MADRID 2023 ESMO congress

Combining the antigen-presenting cell activator eftilagimod alpha (soluble LAG-3) and pembrolizumab: overall survival data from the 1st line non-small cell lung carcinoma cohort of TACTI-002

Phase II study of soluble LAG-3 combined with an anti-PD-1 antibody in 1st line metastatic NSCLC

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DECLARATION OF INTERESTS

Enric Carcereny

Consultant or Advisory Role: AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, MSD, Novartis, Roche, Takeda.

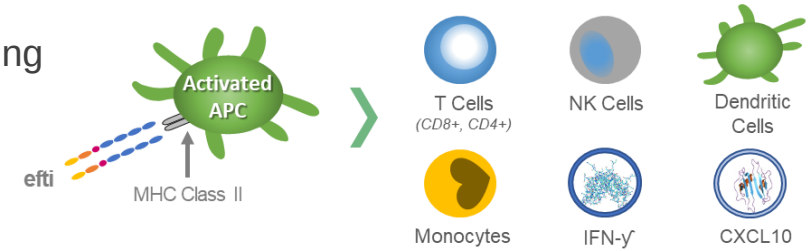
Speaking: AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, MSD, Novartis, Pfizer, Roche, Takeda.

Grant support: Merck KGaA.

Other: Bristol-Myers Squibb, Pfizer, Roche, Takeda.

Eftilagimod alpha (efti) & Trial Design

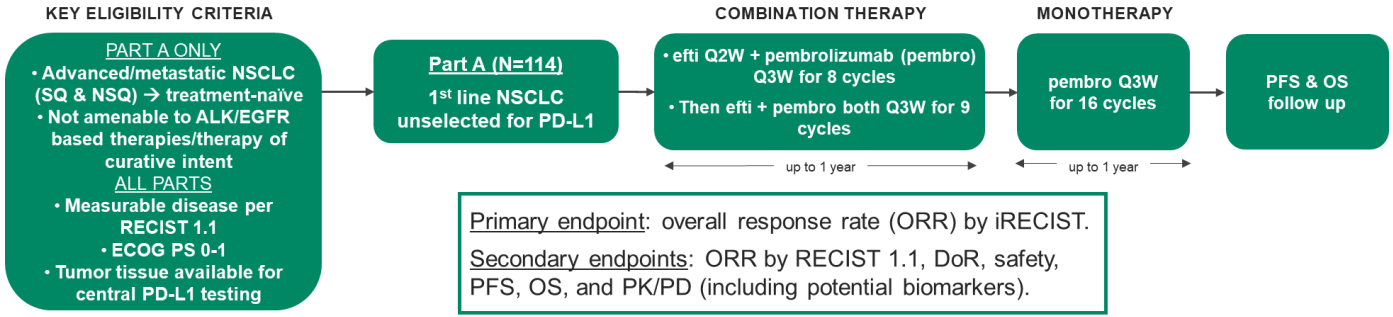
- **efti:** a **soluble LAG-3 protein** and **MHC Class II agonist** that leads to a broad anti-cancer immune response, including CD8+ T cell activation & proliferation, through activating antigen presenting cells (APC).
- **Distinct from anti-LAG-3:** efti targets MHC Class II on APCs, unlike LAG-3 antagonists that target T cells.



- **Rationale:** efti activates APCs, leading to an increase in activated T cells, augmenting responses and disease control when combined with PD-1/PD-L1 antagonists.

Trial Design

TACTI-002 (Part A)



Primary endpoint: overall response rate (ORR) by iRECIST.

Secondary endpoints: ORR by RECIST 1.1, DoR, safety, PFS, OS, and PK/PD (including potential biomarkers).

Note: Pts were recruited according to Simon's optimal two-stage design: during the first stage, 17 pts were recruited; second stage recruitment (n=19) was opened only after the number of responses was above 4. An extension stage (n=78) could be added if there were above 12 responses. In total, 114 pts were enrolled. True response rates sources/assumptions: KN-001 &-042 (KN-001: Lancet Respir Med, 2019; 7(4): 347-357; KN-042: Lancet 2019;393(10183:1819-1830), expecting that ~70% of patients had PD-L1 TPS <50%.

Baseline Disease Characteristics, Exposure & Safety

Baseline parameters		N=114	
Age, median (range), years		67 (44-85)	
Sex, %	Female / Male	26.3 / 73.7	
ECOG PS score, %	0 / 1	37.7 / 62.3	
Smoking status, %	Current or Ex-smoker / Non-smoker	94.7 / 5.3	
Histology, %	Squamous / Non-squamous / Not otherwise specified	35.1 / 63.1 / 1.8	
Metastatic disease, %	Yes / No	99.1 / 0.9	
		Central[1] (N=90)	Central + Local[2] (N=108)
PD-L1 expression TPS, %	<1%	35.6	34.3
	1-49%	42.2	38.9
	≥50%	22.2	26.9
Previous therapy, %	Radiotherapy	33.3	
	Surgery	20.2	
	Systemic therapy for non-met. disease	22.8	

[1] N=90; Central assessment of PD-L1 TPS using Dako IHC 22C3 pharmDx.
[2] N=108; Central assessment as per footnote 1 for 90 pts. For 18 patients, local assessment used predominantly Dako IHC 22C3 pharmDx due to non-evaluable central assessment results.

