595 BIOMARKER RESULTS FROM THE 1ST LINE NON-SMALL CELL LUNG CANCER COHORT OF TACTI-002: PHARMACODYNAMIC EFFECTS OF COMBINING EFTILAGIMOD ALPHA (SOLUBLE LAG-3) AND PEMBROLIZUMAB

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Background Eftilagimod alpha (E, LAG-3Ig) is a soluble LAG-3 protein binding to MHC class II and stimulates antigen-presenting cells (APC). Thus T cells (CD4/CD8) are recruited, leading to stronger anti-tumor response than with pembrolizumab (P). Clinical studies with E have shown increased IFN-gamma, CXCL10 and absolute lymphocyte count (ALC). We report biomarker results from the 1st line non-small cell lung carcinoma (NSCLC) cohort in TACTI-002 (NCT03625323).

Methods Pts with measurable, 1st line metastatic NSCLC unselected for PD-L1 were recruited. Exploratory endpoints included analyses of Th1 biomarkers (IFN-gamma; CXCL10), ALC and gene expression profile (GEP). Pts received E (30 mg SC q2w 8 cycles [1 cycle= 3 weeks], then q3w) with P (200 mg IV q3w). Th1 samples were collected early (pre-dose; 8x within 96 h) and late (pre-dose at 3 and 6 mts). Th1 levels were assessed centrally by electrochemiluminescence immunoassay. ALC was locally tested on day 1 of each cycle. GEP samples were collected (pre-treatment and at 3 mts) for central testing (Nanostring nCounter® PanCancer Immune Profiling Panel).

Results 114 pts were enrolled. Median age was 67 yrs (44–85) & 74% were male. ECOG PS was 0 & 1 in 37% & 63% of pts. IFN-gamma and CXCL10 significantly increased soon after first E administration (up to 96 h; table 1) and remained significantly elevated at 3 and 6 mts (table 1) pre-dose.

ALC increase from baseline was observed at 1st assessment and was maintained. When separating pts by disease control (CR, PR & SD versus PD, NA & NE, by iRECIST), ALC change was significantly higher in pts with disease control (0.43 vs 0.04; p=0.01). PFS was significantly prolonged in pts with ALC increase (≥0.2 versus <0.2x109/L pre-defined cut-off), on treatment (mPFS 9.8 mts vs. mPFS 6.9 mts, respectively). OS was immature at data cut-off (31-Mar-23).

GEP analysis showed upregulated expression of genes related to T-cell functions, cytotoxicity functions, cytotoxic cells, or TH1 cells which are more pronounced in pts with PR/CR.

Conclusions Significant early and sustained increases of circulating biomarkers and ALC substantiate the systemic stimulation via the APC activator efti and show that repeated minimally-invasive liquid biopsies, i.e., blood samplings, are key in detecting this systemic stimulation.

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Trial Registration The trial identifiers are TACTI-002 (sponsor code), IMP321-P015 (Sponsor code),Keynote-PN798 (MSD code), 2018–001994-25 (EudraCT) and NCT03625323 (ClinicalTrials.gov)

Abstract 595 Table 1 Mean fold change from baseline of IFN-gamma and CXCL10 at various timepoints

Time from baseline	Biomarker	Mean fold change ± SEM	p-value [signed-rank Wilcoxon test]
Pre- first E dose (max value within 96 hours); N=20	IFN-gamma	2.5 ±0.4	0.0003
	CXCL10	2.0 ±0.2	<0.0001
At 3-mts (pre-E dose 7); N=68	IFN-gamma	1.7 ±0.2	0.0020
	CXCL10	1.6 ±0.2	0.0014
At 6-mts (pre-E dose 13); N=36	IFN-gamma	1.5 ±0.2	0.0345
	CXCL10	1.6 ±0.2	0.0021

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