noncoplanar 6 MV photon beams were used for 3DCRT plan. 70 Gy at 2 Gy per fraction was prescribed to 90% of PTV. Five to seven non-opposing 6 MV photon beams were used for IMRT plans. Seventy segments were assigned before optimization. Dosimetric parameters including EUD, maximum and minimum dose, heterogeneity index, mean lung dose, NTCP for lung and normal lung volume% were compared between 3DCRT and IMRT plan. In addition, iso-NTCP dose escalation was conducted by two ways (increasing the fraction number or the fraction size) while considering the accelerated repopulation and overall treatment time.
Results: PTV volume ranged from 185–618 cm^3. By optimization objectives, IMRT and 3DCRT plan showed no difference for the target coverage (EUD_PTV; 69.8 Gy for IMRT and 69.5 Gy for 3DCRT, $p = 0.667$)). But, IMRT plan showed lower NTCP for lung and it was statistically significant ($p = 0.019$). Mean TCP for 3DCRT and IMRT was 32% and 29% respectively. By increasing the fraction number and fraction size, mean TCP was elevated to 47% and 81% and these were statistically significant ($p < 0.001$).
Conclusions: It was revealed that the respiratory-gated IMRT plan could increase the therapeutic ratio of NSCLC, especially by the reduction of lung NTCP. Further studies are going to be performed about the effect of the intrafractional uncertainties on the IMRT plan and the feasibility of the gated IMRT delivery.

6625 POSTER

Gefitinib (G) treatment outcome after progression on erlotinib (E) in patients with advanced non-small-cell lung cancer (NSCLC)

F. Grossi, A. Brianti, C. Defferrari, M.G. Dal Bello, M. Loprevite, G. Catania, P. Pronzato. *National Institute for Cancer Research, Medical Oncology, Genoa, Italy*

Background: Two case reports describe a response to E after failure of G (Garfield DH, J Clin Oncol 2005) or to G after failure of E (Choong NW et al„ Nat Clin Pract Oncol 2006) in patients (pts) with advanced NSCLC. Otherwise, a limited experience in 5 pts suggests that E is not effective in pts progressing on G (Viswanathan A et al„ Lung Cancer 2005). Aim of this study was the evaluation of response and time to progression (TTP) in advanced NSCLC pts treated with G after failure of E.
Materials: Pts received G 250 mg/day after disease progression (PD) with E 150 mg/day. Pts accrual was stopped on August 2006 after the approval of E for use in Italy and the consequent closure of the G compassionate-use program.
Results: From May 2005 to August 2006, 15 pts were enrolled. Median age 65 years (50−85); males = 14 pts (93%); never/former smokers = 4/10 pts (26/67%); adenocarcinoma = 10 pts (67%); PS 0/1 = 5/10 pts (33/67%); in 2 pts (13%) E was administered as first-line therapy, 8 pts (53%) received 2 prior lines of chemotherapy (CT) and 3 pts (20%) received CT between E and G. One patient (7%) had a partial response (PR) and 5 pts (33%) had disease stabilization (SD) with E; with G no PR and 6 SD (40%) were obtained. Five out of 6 RP/SD pts with E, had SD with G; 8 out of 9 PD pts with E, had PD with G; 1 SD patient with E, progressed with G and 1 vice versa. TTP in RP/SD pts was 7.2 and 3.4 months for E and G respectively; in PD pts TTP was 1.7 and 1.6 for E and G respectively.
Conclusions: Our data suggest that there is a benefit with G in pts who had RP/SD with E and that is associated with a good TTP. Conversely G is not recommended in pts who immediately progressed after E. An analysis of the role of mutational status and other biomarkers in predicting clinical outcome is currently underway.

Melanoma

Oral presentations (Wed, 26 Sep, 09.00−10.45) **Melanoma**

7000 ORAL

A phase I/II study to determine the feasibility and efficacy of the triple combination of Oblimersen (OBL), Abraxane (ABX), and Temozolomide (TMZ) in metastatic melanoma

A. Pavlick[1], M. Volm[2], T. Ryan[2], J. Escalon[2], L. Lee[2], L. Liebes[2]. *[1]NYU Cancer Institute, Medical Oncology and Dermatology, New York, USA; [2]NYU Cancer Institute, Medical Oncology, New York, USA*