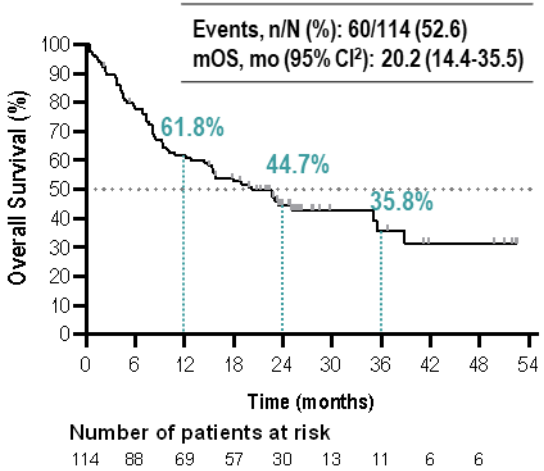
- 114 patients recruited at 18 sites across 6 countries between Mar 2019-Nov 2021.
- Unselected for PD-L1 expression including ~75% of patients with a PD-L1 Tumor Proportion Score (TPS) of <50%.
- Median exposure for efti of 24.7 weeks (range: 0.1-59.1) and for pembrolizumab 24.4 weeks (0.1-113.1).
- No new safety signals.

Data cut-off date: August 15, 2023 with median follow-up of 25.1 mo.

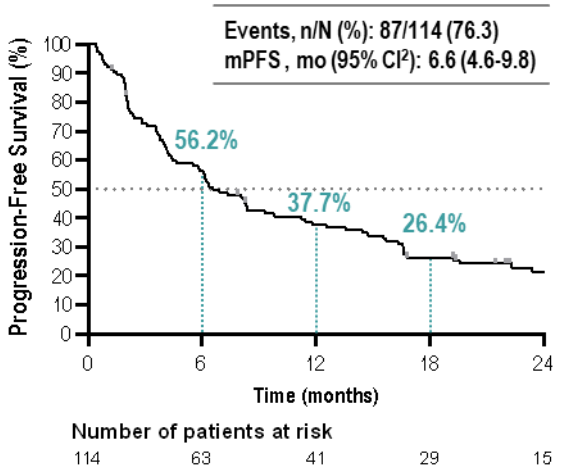
Efficacy - ITT

- Median OS of 20.2 mo in ITT where ~75% of patients had PD-L1 TPS score <50%, including ~35% with PD-L1 TPS of <1%.
- 45/114 (39.5%) received 2nd line therapy → mostly chemotherapy-based (42/45; 93.3%).
- Median DoR of 21.6 mo in the ITT.

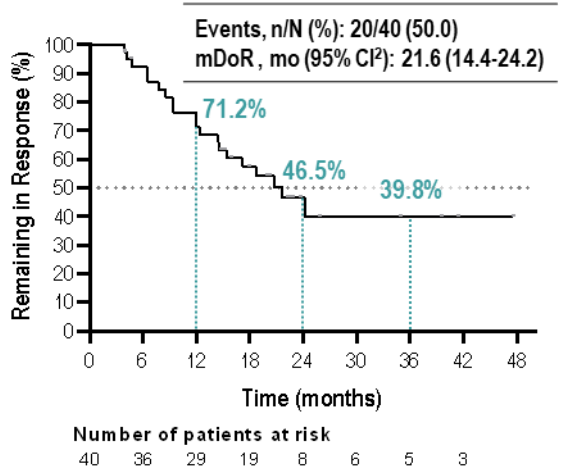
Overall survival, ITT (N=114)



Progression-free survival[1], ITT (N=114)



Duration of response[1], N=40



[1] according to iRECIST.
[2] 95% CIs calculated using Kaplan-Meier survival analysis method.

Note: mOS for squamous and non-squamous histology was 20.2 and 19.8 mo.
Data cut-off date: August 15, 2023 with median follow-up of 25.1 mo.

