dian survival of the subset of patients with stage IIIB locoregional (LR) disease. The results for this subgroup are now available and are reported here together with the updated survival for the overall population.

Method: 171 patients with ECOG 0-2 stage IIIB/IV NSCLC that had stable or responding disease after any first-line chemotherapy (CT) with or without radiotherapy were randomized 1:1 to receive either L-BLP25 plus best supportive care (BSC) or BSC alone. Randomization was stratified by stage of disease (IIIB LR or stage IIIB with malignant pleural effusion and stage IV). Patients in the L-BLP25 arm received a single i.v. dose of cyclophosphamide 300mg/m^2 followed by 8 weekly sc immunizations with L-BLP25 (1000µg). Subsequent immunizations were administered at 6-wk intervals. An analysis of 65 patients with stage IIIB LR disease was conducted, and the results are shown in the table below together with the updated 3 year survival for the overall population.

Results:

	Overall Population			Stage IIIB subgroup		
	BSC	L-BLP25 + BSC	Total	BSC	L-BLP25 + BSC	Total
N	83	88	171	30	35	64
Median follow up (mths)	56	51	52	57	53	53
Median Survival (mths)	13.0	17.2	p=0.085*	13.3	30.6	p=NS**
95% CI	11.2, 16.2	12.9, 24.2		9.6, 28.1	13.4, -	
Hazard Ratio			0.75			0.55
95% CI			0.53, 1.04			0.30, 1.00
1 yr OS	46 (55)	55 (63)		17 (57)	24 (69)	
2 yr OS	22 (27)	36 (41)		10 (33)	20 (57)	
3 yr OS	14 (17)	27 (31)		8 (27)	17 (49)	

* P-value; adjusted for multiple comparisons. Unadjusted p-values for this subgroup based on a Cox model including response to first-line treatment; 0.0497

**P-value of the primary analysis (March 2004) was p=0.112

Conclusion: A 17.3 month difference in median survival and 45% reduction in mortality were seen with maintenance therapy with L-BLP25 in patients with stage IIIB LR NSCLC. The difference in efficacy identified in this subgroup versus patients with IIIB MPE or stage IV disease, could potentially be a result of lower tumor burden or less advanced disease. On the basis of these results, a phase III trial ("START") has been initiated to investigate the addition of maintenance therapy with L-BLP25 to BSC in patients with unresectable stage III NSCLC.

B1-02 **Novel Therapeutics I, Tue, 13:45 - 15:30**

A Phase 1-2 study of the anti-sense oligonucleotide OGX-011 in combination with a platinum/gemcitabine regimen as first-line therapy for advanced non-small cell lung cancer

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Background: The clusterin gene is frequently expressed in NSCLC and encodes a cytoprotective chaperone protein that is upregulated in response to apoptotic stimuli such as chemotherapy. OGX-011 is a second-generation antisense oligonucleotide that inhibits clusterin expression, thus enhancing the apoptotic effects of chemotherapy. Previous phase I studies with docetaxel suggested an OGX-011 dose of 640mg was feasible and biologically active; therefore, the current study began with a run-in phase with 480mg of OGX-011.

Methods: Eligibility criteria: stage IIIB/IV NSCLC; no prior chemotherapy; ≥ 1 measurable lesion; ECOG ≤1; adequate organ function; no active CNS metastasis. Treatment: OGX-011 is given as a 2-hour infusion. There is an initial loading phase with 3 doses of OGX-011 alone in 1 week, followed by weekly OGX-011 with standard chemotherapy: gemcitabine (1250 mg/m^2) Days 1+8 and either cisplatin (75 mg/m^2) or carboplatin (AUC=5) Day 1 q21 days, (maximum 6 cycles).

Results: 85 pts (phase 1=10 and phase 2=75) were enrolled between Dec, 2004 and Nov, 2006. As no unexpected dose limiting toxicities were noted in the first 3 patients who received 480mg of OGX-011, the dose was escalated, as planned, to 640 mg for the remaining patients. Data are available on the first 53 pts; all received ≥1 dose of OGX-011 and were considered evaluable for safety and efficacy. Demographics: female (47%); stage IV (87%); median age 61 (45-79) yrs; ECOG PS = 1 (62%). The median number of cycles delivered was 4. Principal grade 3/4 toxicities were hematologic: neutropenia (32%) + thrombocytopenia (17%). Other common toxicities included fatigue, nausea, vomiting, fever, chills, constipation, + anorexia. Two Serious Adverse Events previously reported as associated with gemcitabine/platinum therapy were documented: acute cortical blindness with stroke + thrombotic thrombocytopenic purpura. Responses: confirmed PRs 13 (ORR = 24%); median duration of PR: 105 days (46-336+); median PFS: 140 days (2-422+); 79% of pts have progressed; 47% have died. Of the first 34 patients who have all been followed for ≥ 1 yr, 18/34 (53%) survived > 1 yr; 14/18 (78%) remain alive as of March 06, 2006. Data will be presented for all 85 patients.

Conclusions: This combination is feasible and tolerable. The 1-yr survival rate ≥50% may justify a randomized phase III trial. OGX-011 is being developed by OncoGenex Technology Inc. + Isis Pharmaceuticals Inc.

B1-03 **Novel Therapeutics I, Tue, 13:45 - 15:30**

Phase II double blind study to investigate efficacy and safety of the triple angiokinase inhibitor BIBF 1120 in patients suffering from relapsed advanced non-small cell lung cancer (NSCLC)

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Background: Angiogenesis, the formation of new blood vessels, is an essential process during growth and progression of different solid

tumors. Vascular endothelial growth factor (VEGF) induces vascular permeability and plays a major role in vasculogenesis, angiogenesis, and endothelial integrity and survival. Besides VEGF-, other proangiogenic factors such as platelet derived- (PDGF), and fibroblast growth factor (FGF) with their receptors compose critical cellular pathways controlling lung cancer vascularization, growth and progression. BIBF 1120 is an oral potent triple angiokinase inhibitor targeting VEGFR, PDGFR, FGFR kinases.

