Exploration of potential biomarkers correlated with efficacy of ociperlimab (anti-TIGIT) plus tislelizumab (anti-PD1) in 1L PD-L1+ non-small cell lung cancer (NSCLC)

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Background: PD-L1 expression was associated with anti-immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domains (TIGIT) + anti-PD-(L)1 treatment, in which a high PD-L1 subgroup showed improved efficacy. We investigated if anti-TIGIT mechanism of action (MOA)-related markers were associated with the efficacy of ociperlimab + tislelizumab in Cohort 3 (1L PD-L1+ NSCLC) of the phase 1/1b AdvanTIG-105 trial (NCT04047862) and evaluated a potential patient-enrichment strategy based on tumor tissue gene expression profile (GEP).

Methods: Tumor tissue GEP was tested using TruSeq RNA Access technology. Ventana SP263 PD-L1 immunohistochemistry (IHC) assay was used to evaluate PD-L1 expression. Median progression-free survival (mPFS) by investigator was calculated descriptively by Kaplan-Meier methodology. 95% confidence intervals for mPFS were generated using the Brookmeyer method. The primary inferential PFS comparison used unstratified log-rank test with 2-sided descriptive *P*-values.

Results: At data cutoff (Feb 2, 2023), 24 of 45 patients had GEP results. Anti-TIGIT MOA-related genes and signatures correlated with ociperlimab + tislelizumab treatment response. Patients with high (H) vs low (L) expression of TIGIT, CD226, CCR8, or a tumor-associated macrophage (TAM) signature had significantly longer mPFS (**Table**). Dual biomarkers combining both anti-PD-L1 (PD-L1 IHC) and one of the anti-TIGIT MOA-related factors (TIGIT, CCR8, TAM signature GEP) identified subgroups of PD-L1 H + TIGIT MOA-related factor H patients with improved PFS vs other subgroups (**Table**). A highly overlapped PD-L1 H + TIGIT H + CCR8 H + TAM signature H patient population was observed in dual biomarker analyses.

Conclusions: Anti-TIGIT MOA-related genes and signatures correlated with efficacy in ociperlimab + tislelizumab-treated 1L PD-L1+ NSCLC. Combining anti-TIGIT MOA-related factors with PD-L1 expression identified a subgroup of patients with improved efficacy.

Table. Efficacy Analyses in Patient Subgroups

	TIGIT[a]		CD226[b]		CCR8[b]		TAM[b]					
Subgroup	H	L	H	L	H	L	H	L				
n	8	16	12	12	12	12	12	12				
mPFS, months (95% CI)	NR (2.6, NR)	5.26 (2.07, 11.86)	NR (4.21, NR)	4.68 (1.41, 15.05)	15.21 (2.6, NR)	4.7 (1.71, 7.16)	15.21 (4.21, NR)	4.17 (1.71, 5.45)				
PFS, *P*-value	0.0326		0.0327		0.0131		0.0153					
	PD-L1[c] + TIGIT[b]				**PD-L1[c] + CCR8[b]**				**PD-L1[c] + TAM[b]**			
Subgroup	$TIGIT^{H}$ $PD\text{-}L1^{H}$	$TIGIT^{H}$ $PD\text{-}L1^{L}$	$TIGIT^{L}$ $PD\text{-}L1^{H}$	$TIGIT^{L}$ $PD\text{-}L1^{L}$	$CCR8^{H}$ $PD\text{-}L1^{H}$	$CCR8^{H}$ $PD\text{-}L1^{L}$	$CCR8^{L}$ $PD\text{-}L1^{H}$	$CCR8^{L}$ $PD\text{-}L1^{L}$	TAM^{H} $PD\text{-}L1^{H}$	TAM^{H} $PD\text{-}L1^{L}$	TAM^{L} $PD\text{-}L1^{H}$	TAM^{L} $PD\text{-}L1^{L}$
n	8	4	8	4	11	1	5	7	9	3	7	5
mPFS, months (95% CI)	NR (1.41,NR)	4.76 (2.6,NR)	8.62 (2.07,NR)	2.94 (1.25,NR)	NR (1.41,NR)	2.6 (NR,NR)	5.19 (2.07,NR)	4.21 (1.25,7.16)	23.89 (1.41,NR)	5.32 (4.21,NR)	5.29 (2.07,NR)	2.6 (1.25,NR)

Cutoff: [a]Top 1/3; [b]Median; [c]TC≥25%