groups were equally distributed according to age, sex, histology, ECOG PS and co-morbidity (hypertension, diabetes and VTE). VEGF serum levels were detected by a commercially available ELISA kit (Quantikine Human VEGF Immunoassay R&D systems, Minneapolis, MN, USA) according to the manifacturer's instructions. S100 B serum levels were measured by the enzyme immunoassay Kit NEXUS Dx ™ (SynX Pharma Inc., Toronto, Canada).

Results: Median age was 60.5 years (range 24–79), M/F 57/16, squamous/adeno/large-cell/non specified NSCLC 18/19/11/26, ECOG PS ⩽2: 64 pts (33 pts with BM and 31 pts without BM), ECOG PS 3: 9 pts (5 pts with BM and 4 pts without BM). Three pts had only BM, while the other were plurimetastatic: bone (24 pts (lung (21 pts), liver (11pts) and adrenal glands (16 pts). The mean value (±SD) of serum VEGF was 506 (±432) pg/ml. VEGF levels showed significant association with large cell histotype ($p = 0.041$). Baseline VEGF serum levels were also correlated with ECOG PS ($p = 0.040$) (pts with ECOG PS 0 had lower VEGF levels (417±364 pg/ml) while pts with ECOG PS 3 had higher VEGF levels (944±699 pg/ml). There was also an association between white blood cells and ECOG PS status ($p = 0.040$). An inverse correlation between serum VEGF levels and haemoglobin was found ($r = -0.24$, $p = 0.046$). No difference in VEGF serum levels was found between pts with BM [501 (±443) pg/ml] and without BM [511(±427) pg/ml] ($p = 0.9$). There was a difference between mean VEGF values in the subgroup of pts with only one BM (300±231 pg/ml) vs pts with multiple BM (506±332 pg/ml) even if it doesn't reach a statistical significance ($p = 0.069$). The S100B serum levels for both groups were <0.01 ng/ml.

Conclusions: No significant association was found between S100 beta levels and the patients' clinical parameters. In particular S100B levels does not seem to discriminate pts with and without BM. Elevated baseline serum VEGF levels appear to be related with the degree of metastatic involvement.

1162 POSTER

Weekly Combretastatin A4 Phosphate (CA4P) in combination with radiotherapy (RT): tumour antivascular effects as demonstrated using perfusion computed tomography (p-CT)

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Purpose: The vascular disrupting agent CA4P, when used as a single agent, causes transient reduction in tumour perfusion. CA4P may act synergistically with RT. Tumour vascular changes that occur during treatment with once-weekly CA4P in combination with RT have been measured using p-CT.

Methods/Materials: Following Local Research Ethics Committee approval and written informed consent, patients with histologically confirmed, advanced non small cell lung cancer were enrolled into a Phase IB clinical trial of CA4P combined with external beam RT. They received twice-weekly palliative RT (27 Gy in 6 fractions) over three weeks. Six patients in the first cohort received a single dose of CA4P (50 mg/m^2) after the first 2nd fraction of RT. Six patients in the second cohort received the same dose of CA4P after the 2nd, 4th, and 6th fractions of RT. Quantitative p-CT measurements of whole tumour blood volume and permeability were performed prior to treatment, after RT, before CA4P and at 4 and 72 hours after every CA4P dose.

Results: After the 2nd, 4th and 6th fraction of RT prior to CA4P, tumour blood volume increased by 13% (paired t-test, $p = 0.16$), 34% ($p = 0.06$), and 26% ($p = 0.05$) respectively. Increases in permeability were seen after RT but failed to reach significance. 4 and 72 hours after receiving the 1st dose of CA4P, tumour blood volume decreased by 15% ($p = 0.03$) and 19% ($p = 0.02$) respectively; after the 2nd dose by 9% ($p = 0.04$) and 32% ($p = 0.02$) respectively; and after the 3rd dose by 7% ($p = 0.3$) and 23% ($p = 0.06$) respectively. At the end of treatment, there was an overall reduction in blood volume of 33% from baseline ($p = 0.04$). Increase in permeability after RT correlated to subsequent reduction in blood volume after CA4P ($r = 0.76$, $p = 0.004$).

Conclusion: Weekly CA4P with RT caused a sustained reduction in tumour blood volume that is measurable using p-CT. Repeated doses of CA4P resulted in additional decrease in blood volume. Changes in tumour permeability after RT may predict for subsequent tumour response to CA4P. There is potential synergy between CA4P and RT.

