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TACTI-004, a double-blinded, randomised phase 3 trial of eftilagimod alfa plus pembrolizumab (P) + chemotherapy (C) vs placebo + P + C in 1st line advanced/ metastatic NSCLC

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Objective

- **TACTI-004** (**NCT06726265**; **KN-F91)** is a **Phase 3**, double-blinded, randomized, placebo-controlled, multicenter trial assessing the effectiveness of eftilagimod alfa (efti) in combination with pembrolizumab (P) & chemotherapy (C) compared to placebo plus P & C in subjects with advanced/metastatic non-small cell lung cancer (NSCLC).

Summary

- Data suggests combining an APC activator (efti) with current standard-of-care treatments P & C enhances anti-tumor effects.
- Based on results from the TACTI-002 and INSIGHT-003 studies, the TACTI-004 trial will analyze treatment of efti plus P & C in subjects with metastatic NSCLC.
- TACTI-004 is currently enrolling subjects.

Plain Language Summary

Why are we performing this study?

NSCLC is one of the most frequently diagnosed cancers worldwide and is commonly treated with immunotherapy (pembrolizumab) or chemo-immunotherapy.

***Efti** is a drug that helps the immune system fight tumors. Prior studies have shown that efti + pembrolizumab and/or chemotherapy may help immune cells to kill cancer cells.*

How the study will be performed?

Subjects with NSCLC will receive either:

- *efti + chemotherapy + pembrolizumab*
- *placebo + chemotherapy + pembrolizumab*

This study will test the effectiveness of these treatments.

Where can I access more information?

More info at: https://clinicaltrials.gov/study/NCT06726265.

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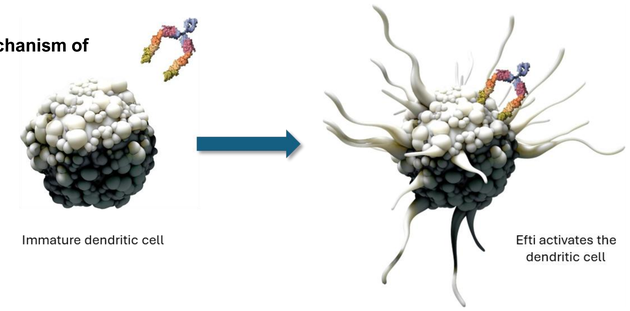
BACKGROUND

- **Eftilagimod alfa (efti):** is an antigen presenting cell (APC) activator that binds to a subset of MHC class II molecules. Activating APCs with efti leads to a broad immune response to fight cancer, including increases in activated T cells (CD4/CD8) and other important immune cells/cytokines[1,2] (**Figure 1**).
- In a previous study (NCT03625323), efti plus pembrolizumab (PD-1 inhibitor), as a first-line therapy for NSCLC subjects, demonstrated an excellent safety profile and encouraging antitumor activity. Subjects with TPS ≥1% had an ORR of 48.3%, median PFS of 11.2 months and median OS of 35.4 months. Antitumor effects were seen across all PD-L1 levels, including no PD-L1 expression (TPS <1%)[3].
- Non-squamous NSCLC subjects treated with efti plus chemotherapy and pembrolizumab (NCT03252938) also reported no safety concerns. Efficacy results were promising, especially in subjects with TPS <50% (median PFS of 10.9 months and median OS not reached)[4].
- Therefore, efti combined with pembrolizumab plus chemotherapy may provide a safe treatment option that optimizes clinical benefit for NSCLC patients, irrespective of their tumor PD-L1 expression.

Figure 1: Mechanism of action of efti

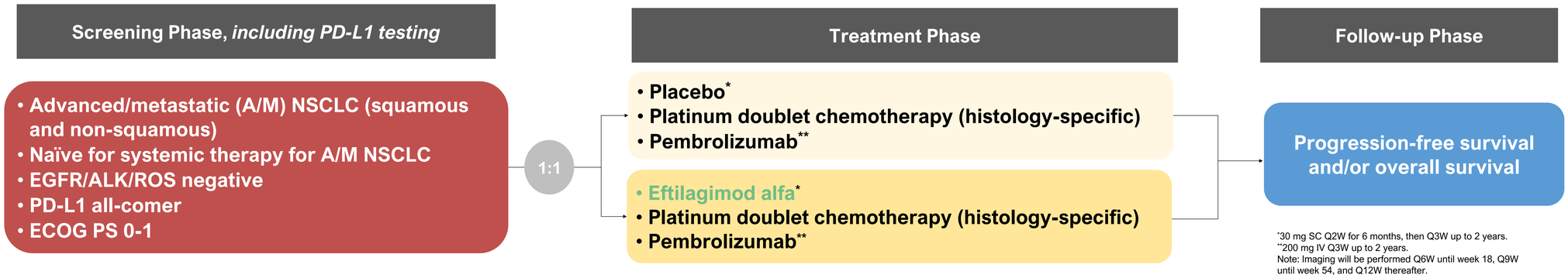


TACTI-004 (Two ACTive Immunotherapies-004)

TRIAL DESIGN

- The **TACTI-004 (NCT06726265**; **KEYNOTE-F91)** trial will recruit approximately 756 subjects in >25 countries (**Figure 4**).
- Prior to randomization, subjects' tumor tissue will be centrally assessed for PD-L1 (all) and mutations (as needed).
- Subjects will be randomized 1:1 (**Figure 2**).
- Stratification factors include PD-L1 expression level, tumor type, ECOG, and geographical region.
- Study endpoints are described in **Figure 3** with PFS and OS being dual primary endpoints.

