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)

**KEY ELIGIBILITY CRITERIA**

- Advanced/metastatic NSCLC (SQ & NSQ) → treatment-naive
- Not amenable to ALK/EGFR based therapies/therapy of curative intent
- Measurable disease per RECIST 1.1
- ECOG PS 0-1
- Tumor tissue available for central PD-L1 testing

**COMBINATION THERAPY**

- **Part A (N=114)**
  1st line NSCLC unselected for PD-L1

- efti Q2W + pembrolizumab (pembro) Q3W for 8 cycles
- Then efti + pembro both Q3W for 9 cycles

**MONOTHERAPY**

- pembro Q3W for 16 cycles

**PFS & OS follow up**

**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

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N=114</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range), years</td>
<td>67 (44-85)</td>
</tr>
<tr>
<td>Sex, %</td>
<td>Female / Male</td>
</tr>
<tr>
<td>ECOG PS score, %</td>
<td>0 / 1</td>
</tr>
<tr>
<td>Smoking status, %</td>
<td>Current or Ex-smoker / Non-smoker</td>
</tr>
<tr>
<td>Histology, %</td>
<td>Squamous / Non-squamous / Not otherwise specified</td>
</tr>
<tr>
<td>Metastatic disease, %</td>
<td>Yes / No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PD-L1 expression TPS, %</th>
<th>Central¹ (N=90)</th>
<th>Central + Local² (N=108)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1%</td>
<td>35.6</td>
<td>34.3</td>
</tr>
<tr>
<td>1-49%</td>
<td>42.2</td>
<td>38.9</td>
</tr>
<tr>
<td>≥50%</td>
<td>22.2</td>
<td>26.9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Previous therapy, %</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiotherapy</td>
<td>33.3</td>
</tr>
<tr>
<td>Surgery</td>
<td>20.2</td>
</tr>
<tr>
<td>Systemic therapy for non-met. disease</td>
<td>22.8</td>
</tr>
</tbody>
</table>

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.

- 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.

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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)**

Events, n/N (%): 60/114 (52.6)
mOS, mo (95% CI): 20.2 (14.4-35.5)

**Progression-free survival\(^1\), ITT (N=114)**

Events, n/N (%): 87/114 (78.3)
mPFS, mo (95% CI): 6.6 (4.6-9.8)

**Duration of response\(^1\), N=40**

Events, n/N (%): 20/40 (50.0)
mDoR, mo (95% CI): 21.6 (14.4-24.2)

\(^1\) 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.

Enric Carcereny
Efficacy by PD-L1

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

Tumor Response by central PD-L1\(^1\), N=90

<table>
<thead>
<tr>
<th>Efficacy parameter</th>
<th>&lt;1%(^1), n (%) N=32</th>
<th>1-49%(^1), n (%) N=38</th>
<th>$\geq$50%(^1), n (%) N=20</th>
<th>$\geq$1%(^1), n (%) N=58</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR(^2,3), % (95% CI)(^4)</td>
<td>31.3 (16.1-50.0)</td>
<td>44.7 (28.6-61.7)</td>
<td>55.0 (31.5-76.9)</td>
<td>48.3 (35.0-61.8)</td>
</tr>
<tr>
<td>mPFS(^2), mo (% events)</td>
<td>4.2 (90.6)</td>
<td>9.3 (71.1)</td>
<td>16.5 (70.0)</td>
<td>11.2 (70.7)</td>
</tr>
<tr>
<td>mDoR(^2), mo (% events)</td>
<td>20.7 (57.1)</td>
<td>NR (35.7)</td>
<td>18.7 (63.6)</td>
<td>24.2 (48.0)</td>
</tr>
<tr>
<td>mOS, mo (% events)</td>
<td>15.5 (71.9)</td>
<td>23.4 (52.6)</td>
<td>NR (40.0)</td>
<td>35.5 (48.3)</td>
</tr>
</tbody>
</table>

\(^1\) 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\% / $\geq$50\% / $\geq$1\%):

Overall survival by central PD-L1\(^1\)

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

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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 monotherapy¹.
• 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 regimens¹.
• 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.

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