Methods: In this double blind multi-centre trial, patients with an ECOG score of 0-2 with locally advanced or metastatic (stage IIIB/IV) relapsed NSCLC after failure of first or second line chemotherapy were randomly assigned to daily treatment with 2x250 mg or 2x150 mg of BIBF 1120 until progression. In the event of dose limiting toxicity, a single dose reduction to open label treatment with 2x150 or 2x100 mg of BIBF 1120 was allowed. Patients with stable brain metastases or squamous cell carcinoma were not excluded. The primary endpoints were progression free survival (PFS) and objective tumour response according to RECIST (determined every 6 weeks).

Results: A total of 74 patients were enrolled and 73 patients treated with BIBF 1120 (61% males, median age: 64 years, range 36-80). The most common histology was adenocarcinoma (55%), followed by squamous cell carcinoma (23%). The median PFS of all patients (n= 73) was 1.6 months without significant difference between both treatment arms. The stable disease rate was 48%. One confirmed partial response was observed.

Patients with an ECOG performance status of 0 or 1 (n= 57) had a median PFS of 2.9 months and a three- and five months PFS rate of 46% and 31%, without any difference between both treatment arms. The stable disease rate in this group of patients was 59% and the median overall survival was 144 days.

Patients treated with 2x250 mg per day had more CTCAE Grade 3 and 4 toxicities as compared to patients treated with 2x150 mg (27% versus 2.8%, p=0.006, two-sided Fisher-test). The most frequent adverse events irrespective of relatedness observed in 73 patients were of CTCAE Grade 1 or 2 and included nausea (41%), diarrhoea (41%), vomiting (33%), fatigue (29%), and abdominal pain (22%). Grade 3 and 4 toxicities included nausea (8%), diarrhoea (7%), vomiting (4%), abdominal pain (4%) and AST and/or ALT elevations (5.4%) which were fully reversible.

Conclusions: These results suggest that continuous treatment with BIBF 1120 is safe and well tolerated, and showed promising efficacy in ECOG 0-1 patients. A considerably high rate of disease control could be observed in this study.

B1-04 **Novel Therapeutics I, Tue, 13:45 - 15:30**

DN-101-004: a multicenter, open label, dose ranging study of DN-101 (ASENTAR™) and docetaxel in patients with stage IIIB or IV non-small cell lung cancer (NSCLC) after platinum-based chemotherapy

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Background: DN-101 is a high dose oral formulation of calcitriol, the most potent ligand of vitamin D receptor. Calcitriol has various antineoplastic effects on malignant cells and increases activity of cytotoxic agents, including taxanes. DN-101 in combination with docetaxel increased survival in a phase 2 study in androgen-independent prostate cancer and ASCENT 2, a phase 3 confirmatory study is underway. The objective of the study was to determine the maximum tolerated dose, response rate (ORR), progression-free survival (PFS), and overall survival (OS) of DN-101 in combination with docetaxel in advanced NSCLC patients (pts).

Methods: Eligible pts had Stage IIIB or IV NSCLC that progressed on or after platinum-based chemotherapy, ECOG ≤ 1, and measurable disease by RECIST criteria. DN-101 was administered on day 1 in doses of 45 (n=5), 75 (n=4), 135 (n=3), or 180 μg (n=53) in the q21d group, or 180 μg on day 1, followed by 45 (n=5), 90 (n=4), or 180 μg (n=12) on days 8 and 15 in the q7d group. Docetaxel (75 mg/m^2 BSA) was given on day 2 q21d for all pts.

Results: A total of 86 pts were treated. No unexpected toxicities were reported with DN-101. Grade (G3/4) toxicities and fatal adverse events (AEs) were consistent with the reported toxicity of docetaxel alone. Stomatitis (0% in q7d, 9% in q21d) and G3/4 asthenia and fatigue (5% in q7d, 14% in q21d) were less frequent on DN-101 compared to published reports on docetaxel. No pt on DN-101 q21d developed hypercalcemia while 2 pt on DN-101 q7d (180 μg cohort) developed G3/4 hypercalcemia. Three fatal AEs included 2 on DN-101 q21d (1 lung infiltration, 1 pneumonitis) and 1 on DN-101 q7d (intestinal perforation). The ORR was 5.9% (CI 0.1%, 28.7%) and 6.6% (1.8%, 15.9%), median PFS 14.1 (6.0, 20.0) and 11.6 (8.4, 17.4) weeks, median OS 8.8 (7.1, NA) and 6.9 (5.5, 9.7) months, and 1 year survival rate 40% (15.2%, 64.8%) and 31% (18.9%, 42.2%) for the q7d and q21d group, respectively.

Conclusion: DN-101 in combination with docetaxel is well-tolerated in advanced NSCLC. The observation of improved PFS, OS, and 1 year survival rate with weekly DN 101 supports further investigation, as does the appearance of ameliorated docetaxel-induced toxicity when combined with DN-101.

B1-05 **Novel Therapeutics I, Tue, 13:45 - 15:30**

Activity of MAGE-A3 cancer immunotherapeutic as adjuvant therapy in stage IB/II non-small cell lung cancer (NSCLC): final results of a multi-center, double-blind, randomized, placebo-controlled phase II study

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Background: NSCLC is associated with poor outcome: even after complete surgical resection, about half of the patients with stage IB or II NSCLC relapse and die within 5 years. Cisplatin-based adjuvant che-