1163 POSTER

Relation between P53 codon 72 polymorphism and somatic P53 gene mutation in non-small cell lung cancer (NSCLC)

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Background: *P*53 gene mutation is among the most frequent molecular abnormalities in lung cancer and is strongly associated with cigarette smoking. A relation between *P*53 gene polymorphism and mutation was postulated recently in breast carcinoma but data on this subject in NSCLC have been scarce. The aim of this study was to assess the association between constitutional pro72codon polymorphic variant of *P*53 gene and the risk of somatic *P*53 gene mutations in NSCLC.

Material and methods: Study group included 240 NSCLC patients (52 females and 188 males) who underwent curative pulmonary resection between 1996 and 2000. Arg72Pro *P*53 polymorphism analysis was performed using peripheral blood samples. In 31 NSCLC cases for whom blood samples were not available, tumor-free lung tissue was used for polymorphism analysis. *P*53 gene codon 72 polymorphism was evaluated by allele specific amplification-polymerase chain reaction (ASA-PCR) with Taq DNA polymerase and allele-specific primers. The results were confirmed by denaturing high-performance liquid chromatography (DHPLC). Somatic *P*53 mutation analysis included sequencing of exons 5–8 in tumor DNA.

Results: The frequencies of *P*53 gene Arg72Pro genotypes (Arg/Arg, Arg/Pro, Pro/Pro) in NSCLC patients were 46%, 50% and 4%, respectively. No relationship was found in NSCLC patients between polymorphic variants and clinical characteristics, such as age, sex, pT, pN, histological type and smoking, and neither was there a correlation between polymorphic variants and overall survival. *P*53 gene somatic mutations were found in 76 out of 240 NSCLC patients (32%). Most common were missense mutations. There was no correlation between *P*53 somatic mutations and overall survival. The mutations were more frequent in pro72codon carriers (49/130 patients – 38%) than in arg72codon homozygotes (27/110 patients – 25%). The odds ratio for mutations of *P*53 gene in tumor cells in Pro allele carriers was 1.80 (95% CI: 1.03–3.16).

Conclusions: Arg72Pro *P*53 gene polymorphism may increase the risk of somatic *P53* gene mutations in NSCLC patients. The biological significance of this finding warrants further studies.

1164 POSTER

Can brain metastases (BM) timing presentation influence on survival in patients with lung cancer treated by radiosurgery (RS) ? Long term results

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Purpose: To determine if BM timing presentation (synchronous vs. metachronous) in patients affected of lung cancer treated by RS can influence on overall survival (OS).

Patients and Methods: One hundred consecutive patients (p) have been included; 10% of cases had SCLC. Synchronous BM were observed in 43 cases, and metachronous in 57cases. KPS were as follows: 10 p had 60, 23 p had 70, 34 p had 80, 23 p had 90, and 10 p had 100. Only in 6 p primary tumour was considered in progression. RTOG RPA classes were: class I 31 p, class II 59 p, and class III 10 p. Ninety one percent of patients received WBI (sequential in 63 p). Number of BM previous RS were: one in 59 cases, two in 29 cases, three in 8 cases, and four in 4 cases. Median treated BM volume for RS was 2.7 cc (0.1–23.8). RS doses administered at isocenter was: 22.6 Gy (19–27.3).

Results: median follow-up was 19 m (2–124) (6% lost of follow-up); 28 p were alive at the end of analysis. KPS at last F-U was: 40–60 in 13 p, 70–100 in 14 p, and unknown in 1 p. Median survival time since RS was 10.3 months.

Local control at final analysis: 40 cases (11% in CR) did not progress in brain, 46 progressed, and 14 can not be evaluated because of rapid lethal events. Six patients received RS again as a salvage treatment.

Causes of death: 25 p because brain progression, 26 p because systemic progression, 17 p both causes, 1 p due to intercurrent disease, and 3 p with unknown reason.

On multivariate analysis we observed, as independent prognostic variables for OS, progression of the primary tumour (RR 4.38, CI 1.7–10.9), KPS 60–70 (RR 2.32, CI 1.4–3.9), and absence of WBI (RR 2.8, CI 1.1–6.9).

When we performed an exclusive analysis for NSCLC patients, MST was 10.6 months, and multivariate analyses showed that progression of the primary tumor (RR 4.87, CI 1.7–13.5), and KPS 60–70 (RR 2.16, CI