(25 patients). In the latter dose range the FSRT was partially delivered concurrently with the CRT. Concurrent chemotherapy was administered to 47% (41) and neoadjuvant chemotherapy to 4% (3) . Two year actuarial rates of overall survival and disease free survival were 98% and 83%. Local, nodal and distant control rates at 2 years were 86%, 98% and 94%. Two year local control rates by T category were: T1: 95%, T2A: 83%, T2B: 88%, T3:100%, T4: 66%. Means of the maximum point dose to brainstem and optic chiasm were 56% and 34% of the prescribed FSRT dose. FSRT delivered with IMRT allowed larger CTV's to be treated (median volumes: 48 ml IMRT, 38 ml XPlan, 37 ml XKnife) permitting the inclusion of involved retropharyngeal nodes in the volume treated with FSRT. No patients have developed significant late toxicity at the time of this review.

Conclusion: FSRT has been successfully integrated with CRT for the initial management of NPC. Coverage of larger volume tumours was better achieved with stereotactic IMRT than Xknife or XPlan. Sparing of critical normal structures without compromise of dose delivered to the tumour was achieved. A comparison of FSRT to CRT and large volume nonstereotactic IMRT will be presented.

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Radiotherapy combined with cisplatin, carboplatin, mitomycin C, and 5-FU single drug or two drug chemotherapy compared to radiotherapy alone in unresectable head and neck cancer - a meta-analysis

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Background: Former meta-analysis on the addition of chemotherapy to radiotherapy in unresectable squamous cell cancer of the head and neck showed a small but significant survival advantage in favour of simultaneous chemotherapy. However, the meta-analysis included studies with older bleomycin and MTX containing chemotherapies that are not longer considered standard and did not take into account differences in the fractionation schedules used in the studies. Therefore, we performed a meta-analysis based on published data on modern chemotherapeutic regimens in combination with different radiation schedules.

Methods: Randomised trials comparing radiotherapy alone with simultaneous or alternating chemo-radiotherapy using cisplatin, carboplatin, mitomycin C, and 5-FU as single drug or combinations of 5-FU with one of the other drugs were included into the analysis. Group I trials included studies with conventionally fractionated radiotherapy (CF-RT) with or without single drug simultaneous chemotherapy. Group II consisted of trials with CF-RT in combination with or without simultaneous two drug chemotherapies or CF-RT compared to alternating chemo-radiotherapy (two drugs). Group III analysed studies of hyperfractionated-accelerated radiotherapy (HFX/AFX-RT) compared to HFX/AFX-RT in combination with simultaneous single or two drug chemotherapy. Survival data were fitted to a log-normal distribution to assess differences in survival in the respective study. The mean difference in overall survival of the pooled data in groups I-III were estimated using a maximum likelihood method.

Results: 20 trials with a total of 3513 patients were included into the analysis. Group I, II, and III consisted of 7, 6, and 7 studies including 1229, 951, and 1333 patients, respectively. Single drug chemotherapy in combination with CF-RT (group I) resulted in a survival benefit of 18.8 months (14.6 - 23.7 months 95% CL) compared with CF-RT ($p<0.00001$). The use of two drug chemotherapy in combination with simultaneous or alternating CF-RT (group II) was associated with an 8.8 months (5.4 - 12.8 months 95% CL) survival advantage compared with CF-RT alone ($p<0.001$). HFX/AFX-RT in combination with single or two drug simultaneous chemotherapy (group III) resulted in a 12.1 months (8.9 - 15.9 months 95% CL) longer survival than HFX/AFX-RT alone ($p<0.0001$).

Conclusions: Cisplatin, carboplatin, mitomycin C, and 5-FU single drug or combinations of 5-FU with one of the other drugs combined with simultaneous radiotherapy leads to a profound survival benefit in unresectable head and neck cancer patients irrespective the fractionation schedule of the radiotherapy.