Figure 2: Trial flow chart



*30 mg SC Q2W for 6 months, then Q3W up to 2 years.
**200 mg IV Q3W up to 2 years.
Note: Imaging will be performed Q6W until week 18, Q9W until week 54, and Q12W thereafter.

PARTICIPATION CRITERIA

Key inclusion criteria

- ≥18 years of age.
- Advanced/metastatic (A/M; stage IIIB/C or IV) NSCLC (squamous or non-squamous), not amenable to curative treatment nor locally available oncogenic driver mutation-based first-line therapy.
- ECOG performance status 0 or 1.
- Expected survival >3 months.
- Measurable disease as defined by RECIST 1.1.
- Tumor tissue available for PD-L1 central testing.
- Stable brain metastasis is acceptable.
- Prior anti-PD-L1 after 12-month washout is permitted.

Key exclusion criteria

- Tumors with EGFR mutations, or ALK/ROS1 translocations.
- Prior systemic therapy for A/M NSCLC (previous palliative radiotherapy for A/M disease acceptable).

STATISTICAL METHODS

- Main analyses will be performed in the intent-to-treat population.
- Prior to the final analysis, there will be 3 predefined interim analyses. Timing of analyses will be event-driven.
- The overall type I error rate of the primary endpoints will be strongly controlled at a 2-sided alpha level of 0.05. The trial is powered to show superiority in terms of OS at the final analysis and will be considered successful if one of the dual primary endpoints is positive.

Figure 3: Trial endpoints

DUAL PRIMARY ENDPOINTS

- **PFS by RECIST 1.1 and OS**

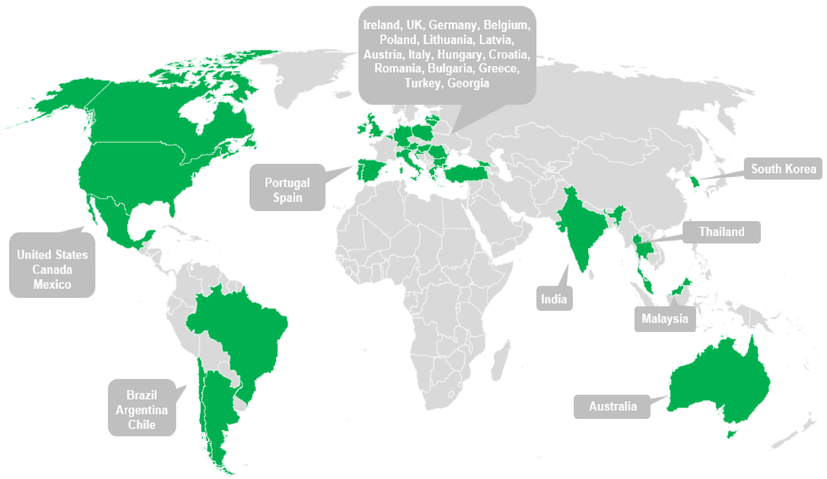
KEY SECONDARY ENDPOINTS

- ORR by RECIST 1.1
- Safety and tolerability
- DCR, DoR and TTR by RECIST 1.1
- Quality of life

EXPLORATORY ENDPOINTS

- Characterization of immunogenic properties of efti
- Pharmacokinetic and pharmacodynamic characterization of efti

Figure 4. Trial site locations



Abbreviations

ALK… Anaplastic Lymphoma Kinase
APC… Antigen presenting cell
CXCL-10… C-X-C motif chemokine ligand 10
DCR… Disease control rate
DoR… Duration of response
ECOG…Eastern Cooperative Oncology Group
EGFR… Epidermal Growth Factor Receptor
IFN-γ… Interferon-gamma
LAG-3… Lymphocyte Activation gene-3
MHC… Major Histocompatibility Complex
NK… natural killer
ORR… objective response rate
OS… overall survival
PFS… progression-free survival
ROS1… c-ros oncogene 1
TPS…Tumor proportion score
TTNT… time to next treatment
TTR…time to response

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Disclosures

- **Invited Speaker**: AstraZeneca, BMS, Lilly, Pfizer, Roche, Sanofi/Aventis, Takeda
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