Eftilagimod alpha (soluble LAG-3 protein) combined with 1st line chemo-immunotherapy in metastatic non-squamous non-small cell lung cancer (NSCLC) – Updates from INSIGHT-003 (IKF-s614)

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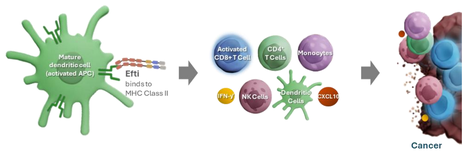
BACKGROUND

Stratum C of the INSIGHT multicenter platform trial evaluates eftilagimod alpha (efti) combined with standard of care (SOC) 1st line chemo-immunotherapy (CIT) in metastatic non-squamous (NSQ) NSCLC patients (pts). Efti is an MHC class II agonist (soluble LAG-3 protein) activating antigen-presenting (APCs) cells followed by T-cell (CD4/CD8) activation. Efti aims to enhance efficacy of IC. We hereby report the initial results from the full cohort of 54 pts.

Figure 1: Mechanism of action of efti

Efti is a soluble LAG-3 protein (LAG-3 domains fused to human IgG backbone). Activating APCs with efti leads to a broader immune response, including an increase in activated T cells (CD4/CD8) to fight cancer.

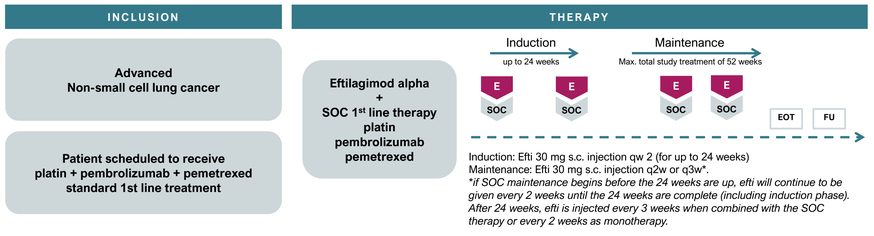


METHODS

Patients with 1st line advanced or metastatic NSCLC adenocarcinomas (non-squamous) receive carboplatin AUC5 / pemetrexed 500 mg/m² / pembrolizumab 200 mg q3w 4 cycles followed by maintenance pembrolizumab q3w and optional pemetrexed 500 mg/m² q3w combined with s.c. efti (30 mg) (q2w for 24 weeks; thereafter q3w till week 52; SOC thereafter). Imaging: q8w. Primary endpoint: feasibility (safety / tolerability). Secondary endpoints include ORR*, PFS* and OS.

* Per RECIST 1.1.

Figure 2: Study Design



SUMMARY & CONCLUSION

- **Eftilagimod alpha combined with SOC (carboplatin/pemetrexed/ pembrolizumab) in NSQ 1st line NSCLC led to encouraging ORR (unconf. 62.7% & conf. 58.8%) overall.**
- **More importantly ORR was comparable among TPS strata with conf. ORR of 54.5% on TPS < 1%; 60 % in TPS 1-49% and 75% in TPS ≥ 50%, respectively.**
- **Efti does not increase toxicity of the chemo-immunotherapy SOC.**
- **This combination is feasible and safe to administer, showing very encouraging ORR especially in pts with TPS score <1% and TPS 1-49%, where the unmet medical need is high. Phase 3 study TACTI-004 is underway (NCT06726265).**

RESULTS

From August 2021 until December 2024, 54 patients were enrolled and received treatment. Data cut-off was September 2025.

Baseline characteristics are reported in **Table 1.**

Overview of Adverse-Events is shown in **Table 2**.

