

**Feasibility of eftilagimod alpha (soluble LAG-3 protein) combined with standard-of-care-therapy in advanced non-small-cell lung cancer (NSCLC) adenocarcinomas. Initial results from INSIGHT-003**

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**Background:**

*Eftilagimod alpha (efti; IMP321) is a MHC II class agonist (soluble LAG-3 protein) which activates antigen-presenting cells followed by T-cell (CD4/CD8) activation. Data from the TACTI-002-trial (NCT03625323) and INSIGHT-004 of the current multiple-strata INSIGHT phase-I platform-study revealed that the combination of 30 mg efti subcutaneous (s.c.) with anti-PD-(L)1-checkpoint-inhibitor is well tolerated with encouraging efficacy especially in NSCLC. Stratum-C (INSIGHT-003) of the INSIGHT-study aims to evaluate the feasibility and tolerability of s.c. injections with efti combined with Standard-of-Care (SOC) chemo- and immuno-therapy in 1<sup>st</sup>-line NSCLC-patients (pts).*

**Methods:**

*In Stratum-C, pts with metastatic NSCLC adenocarcinomas are treated with: SOC-chemotherapy (carboplatin AUC5 / pemetrexed 500 mg/m<sup>2</sup> q3w for 4 cycles + 500 mg/m<sup>2</sup> q3w for maintenance) plus pembrolizumab 200 mg q3w combined with s.c. injections of efti (30 mg) (q2w for 24 weeks; thereafter q3w till week 52). Imaging is performed every 8 weeks and assessed locally. The primary endpoint is feasibility (defined by safety & tolerability) while secondary endpoints include objective response acc. to RECIST 1.1 and other efficacy parameters. In total 20 pts will be enrolled.*

**Results:**

*From 02Aug2021 till 22Jul2022, 14 pts have been enrolled. Median age is 66 years and 71.4% are male. Eleven (78.6 %) pts had PD-L1 TPS <50%. No occurrence of unacceptable toxicities (i.e., causally related to efti AND resulting in permanent discontinuation of combination-treatment before administration of two complete cycles). Two serious adverse events (1 thromboembolic event, grade 3; 1 bronchial infection grade, 3) were reported, both unrelated to efti. In total, 69 adverse events (grade 1-2: 29; grade 3: 38; grade 4: 2) were documented. The most frequent AEs were platelet-count decreased in three pts (21.4%, grade 1-3) and anemia (grade 2-3), white-blood-cell decreased (grade 3), and neutrophil-count decreased (grade 3-4) in four pts (28.6%). One grade 3 AE was considered related to efti (insomnia). 10/14 pts are currently evaluable for efficacy (four did not yet have any on-treatment tumor-staging): Seven (70 %) partial responses, two (20%) stable diseases, one (10%) progressive disease as best overall response acc to RECIST 1.1.*

**Conclusions:**

*To date, 30 mg efti combined with SOC appears to be feasible and safe with first promising signals of efficacy.*

**Key-words:**

- Eftilagimod alpha
- LAG-3lg fusion protein
- Advanced solid tumors
- Immunotherapy

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This abstract reports on original research.

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