of <0.001, 0.014 and 0.003 respectively. However, in the final multivariate Cox regression, N-stage was no longer significant. A comparison was made between three multivariate models each consisting of gender, WHO-performance status, $EQD_{2,T}$ and only one of the following combinations: (1) total tumor volume and PLNS, (2) T-stage and N-stage, (3) UICC overall stage. The AIC of the models was 1965.8, 1989.9 and 2001.2 respectively. It was therefore concluded that model 1 was the best for predicting overall survival.
Conclusions: The best prediction for survival in NSCLC patients treated with (chemo)radiation is based on total tumor volume, number of positive lymph node stations, gender, performance status and equivalent radiation dose corrected for time ($EQD_{2,T}$).

6506 ORAL

A prognostic model based on BRCA1 mRNA expression: a new determinant of outcome in early non-small-cell lung cancer (NSCLC)

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Background: Following surgical resection in operable NSCLC, 5-year survival is 60% in stage I, 39% in stage IIB and 23% in stage IIIA, with relapse commonly as distant metastases. The average benefit of adjuvant chemotherapy is 5%, ranging from nil in stage I to 15% in stage II-IIIA. Caretaker genes involved in keeping genetic alterations to a minimum include the nucleotide excision repair genes ERCC1 and myeloid zinc finger 1 (MZF1), which mediates ERCC1 expression, and other stability genes, such as BRCA1, which control processes involving large portions of chromosomes. Thioredoxin-1 (TRX1) is a redox protein overexpressed in NSCLC that is correlated with poor prognosis, and TWIST contributes to metastasis by promoting epithelial-mesenchymal transition.
Methods: In order to identify p with a high risk of relapse, we investigated the expression of these 5 transcripts in frozen resected tumors from 126 resected NSCLC p by real-time quantitative PCR. Gene expression was normalized using beta-actin and 18SrRNA expression as internal references.
Results: Adenocarcinoma (adeno), 33 p; squamous cell carcinoma (SCC), 93 p. Stage: IA, 18 p; IB, 53 p; IIB, 33 p; IIIA, 22 p. Tumoral transcript expression with ?-actin: ERCC1, 1.23; MZF1, 0.53; BRCA1, 3.65; TRX1, 1.82; TWIST, 7.75. A strong correlation was observed between the expression of ERCC1, MZF1 and BRCA1 ($P < 0.001$). Expression of each of the 5 transcripts was higher in SCC than in adeno ($P < 0.001$). Median survival (MS): low ERCC1 (<1.5) = not reached (NR), high ERCC1 = 33 months (m) ($P = 0.21$); low MZF1 (<0.5) = NR, high MZF1 = 33 m ($P = 0.04$); low BRCA1 (<5) = NR, high BRCA1 = 22 months (m) ($P = 0.01$); low TRX1 (<0.8) = NR, high TRX1 = 39.5 m ($P = 0.02$); no differences in MS according to levels of TWIST. In a multivariate Cox model for survival, BRCA1 and stage emerged as independent prognostic variables (Table). The prognostic value of BRCA1 has been validated in a separate set of 58 NSCLC p.

		HR	95% CI	p
Stage	IA-IB	1		
	IIA-IIIA	1.75	1.02−3.06	0.04
BRCA Level	<5	1		
	>5	1.77	1.02−3.06	0.04

Conclusion: Increased BRCA1 is associated with shorter survival, and BRCA1 assessment could be useful for customizing adjuvant chemotherapy.

6507 ORAL

Phase III study of IV vinflunine (VFL) versus IV docetaxel (DTX) in patients (pts) with advanced or metastatic non-small cell lung cancer (NSCLC) previously treated with a platinum-containing regimen

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Background: VFL is a novel microtubule inhibitor of the vinca alkaloid class with clinical activity in NSCLC (J. Bennouna, BJC, 2006). Single-agent safety and efficacy of VFL and DTX were compared in 2nd line NSCLC.
Methods: Open-label, multi-centre, randomised, Phase III study in platinum pre-treated advanced/metastatic NSCLC pts; 550 pts were to be randomised to receive VFL (320 mg/m^2, 20' infusion) or DTX (75 mg/m^2, 1-hour infusion with dexamethasone over 3 days) every 3 weeks. The primary endpoint was to compare PFS, with a non-inferiority analysis based on a 10% difference (types I/II error rates: 5%/20%); response, stable disease, overall survival and safety were assessed (RECIST and NCI CTC [version 2.0] respectively).
Results: From 06/03 to 03/05, 551 pts were randomised (VFL: 274; DTX: 277) and 547 treated (411 men, 136 women; median age 61 y [range 21−83]; ECOG PS 0−1: 89%; metastatic: 90%). All pts were platinum pre-treated, in combination with a vinca alkaloid (22%), paclitaxel (21%), gemcitabine (48%) or other excluding DTX (9%). A total of 950 [1−20] and 1025 [1−18] cycles were given with VFL and DTX respectively.
Safety: Grade 3/4 toxicities (VFL vs DTX): neutropenia (33% vs 30%), anaemia (8% vs 3%), thrombocytopenia (2% vs <1%), febrile neutropenia (3% vs 5%), fatigue (10% vs 6%), vomiting (2% vs 1%), abdominal pain (4% vs <1%), constipation (7% vs <1%) and all grades >0: alopecia (20% vs 35%), nail disorders (1% vs 5%), injection site reaction (25% vs 1%), peripheral neuropathy (11% vs 15%), diarrhoea (6% vs 12%) were observed.
Efficacy: Efficacy endpoints were similar): median PFS (2.3 vs 2.3 months, HR: 1.004 [0.841−1.199]), response rate (4.4% vs 5.5%), stable disease (36.0% vs 39.6%), median overall survival (6.7 vs 7.2 months, HR: 0.973 [0.805−1.176]). No significant difference was observed in the rate of Patient Benefit (PB) and Quality of Life (QOL)(FACT-L) assessment between the VFL and the DTX arms.
Conclusion: Vinflunine 320 mg/m^2 every 3 weeks was found to be similar in terms of efficacy to docetaxel 75 mg/m^2 when administered every 3 weeks in patients previously treated with a platinum-containing regimen for advanced NSCLC patients. PB and QOL were also comparable for the two study treatments. Manageable but different toxicity profiles were observed in either arm allowing a good median relative dose intensity >98%. Therefore, vinflunine offers a new treatment option for patients with advanced NSCLC in the second line setting.

Oral presentations (Wed, 26 Sep, 09.00−11.00)
Lung cancer (2)

6508 ORAL

CP-751,871, an anti-IGF-IR antibody, in combination with paclitaxel and carboplatin or paclitaxel and carboplatin alone as first-line treatment for advanced non-small cell lung cancer (NSCLC): A phase Ib/randomized phase II, non-comparative, open label trial

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Background: CP-751,871 is a fully human, IgG2 monoclonal antibody against the IGF-IR active in preclinical models of NSCLC. We report the