Efficacy results for the evaluable population (pts with ≥1 evaluable post-baseline scan; N=51) are presented in **table 3.**

Table 1: Baseline Characteristics

Baseline parameters		EVAL N=51
1L NSQ NSCLC, %		100
Age, median (range), years		65 (52-81)
Sex, (%)	Female / Male	45.1 / 54.9
ECOG PS score, (%)	0 / 1	49.0 / 51.0
PD-L1 expression TPS, (%)	<1% 1-49% ≥50%	43.1 49.0 7.8
Smoking status, % Current / Ex / Never / Unknown		17.6 / 74.5 / 3.9 / 3.9
Brain metastasis, % Liver metastasis, %		3.9 11.8

Table 2: Safety overview

Total N=54	N	%
Total AEs	799	
Any AEs	54	100.0
Grade 1 - 2	52	96.3
Grade 3 – 4	43	79.6
Grade 5*	5	9.3
TRAE leading to discontinuation of any treatment component	15	27.8

AE: Adverse Event
TRAE: Treatment Related Adverse Event

*No Grade 5 AE was considered treatment-related

Figure 3: Case study of a 75-year-old male with PR

- 75-year-old male, TTF1 pos. Adeno-Ca, G3
- PD-L1 TPS 0%, no actionable genetic alterations
- ECOG PS 1
- cT1c pN2 cM1c (PLE, LYM, OSS, HEP, PUL), stage IVb
- Partial Response after treatment cycle 3, maintained until planned end of treatment (week 52)

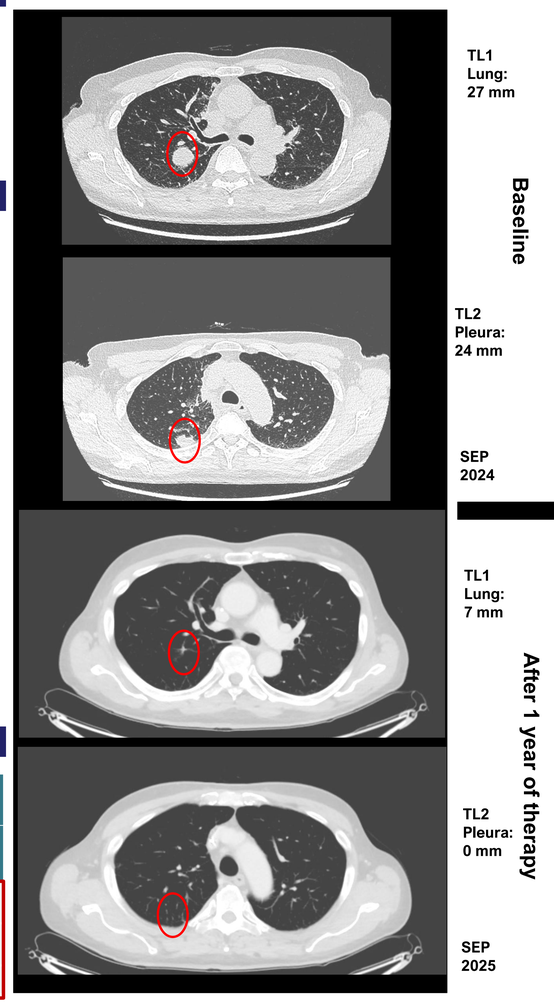
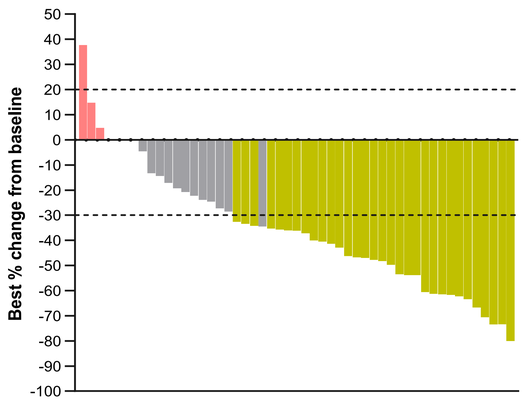


Figure 4: Best change in tumor size by RECIST 1.1



44 of 51 patients (86.3 %) experienced tumor shrinkage **(Figure 4)**.

Table 3: Efficacy Overview by PD-L1 status

Tumor Response	PD-L1 expression level (TPS)				
	EVAL (N=51)	<1%, N=22	1-49%, N=25	≥50%, N=4	<50%, N=47
ORR* confirmed, %	58.8	54.5	60.0	75.0	57.4
ORR* unconfirmed, %	62.7	54.5	68.0	75.0	61.7
DCR* %	90.2	86.4	92.0	100.0	89.4

* Per RECIST 1.1.

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Disclosures

TOG: no conflict of interest.
AA: no conflict of interest.

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