ASCO 2022 Abstract: Tacti-002 Part A

A Phase II study (TACTI-002) in 1st line metastatic non-small cell lung carcinoma investigating eftilagimod alpha (soluble LAG-3 protein) and pembrolizumab: updated results from a PD-L1 unselected population

Short title: Phase II study of eftilagimod alpha and pembrolizumab in 1st line metastatic NSCLC

Background: Eftilagimod alpha (E) is a soluble LAG-3 protein binding to a subset of MHC class II molecules to mediate antigen presenting cell (APC) / CD8 T-cell activation. Stimulation of the APCs & subsequent T cell recruitment with E may lead to stronger anti-tumor responses than observed with pembrolizumab (P) alone. We hereby report results of the extended 1st line non-small cell lung carcinoma (NSCLC) cohort of the TACTI-002 ("Two ACTive Immunotherapies") phase II trial.

Methods: Pts with untreated metastatic NSCLC, unselected for PD-L1 expression were recruited. Objective response rate (ORR) by iRECIST was the primary endpoint (EP) & secondary EPs include ORR by RECIST 1.1, tolerability, disease control rate (DCR), progression free survival (PFS), overall survival (OS) & exploratory biomarker. Pts received 30 mg E SC q2w for 8 cycles (1 cycle= 3 weeks) & then q3w for up to 1 year with P (200 mg IV q3w for up to 2 years). Imaging was done every 8 weeks. PD-L1 was assessed centrally. This has been approved by relevant CAs, ECs, & IRBs.

Results: From Mar 2019 - Nov 2021 114 pts were enrolled. Median age was 67 years (44-85) & 74% were male. ECOG PS was 0 & 1 in 37% & 63% of pts, respectively. Pts presented squamous (35%) or non-squamous (62%) NSCLC with 88% of pts at stage IV at the time of study entry. All PD-L1 subgroups were represented (Table 1). Pts received median 6.0 (range 1–35) P & 7.0 (1-22) E administrations. 19 (17%) pts discontinued treatment due to adverse events (AEs). The most common (≥15%) AEs were dyspnea (33%), asthenia (30%), decreased appetite (22%), cough (20%), anemia (20%), fatigue (19%), pruritus (18%), constipation (17%) & diarrhea (15%).
At data cut-off (Jan 2022), 75 pts with a minimum follow-up of 6 months were evaluated for efficacy. ORR (iRECIST) was 37.3% in the ITT & 41.8% in the evaluable pts assessed by local read. DCR 73.3% was reported. Response rate for squamous & non-squamous pathology were 33.3 % & 40.3 %, respectively. Results according to RECIST 1.1 were comparable. Responses were observed in all PD-L1 subgroups (Table 1). 24/28 (86%) responses were already confirmed while median duration of response was not yet reached (5 events).

Table 1. ORR/DCR by iRECIST and PD-L1 subgroup

ORR / DCR by iRECIST	N (%) [95 % CI[&]]
ORR ITT* (N=75)	28 (37.3) [26.4-49.3]
DCR ITT* (N=75)	55 (73.3) [61.9-82.9]
ORR evaluable[$] (N=67)	28 (41.8) [29.8-54.5]
ORR ITT*[#] (TPS < 1%); n=22	6 (27.3) [10.7-50.2]
ORR ITT*[#] (TPS ≥ 1%); n=50	22 (44.0) [30.0-58.8]
ORR ITT*[#] (TPS < 50%); n=50	16 (32.0) [19.5-46.7]
ORR ITT*[#] (TPS ≥ 50%); n=22	12 (54.5) [32.2-75.6]
* - intent to treat population; $ - ≥ 1 post baseline tumor imaging & - Clopper-Pearson; # - ITT with available PD-L1 results (n=72)	

Conclusions: E + P is safe & shows encouraging antitumor activity in 1st line metastatic NSCLC patients unselected for PD-L1, warranting further investigation.

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