FPN: 131TiP

TACTI-004: a double-blinded, randomized phase 3 trial in patients with advanced/metastatic non-small cell lung cancer receiving eftilagimod alfa (MHC class II agonist) in combination with pembrolizumab (P) and chemotherapy (C) versus placebo + P + C

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Objective

- **TACTI-004** (**NCT06726265**; **KNF91)** 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 MHC II agonist (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?

Non-small cell lung cancer (NSCLC) is one of the most frequently diagnosed cancers worldwide. NSCLC is commonly treated with pembrolizumab or chemotherapy, however, **new treatment options are needed to improve outcomes for patients.**

Efti is a drug that boosts the immune response to fight tumors. Previous studies have shown that combining efti with 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 aims to test the effectiveness of these treatments.

Where can I access more information?

More info about the TACTI-004 trial can be found at:
https://clinicaltrials.gov/study/NCT06726265

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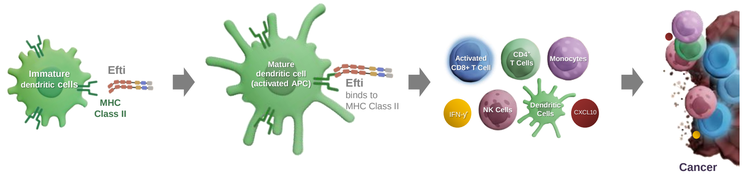
BACKGROUND

- **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-L1 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 35.5 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

TRIAL DESIGN

- The **TACTI-004 (NCT06726265**; **KNF91)** trial will recruit in across 25+ countries approximately 756 subjects (**Figure 5**).
- Prior to randomization, during the screening phase, subjects' tumor tissue will be centrally assessed for PD-L1/mutations (as needed).
- Subjects will be randomized 1:1 (**Figure 2**).
- Stratification factors are PD-L1 expression level (TPS <1% vs 1-49% vs ≥50%), tumor type (squamous vs non-squamous), ECOG (0 vs 1), and geographical region (Europe vs Asia vs rest of the world).
- Imaging will be performed Q6W until week 18, Q9W until week 54 & Q12W thereafter.
- An overview of the treatments' administration schedule is provided in **Figure 3.**
- The primary objective is to compare the efficacy of efti + P & C versus placebo + P & C, using dual primary endpoints (**Figure 4**) of PFS and OS.

Figure 2: Trial flow chart

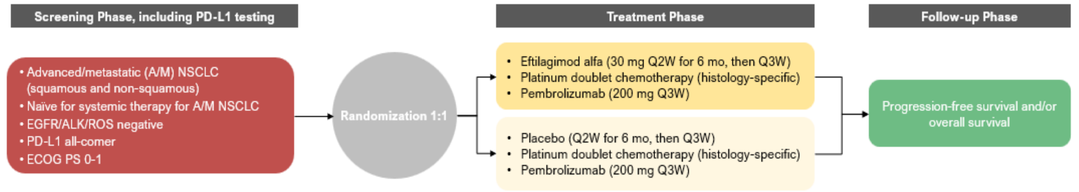


Figure 4: Trial endpoints

DUAL PRIMARY ENDPOINTS	SECONDARY ENDPOINTS	EXPLORATORY ENDPOINTS
• **PFS by RECIST 1.1 and OS**	• ORR by RECIST 1.1 • Safety and tolerability • DCR, DoR and TTR by RECIST 1.1 • TTNT • Quality of life • PFS on next line therapy by RECIST 1.1	• Characterization of immunogenic properties of efti • Pharmacokinetic and pharmacodynamic characterization of efti

STATISTICAL METHODS

- All main analyses will be done in the intent-to-treat population.
- The overall type I error rate of the primary endpoints will be strongly controlled at a two-sided alpha level of 0.05. This alpha will be split between the endpoints. The trial is mainly powered to show superiority in terms of OS at the final analysis. The study will be considered a success if one of the dual primary endpoints is positive.
- Prior to the final analysis, there will be 3 predefined interim analyses (one futility, one efficacy analysis for PFS and one for OS). All analyses will be event-driven and will take place only once the required number of events was reached.

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).

Figure 5. Trial site locations

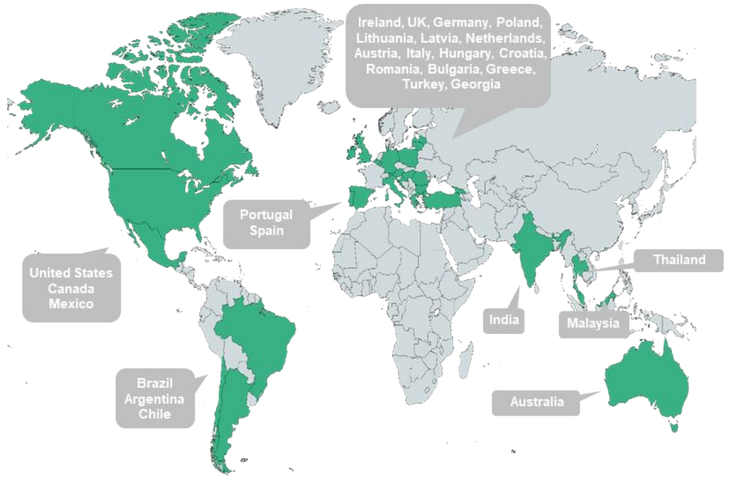
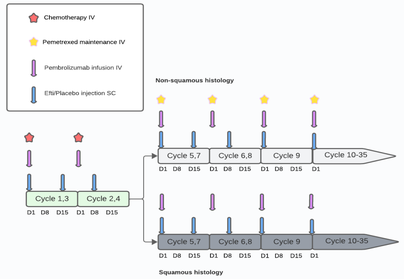


Figure 3: Schedule of treatments



Histology-based chemotherapy

- **Non-squamous NSCLC:** cisplatin (75 mg/m²) or carboplatin (AUC 5 or 6) + pemetrexed (500 mg/m²) Q3W for 3 months, then maintenance pemetrexed Q3W.
- **Squamous NSCLC:** carboplatin (AUC 5 or 6) + paclitaxel (175 or 200 mg/m²) Q3W for 3 months.

Pembrolizumab

- 200 mg will be administrated as intravenous infusion (30 min) Q3W for up to 2 years.

Eftilagimod alfa or Placebo

- 30 mg efti or placebo will be injected subcutaneously Q2W for 6 months, then Q3W for up to 2 years.

Abbreviations

DCR… Disease control rate
DoR… Duration of response
LAG-3… Lymphocyte Activation gene-3
MHC… Major Histocompatibility Complex
NK… natural killer
ORR… objective response rate
OS… overall survival
PFS… progression-free survival
TTNT… time to next treatment
TTR…time to response

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Disclosures

Advisory board: Amgen, Roche, AstraZeneca, Takeda, Janssen, Casen Recordati, BMS, Sanofi, Pfizer.
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