neuropathy (sensory). No deaths were reported. Mean MMB systemic exposure was dose proportional between DL1 and DL2A, and comparable between DL2A and DL2B (200 mg total daily dose). MMB did not affect erlotinib PK. Mean blood pSTAT*3* was maximally decreased by 34.9% at 1 hour postdose and was not dose dependent. As observed for MMB in myelofibrosis, inflammatory cytokines such as CRP, IL-10 and IL-12/-23p40 were reduced, whereas IL-8 was increased. The overall response rate was 54.5% (n=6; all partial responses).

Conclusion: MMB administered in combination with erlotinib had more toxicity than expected at DL2B, including one grade 4 neutropenia. However, grade 2-3 neutropenia without fever was seen in 2 additional patients. The response rate was similar to previous reports with erlotinib, but it is too early in the study to provide progression-free survival with this treatment combination.

Keywords: Erlotinib, EGFR, NSCLC, Momelotinib

P2.06-005
Phase 1 Study of Ramucirumab or Necitumumab in Combination with Osimertinib (AZD9291) in Advanced T790M-Positive EGFR-Mutant NSCLC

Topic: Phase I Trials

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Background: Despite the likelihood of an initial response to 1st or 2nd generation EGFR-TKI, *EGFR* mutant patients develop disease progression. The most frequent mechanism of acquired resistance is the *EGFR* T790M gatekeeper mutation. Novel treatment options are needed in this treatment resistant patient population. Osimertinib, a third-generation EGFR TKI targeting mutant EGFR including T790M, is an oral, irreversible, selective inhibitor. Ramucirumab and necitumumab are human IgG1 monoclonal antibodies to VEGFR-2 and EGFR, respectively. This phase 1, open-label, multicenter study with expansion cohorts (JVDL; NCT02789345) is designed to evaluate the safety and preliminary efficacy of ramucirumab or necitumumab in combination with osimertinib in patients with advanced *EGFR* T790M-positive NSCLC who have progressed after EGFR TKI therapy.

Methods: This study includes patients with advanced or metastatic *EGFR* T790M-positive *EGFR* activating mutant (exon 19 deletions or L858R) NSCLC, with measurable disease and ECOG performance status 0-1 who have experienced disease progression on one prior EGFR TKI regardless of prior chemotherapy. Patients previously treated with an EGFR antibody or 3rd generation EGFR TKI for NSCLC are not eligible. In the phase 1a dose de-escalation portion (3+3 design), all patients (n=6 to 24) will be administered daily oral osimertinib (80 mg) with either an initial dose of 10 mg/kg IV ramucirumab on day 1 of every 2-week cycle or 800 mg IV necitumumab on days 1 and 8 of every 3-week cycle. One level of dose de-escalation is planned for each arm. A dose reduction (level -1) to 8 mg/kg IV ramucirumab or 600 mg IV necitumumab is planned if 2 or more patients have DLTs in either arm. After the DLT evaluation, the study will open a dose-expansion portion (phase 1b) and 25 patients in each Arm will receive study treatment until disease progression or a criterion for discontinuation is met. The primary objective is to assess safety and tolerability of ramucirumab or necitumumab in combination with osimertinib. Secondary endpoints include preliminary efficacy and pharmacokinetics. An exploratory biomarker objective includes the assessment of correlations between *EGFR*-mutations in tissue and serial blood samples with clinical outcomes. Primary analyses will be conducted approximately 6 months after the last patient receives initial dose.

Results: Section not applicable.

Conclusion: Section not applicable.

Keywords: osimertinib, ramucirumab, Necitumumab, T790M

P2.06-006
Phase I/II Dose Escalation Study of L-DOS47 as a Monotherapy in Non-Squamous Non-Small Cell Lung Cancer Patients

Topic: Phase I/II Trials

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Background: L DOS47, a cancer therapeutic designed to exploit the acidic tumor extracellular environment, is a protein conjugate consisting of a urease conjugated to a camelid monoclonal antibody (AFAIKL2) that is targeted to the CEACAM6 antigenic tumor marker. The AFAIKL2 antibody serves as a targeting agent to deliver the enzyme to the tumor sites while the urease enzyme converts urea, an abundant natural metabolite, into ammonia and generates a local pH increase. The combined effect of ammonia toxicity and pH increase is cytotoxic to cancer cells in culture and in xenograft models. This first in human study of L DOS47 was designed to define the maximum tolerated dose of multiple doses of L-DOS47 administered intravenously to patients with non-squamous NSCLC when given as a monotherapy.

Methods: Stage IIIb or IV histologically confirmed non-squamous NSCLC patients (aged $\geq$18 yrs, ECOG PS $\leq$2) receive multiple cycles of L-DOS47 during the study treatment period. L-DOS47 is administered once weekly over 14 days followed by 7 days rest in each treatment cycle. Patients are recruited into cohorts and received the same dose of L-DOS47 on Days 1 and 8 of each treatment cycle. Dose levels of L-DOS47 are escalated in further cohorts following a review of safety data by the Trial Steering Committee.

Results: Fifty-five (55) pts (median age 61, 53% male) were enrolled in sixteen cohorts (dose levels: 0.12 to 13.55 μg/kg) in four Polish centers. L-DOS47 was well tolerated at the dose levels reviewed. One (1) DLT was reported in a cohort 13 patient (spinal pain). None of the patients treated to date have had a partial or complete response as defined by RECIST v1.1. Thirty-two (32) patients had an overall response of stable disease after completing two cycles of L-DOS47. Thirteen (13) of the 32 patients had a decrease in the sum of diameters of target lesions. One (1) patient in cohort 9 was dosed for 10 cycles without disease progression.

Conclusion: L-DOS47 monotherapy is well tolerated at dose levels up to 13.55μg/kg.

Keywords: Non-Squamous non-small cell lung cancer, CEACAM6, tumor microenvironment, camelid monoclonal antibody

P2.06-007
A Phase 1/2 Trial of the Oral EGFR/HER2 Inhibitor AP32788 in Non—Small Cell Lung Cancer (NSCLC)

Topic: Phase I/II Trials

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Background: Approximately 4%—9% of EGFR-mutated NSCLC tumors have *EGFR* exon 20 insertion mutations, and no targeted treatment options are currently approved for patients with these mutations. In addition, approximately 2%—4% of patients with NSCLC have *HER2* mutations, the majority of which are exon 20 insertion mutations. The irreversible EGFR/HER2 inhibitor AP32788 was designed to selectively inhibit EGFR or HER2 kinases with *EGFR*/*HER2* exon 20 mutations. In preclinical studies, investigational agent AP32788 had potent inhibitory activity against all EGFR and HER2 mutants tested, including exon 20 insertion mutants, while sparing wild-type EGFR.

Methods: This phase 1/2 trial is a first-in-human, open-label, multicenter study to evaluate the safety, tolerability, pharmacokinetics, and antitumor activity of orally administered AP32788 (NCT02716116). The study will be conducted in 2 parts: a dose-escalation phase with a 3+3 design and an expansion phase of 4 histologically and molecularly defined cohorts after the recommended phase 2 dose (RP2D) is determined. Patients ($\geq$18 years) must have locally advanced or metastatic NSCLC. In phase 1, the dose-escalation phase, patients refractory