Symptom management/Quality of life

685 ORAL

A phase 3, randomized, double-blind, placebo-controlled study of darbepoetin alfa in patients (pts) with lymphoproliferative malignancies

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Background: Darbepoetin alfa (Aranesp®) is a unique erythropoietic protein that is safe and effective for treatment of chemotherapy-induced anaemia in pts with solid tumors. Results of a phase 2 study suggest that similar outcomes could be achieved in pts with lymphoproliferative malignancies (Hedenus et al, 2002). This confirmatory phase 3 study was designed to evaluate the efficacy and safety of darbepoetin alfa in pts with lymphoproliferative malignancies.

Methods: This multicenter, randomized, double-blind, placebo-controlled study was conducted in anaemic pts (haemoglobin [Hb] $\leq$ 11.0 g/dL) with lymphoma (Hodgkin's disease, non-Hodgkin's lymphoma, or chronic lymphocytic leukaemia) or myeloma who were receiving chemotherapy. No lower limit for Hb concentrations or specific endogenous erythropoietin level requirement was specified at study entry. Pts were required to be red blood cell (RBC) transfusion-free in the 2 weeks before randomization. Pts (n = 349) were randomized to receive darbepoetin alfa 2.25 mcg/kg (n = 176) or placebo (n = 173) by subcutaneous injection once weekly for 12 weeks. Mean change in Hb was calculated by 2 methods: in the intent-to-treat (ITT) analysis, missing values were imputed by last value carried forward; in the completers analysis, missing values were not imputed and only those pts who had a week 13 Hb value were included. Both methods excluded values within 28 days of RBC transfusion.

Results: see table.

The treatment effect of darbepoetin alfa relative to placebo was evident regardless of baseline endogenous erythropoietin level. Efficacy profiles were consistent between pts with lymphoma and myeloma. Improvements in health-related quality of life were also associated with darbepoetin alfa. The overall safety profile of darbepoetin alfa was consistent with that expected for this pt population.

Conclusions: Darbepoetin alfa is well tolerated and effective in increasing haemoglobin and reducing transfusions across a broad population of anaemic pts with lymphoproliferative malignancies.

686 ORAL

Epoetin alfa rapidly increases hemoglobin levels in anemic cancer patients receiving chemotherapy: results from a meta-analysis of nine randomized, placebo-controlled studies

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Background: Because of the relatively short duration of chemotherapy, it is important that any concurrently administered anemia treatment affords a clinically meaningful and rapid increase in hemoglobin (Hb) level to assure optimal patient benefits, including preservation or improvement of quality of life (QOL). Results from two large, multicenter, prospective, open-label, non-randomized, community-based studies (Demetri 1998; Gabrilove 2001) in anemic cancer patients undergoing chemotherapy showed mean Hb increases of ~1 g/dL after 1 month and ~2 g/dL after 2 months of epoetin alfa therapy (mean baseline Hb, ~9.4 g/dL).

Methods: To further characterize the Hb response to epoetin alfa, Hb data were gleaned from 1,646 chemotherapy patients who had received epoetin alfa 150-300 IU/kg three times weekly or placebo in nine randomized studies,

Abstract 685 – Table

	Darbepoetin alfa (n=174)	Placebo (n=170)	
Kaplan-Meier Proportion (95% CI) achieving haemoglobin response[a]	60% (52, 68)	18% (12, 24)	<0.001
Kaplan-Meier Proportion (95% CI) achieving haematopoietic response[b]	65% (57,73)	24% (18, 31)	< 0.001
Mean change (SE) in Hb (g/dL) from baseline to end of treatment (ITT analysis)	1.80 (0.17)	0.19 (0.10)	< 0.001
Mean change (SE) in Hb (g/dL) from baseline at 12 weeks (completers analysis)	2.66 (0.20) (n = 94)	0.69 (0.14) (n = 86)	< 0.001
Incidence (95% CI) of RBC transfusions from week 5 to end of treatment	31% (24, 38) (n = 167)	48% (41, 56) (n = 165)	< 0.001

[a] Increase of * 2.0 g/dL from baseline in the absence of RBC transfusions [b] Increase of * 2.0 g/dL from baseline or a haemoglobin value * 12.0 g/dL in the absence of RBC transfusions