Background: OBL is a bcl-2 antisense oligonucleotide, which has shown efficacy on multiple endpoints in combination with DTIC as compared to DTIC alone in a large randomized study: response rate (RR) 13.5% vs. 7.5% ($p < .01$), median progression free survival (PFS) 2.6 vs. 1.6 months ($p < .001$), median overall survival 9 vs 7.8 months ($p = 0.077$). Patients selected on the basis of normal baseline LDH have a greater benefit. Notably, OBL increases the rate of durable responses. Relative to DTIC, combination therapies generally improve RR only. The addition of OBL to chemotherapy may have an impact on survival. TMZ is an oral drug with a similar mechanism of action as DTIC. The combination of OBL and TMZ+ABX has been shown to be synergistic in preclinical models.
Methods: Two cohorts of 14 cases are being enrolled sequentially. A series of 14 consecutive failures to respond would be considered insufficent activity (RR < 20%, $p < 0.05$). Treatment is as follows: Cohort 1: OBL 7 mg/kg days 1−7 and 22−29 as a continuous infusion, TMZ 75 mg/m^2 p.o. qd days 1−42, ABX 175 mg/m^2 on day 7 and 29. Cohort 2 will have ABX dose escalated to 260 mg/m^2. Eligibility criteria are: metastatic melanoma with baseline LDH <1.1 ULN with no previous chemotherapy, measurable disease by RECIST criteria. Feasibility criterion for each cohort is no observed severe neutropenia (>7 d) in 14 consecutive cases or more than 33% of the patients experience a Gr 3/4 non-hematologic toxicity. RR and PFS at 6 months will be assessed.
Results: Of 5 subjects treated in Cohort 1, one patient achieved a partial response and two, stable disease (RECIST). Pre & post tumor biopsies and PBMCs are being monitored for bcl-2 pathway and proliferation markers. Pharmacokinetics are being accessed for OBL and ABX. Shed cryptic epitopes will be measured serially and correlated with clinical responses.
Conclusion: This regimen includes 3 drugs combined at fully active doses. It will establish the tolerance profile and give a risk-benefit assessment based on tolerability and observed response rate to determine which dose level is most promising.

7001 ORAL

Long-term outcome of 403 patients treated with ruthenium brachytherapy for choroidal melanoma

K.M.S. Verschueren[1], N.E. Schalij[2], C.L. Creutzberg[1], M. Ketelaars[1], F.L.L. Klijssen[2], B.I. Haeseker[2], S.M.B. Ligtenberg[2], C.A.M. Marijnen[3]. *[1]Leiden University Medical Center, Clinical Oncology, Leiden, The Netherlands; [2]Leiden University Medical Center, Opthalmology, Leiden, The Netherlands; [3]Netherlands Cancer Institute, Radiotherapy, Amsterdam, The Netherlands*

Background: Eye sparing treatment using ruthenium-106 plaque brachytherapy has replaced enucleation as standard treatment for intermediate size choroidal melanoma, as it provides equal survival rates, while preserving cosmetic appearance, useful visual function and quality of life. Long-term results were analyzed to evaluate local control (LC), overall (OS) and recurrence-free survival (RFS), complication rates and visual acuity after treatment, and identify prognostic factors.
Materials and Methods: Outcome data of 430 consecutive patients treated between 1993 and 2004 were analyzed. Brachytherapy doses were specified at the scleral surface and ranged from 400 to 600 Gy with TTT, and from 600 to 800 Gy without TTT, depending on the apical height and location of the tumour. Doses were calculated at the sclera and at the tumour apex, and corrected for dose rate. Tumours up to 8 mm apical height and 16 mm basal diameter were treated. Initial visual acuity in the affected eye was >0.50 in 70% and >0.10 in 95%.
Results: At median follow-up of 54 months, an excellent 5-year actuarial LC of 96% was found. OS and RFS rates were 78% and 81% at 5 years. The 5-year rate of distant metastases was 16%. Cosmetic and functional (visual acuity >0.10) eye preservation was obtained in 96% and 62%, respectively. Significant prognostic factors for LC were central or juxtapapillary location of the tumour, and initial visual acuity. Both factors remained significant in the multivariate analyses (MV). For RFS, age, apical height, basal diameter, central or juxtapapillary location and dose to the apex were significant prognostic factors in univariate analyses. Basal diameter and central or juxtapapillary location remained significant in MV. Radiation side effects such as retinopathy, opticopathy and maculopathy were frequent and gradually increased over time, amounting to 2- and 5-year rates of 38% and 64%. Eventually, 17 patients underwent enucleation; 10 for local recurrence, and 7 for severe treatment complications.
Conclusions: Ruthenium-106 plaque brachytherapy is a very effective and safe treatment for choroidal melanoma with excellent local control and cosmetic and functional eye preservation rates. Central or juxtapapillary location and basal diameter of the tumour are significant prognostic factors for RFS.