Efficacy by PD-L1[1]

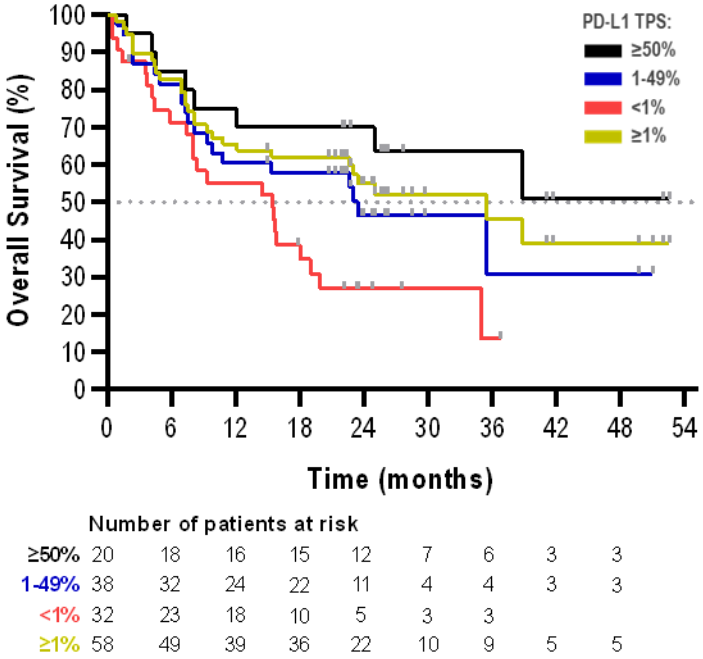
- Promising efficacy (ORR, PFS, OS, DOR) visible across all PD-L1 subgroups[1,2].
- For TPS ≥1%, mOS of 35.5 mo, mPFS[2] of 11.2 mo, mDOR[2] of 24.2 mo.
- For TPS ≥50%, mOS not reached despite long median follow up of 25.1 mo.

Tumor Response by central PD-L1[1], N=90

Efficacy parameter	<1%[1], n (%), N=32	1-49%[1], n (%), N=38	≥50%[1], n (%), N=20	≥1%[1], n (%), N=58
ORR[2,3], % (95% CI)[4]	31.3 (16.1-50.0)	44.7 (28.6-61.7)	55.0 (31.5-76.9)	48.3 (35.0-61.8)
mPFS[2], mo (% events)	4.2 (90.6)	9.3 (71.1)	16.5 (70.0)	11.2 (70.7)
mDoR[2], mo (% events)	20.7 (57.1)	NR (35.7)	18.7 (63.6)	24.2 (48.0)
mOS, mo (% events)	15.5 (71.9)	23.4 (52.6)	NR (40.0)	35.5 (48.3)

[1] N=90; Central assessment of PD-L1 TPS using Dako IHC 22C3 pharmDx; [2] iRECIST; [3] unconfirmed; [4] calculated using Clopper Pearson method; NR: not reached.
Note: results for PD-L1 central + local (N=108) were as follows (<1% / 1-49% / ≥50% / ≥1%):
mOS, mo: 14.4 / 23.4 / 38.8 / 35.5; mPFS[2]: 4.2 / 8.3 / 16.3 / 9.8; mDoR[2]: 20.7 / 21.6 / 18.7 / 21.6.

Overall survival by central PD-L1[1]



Data cut-off date: August 15, 2023 with median follow-up of 25.1 mo.

Conclusions

- Efti plus pembrolizumab lead to promising median overall survival (mOS) in 1st line NSCLC patients with TPS ≥1% (35.5 mo), TPS 1-49% (23.4 mo) and TPS ≥50% (not reached).
- Encouraging efficacy seen across response endpoints (ORR, PFS, DoR and OS) and PD-L1 subgroups (<1%, ≥1%, 1-49% and ≥50%).
- ITT population (N=114; ~75% patients PD-L1 low/negative) showed promising efficacy with mOS 20.2 mo, mDoR 21.6 mo, 12-mo PFS rate of 38% and 36-mo OS rate of 36%.
- In patients with TPS ≥1%, ORR (48.3%), mPFS (11.2 months), and mOS (35.5 months) compare favorably to historical results of anti-PD-1 monotherapy[1].
- In patients with TPS ≥1% mDOR (24.2 months) and mOS (35.5 months) compare favorably to historical results of approved anti-PD-1 + chemo-containing regimens[1].
- Efti plus pembrolizumab (without platinum-based chemotherapy backbone) showed promising efficacy especially in PD-L1 positive (TPS ≥1 %) 1st line NSCLC and should be investigated further.

[1] KN-001: NB Leighl et al, The Lancet 2019, http://dx.doi.org/10.1016/S2213-2600(18)30500-9; KN-042: TSK Mok et al, The Lancet 2019, http://dx.doi.org/10.1016/S0140-6736(18)32409-7); KN-407: Paz-Ares et al, N Engl J Med 2018 Nov 22;379(21):2040-2051.doi: 10.1056/NEJMoa1810865; KN-189: Gandhi et al, N Engl J Med, 2018 May 31;378(22):2078-2092, doi: 10.1056/NEJMoa1801005; EMPOWER-Lung3, Gogishvili et al, 2022 Nov;28(11):2374-2380. doi: 10.1038/s41591-022-01977-y.

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