neck region were treated in a randomised study comparing conventional fractionation (CF, 70 Gy/35 Fractions/7 weeks) with a continuous hyperfractionated accelerated radiotherapy (V-CHART 55.3 Gy/17 consecutive days/33 fractions) and the same fractionation with additional Mitomycin C (MMC: 20 mg/sqm on day 5 = V-CHART + MMC). Patients were stratified for age, gender, stage and site of disease, and performance status. Most patient had large inoperable tumours (T3/T4 84%, N1-3 79%). The mean Karnofsky performance status was 90–100% in all three treatment groups. Sites of origin were: oral cavity 70, oropharynx 95, hypopharynx 39, larynx 25.

Results: Main toxicity from accelerated schedules was confluent mucositis (Grade 3–4 in 95%) requiring naso-gastral tube feeding and analgetics in majority of cases, and moderate haematological toxicity (Grade III–IV: 29%) in those receiving MMC. The administration of MMC did however not influence local toxicity. The duration of mucositis in the three treatment groups was not statistically different.

	CF	V-CHART	V-CHART + MMC
Local tumour control	31%	34%	48%
Survival	27%	28%	39%

Twenty-one patients have experienced distant metastases, 9 patients second primaries, respectively. Follow up was >48 months (median) and assessment performed by January 1999.

Conclusion: Following shortening the overall treatment time from 7 weeks to 17 days and a reduction in dose of 15 Gy the results from the radiation only treatments are comparable. The administration of MMC to our accelerated regimen improves results significantly with regard to local tumour control and to actuarial overall survival.

601 ORAL

Randomized trial evaluating the role of blood transfusion prior to radiotherapy in 414 patients with head and neck carcinoma. A multicenter study by the Danish Head and Neck Cancer Study Group (DAHANCA)

J. Overgaard[1], H. Sand Hansen, M. Overgaard, C. Grau, K. Jørgensen, L. Bastholt, L. Specht. [1]*Danish Cancer Society, Dept. Experimental Clinical Oncology, Aarhus University Hospital, Denmark*

Background: As a part of a randomized trial evaluating role of nimorazole as a hypoxic cell radiosensitizer (Radiother. Oncol. 46: 135–46, 1998), the importance of hemoglobin (Hb) level on the outcome of radiotherapy and its modification with transfusion were also addressed.

Methods: Patients with low pre-irradiation Hb (females < 8 mmol/l, males < 9 mmol/l) were randomized to ± transfusion, prior to final randomization to nimorazole or placebo. Transfusion were given with packed red blood cells to achieve a Hb concentration in the "high" value range. If during the treatment the Hb level fell below the values indicated above, the transfusion was repeated. A total of 414 eligible patients with pharynx and supraglottic larynx carcinoma were included. High Hb was found in 243, and low in 171 pts. Among the latter 82 was randomized to receive transfusion (0–6 units). Compliance to tranfusion was high and all but six patients randomized received the treatment, but only in 29 patients were the required Hb level reached and matained during irradiation. Radiotherapy was conventional radiotherapy alone (62–68 Gy, 2 Gy per fx, 5 fx per week). Median obs. time was 112 months.

Results: Hb levels were not significantly related to any other major prognostic parameter (T-size, Nodal status, Tumorsite). Univariate analysis showed that the outcome (5-year actuarial loco-regional tumor control) was significantly related to Hb concentration (high 46% vs low 37%, p = 0.02), but transfusion to the low Hb group was unable to change the out come (39% vs 35% in transfused and non-transfused pts, respectively. Despite that, nimorazole did significantly enhance the outcome in all Hb strata, indicating the importance of tumor oxygenation and hypoxic cell radiosensitization. The lack of transfusion effect was unexpected, but may be explained by compensatory growth of tumor cells, since transfusion was given prior to start of radiotherapy. This may be avoided by a slow Hb increase during RT. Consequently this mechanism will be explored in a planned trial using EPO rather than transfusion.

Conclusion: Transfusion prior to radiotherapy was unable to improve the effect of radiotherapy of head and carcinomas in patients with low Hb values.

602 ORAL

A systematic review of chemotherapy trials in Head & Neck cancer

A.J. Munro[1]. [1]*R.O.D.S. Ninewells Hospital and Medical School, Radiation Oncology, Dundee, United Kingdom*

A literature-based meta-analysis of 73 randomised trials (11.355 patients) comparing standard treatment alone with standard treatment plus chemotherapy shows that adding chemotherapy improves survival by 8% (5% to 11%: NNT 10 to 20). The magnitude of improvement depends upon the timing of treatment: neoadjuvant 4% (ci 2% to 6%; NNT 16 to 50); synchronous chemo RT 16% (ci 11% to 21%; NNT 5 to 10). Loco-regional control is improved by synchronous chemo RT but not by neoadjuvant therapy: perhaps because the local procedure is compromised by a sense of false security. The modest survival benefit from neoadjuvant chemotherapy is due to a 7% (ci 4% to 11%) reduction in distant metastases. Synchronous chemo RT increases the rate of Grade 3 or 4 mucositis by 16% (ci 10 to 21%) – suggesting that there may be no real improvement in therapeutic ratio with this approach. These results imply that future trials need directly to address issues concerning morbidity and patients, attitudes to functional impairment.

Data from over 600 Phase 2 and Phase 3 studies of chemotherapy have also been systematically reviewed (15.353 patients). CR rate with platinum-based regimens is 32% (ci 31 to 33%); CR rate with regimens not containing platinum is 17% (ci 15 to 19%). CR rate is significantly higher in Phase 2 studies 36% (34 to 37%) than in Phase 3 studies 20% (19 to 22%). Early data, on 421 patients, suggests that Taxanes have significant activity in Head and Neck cancer: local disease CR rate 49% (ci 45 to 54%) for Taxane-based regimens. These data may be useful in putting the design of future trials in Head and Neck cancer on a more rational basis.

603 ORAL

Randomized study of fluconazole (FCA) oral suspension (OS) versus amphotericin b (ab) oral suspension in the treatment of oropharyngeal mucositis in head and neck cancer patients (HNCP)

C. Domenge[1], J.L. Lefebvre[2], Y. Esnault[3]. [1]*Gustave Roussy, chirurgie cervicio faciale, Villejuif;* [2]*Oscar Lambret, Chirurgie cervico faciale, Lille;* [3]*Laboratoire Pfizer, Orsay, France*

Mucositis is a frequent disabiliting side effect of anticancer chemotherapy and of radiotherapy. A randomized French multicentric study was conducted from March 1996 to June 1998 to compare the efficacy and safety of 2 regimen groups, FCA OS 50 mg o.d. vs AB OS 0.5 g q.i.d., for a period of 1 to 2 weeks in the treatment of mucositis in HNCP treated by radiotherapy and/or chemotherapy.

Methods: Inclusion criteria were HNCP with at least grade I mucositis during radiotherapy and/or chemotherapy, and who had direct swab examination and culture. Clinical symptom evaluation, direct swab examination and culture, were performed before treatment, at day 4 and day 7 and day 14 in case of clinical response.

Results: 268 patients (pts) were included in this study, 135 assigned to AB and 133 to FCA. The 2 groups were well balanced. There was no difference according to the gender (87% male), the age (28–90 average 58 ± 11), the weight (average 65 kg), anteriority of mucositis at inclusion (average 9 d ± 16). Mycologycal evaluation was positive before treatment in 46% of pts (C. albicans 65%, C. tropicalis 10%, C. kefir 9%, C. krusei 7%, C. glabrata 6%). Median treatment duration was 10.3 d (0–23) and 96%