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11P Results of a phase II study investigating eftilagimod alpha (soluble LAG-3 protein) and pembrolizumab in second-line PD-1/PD-L1 refractory metastatic non-small cell lung carcinoma pts

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Background: Eftilagimod alpha (efti) is a soluble LAG-3 protein binding to a subset of MHC class II molecules to mediate antigen presenting cell (APC) and CD8 T-cell activation. Stimulating APCs and subsequent T cell recruitment with efti may revert PD-1 resistance. We hereby report results from part B, 2nd line PD-1/PD-L1 refractory non-small cell lung carcinoma (NSCLC), of the TACTI-002 trial.

Methods: Patients (pts) with previously treated metastatic NSCLC, refractory to PD-1/PD-L1 and unselected for PD-L1 expression were enrolled. A Simon's 2-stage design was used, with objective response rate (ORR) by iRECIST as the primary endpoint (EP). Secondary EPs include ORR by RECIST 1.1, tolerability, disease control rate (DCR), progression free survival and overall survival. Pts received 30 mg efti (SC) q2w for 8 cycles (1 cycle= 3 wks) and then q3w for up to one year together with pembrolizumab (200 mg IV q3w for up to 2 years). Imaging was performed every 8 weeks and evaluated locally. The study was approved by relevant authorities and ethics committees.

Results: 36 pts were enrolled in this cohort. Median age was 66 years (50-84) and 61 % were male. The ECOG PS was 0 and 1 in 33 % and 67 % of pts, respectively. Pts had squamous (19 %) and non-squamous (78 %) NSCLC. Pts were pretreated with a PD-1/PD-L1 antagonist alone (33 %) or in combination with platinum-based chemo (67 %). All PD-L1 subgroups were included with 36 % being PD-L1 negative. Pts received a median 4.0 (range 1−18) pembrolizumab and 5.0 (range 1-22) efti administrations. 2 pts discontinued treatment due to adverse reactions (ARs) (5.6 %). The most common (>15 %) AEs were decreased appetite (33 %), dyspnea (31 %), cough (25 %), asthenia (22 %), fatigue (17 %) and weight decreased (17 %). At data cut-off (Nov2021) 36 pts were evaluated for response with a min. follow-up of ≥4 months. ORR (iRECIST) and DCR was 6 % (2/36) and 36 % (13/36), respectively. Both responses were reported in pts pre-treated with chemo + PD-1 and under therapy since 7+ and 12+ months at data cut-off.

Conclusions: Efti in combination with pembrolizumab is safe and shows encouraging signs of antitumor activity in PD-1 refractory 2nd line NSCLC pts.

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Legal entity responsible for the study: Immutep S.A.

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12P A phase II study of atezolizumab in combination with bevacizumab, carboplatin or cisplatin, and pemetrexed for EGFR-mutant metastatic NSCLC patients after failure of EGFR TKIs

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Background: Acquired resistance to EGFR TKI remains a significant barrier for patients with EGFR-mutated lung cancer, especially for those without acquired $EGFR^{T790M}$. The current study explored the safety and efficacy of combinational treatment with atezolizumab, bevacizumab, and pemetrexed-platinum in patients with EGFR-mutated NSCLC after failure of EGFR TKIs.

Methods: NSCLC patients with activated EGFR mutations after failure of EGFR TKIs were recruited, and patients with T790M were excluded. The treatment is to combine atezolizumab, bevacizumab (7.5 mg/kg), and pemetrexed-platinum once every 3 weeks until progression. Endpoints were ORR, PFS, and OS. For comparison, we retrieved a historical control group that enrolled patients with EGFR mutations who received pemetrexed-platinum plus bevacizumab after failure of single using EGFR TKI from 2009 to 2020. This study is active and recruiting patients is still ongoing.

Results: Twenty patients were enrolled, and the median age was 62 years. Seven patients had taken osimertinib before enrollment. PD-L1 expression was ≧ 1% in 35.0%. The median follow-up time was 15.6 months. One patient was excluded from response analysis due to idiopathic thrombocytopenic purpura being diagnosed after 1st-cycle treatment. ORR was 42.1%, and the DCR was 100%. Median PFS was 10.2 months, and OS was not mature yet. Patients with PD-L1 ≧ 1% have a higher ORR than those with PD-L1 < 1% (85.7% vs. 16.7%; $p = 0.003$). Compared with the historical control group (Bev/Pem/Platin) ($n = 53$), the experimental treatment (Atezo/Bev/Pem/Platin) showed significant benefits in DCR (100.0% vs. 64.2%; $p = 0.002$) and PFS (10.2 vs. 5.9 mo.; $p = 0.007$). There were no significant differences in ORR (42.1% vs. 30.2%; $p = 0.401$) and OS (unmatured vs. 19.3 mo.; $p = 0.134$). Grade ≧ 3 adverse events occurred in 40.0% (8/20) patients, especially 2 venous thromboembolism, 1 hydrocephalus, and 1 renal abscess.

Conclusions: The combination treatment of atezolizumab, bevacizumab, and pemetrexed-platinum provided favorable efficacy in EGFR-mutated NSCLC after TKI failure. The DCR and PFS of pemetrexed-platinum plus bevacizumab could be improved by the addition of atezolizumab.

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