AIPAC-003: A randomized, double-blind, placebo-controlled phase 3 trial testing eftilagimod alpha (soluble LAG-3) in HER2-neg/low metastatic breast cancer patients receiving paclitaxel, following an open-label dose optimization

TPS1125

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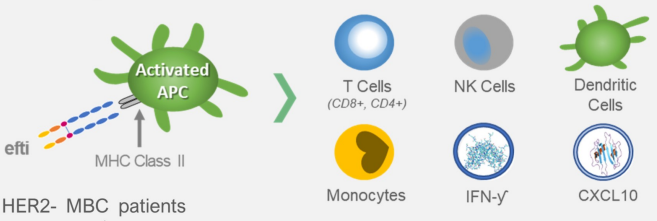
BACKGROUND

Eftilagimod alpha (efti):

- **Mechanism of action:** efti is a soluble LAG-3 protein (LAG-3 domains fused to human IgG backbone) and MHC Class II agonist. Activating antigen presenting cells (APCs: dendritic cells & monocytes) 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 **(Figure 1)**.
- **Synergistic effect with chemotherapy**: efti reinforces long-lasting T cell responses, leading to more durable effects & prolonged survival with minimal related side effects.

Figure 1: Mechanism of action of efti



Rationale for trial:

- Data from predecessor randomized, phase 2b trial of paclitaxel plus either efti or placebo in HR⁺ HER2- MBC patients (AIPAC; NCT02614833) linked sustained pharmacodynamic activity to improved overall survival (OS) in the efti arm[1].
- To address a high unmet medical need in HR⁺ HER2-neg/low metastatic breast cancer (MBC) and metastatic triple negative breast cancer (TNBC) patients eligible to receive chemotherapy.

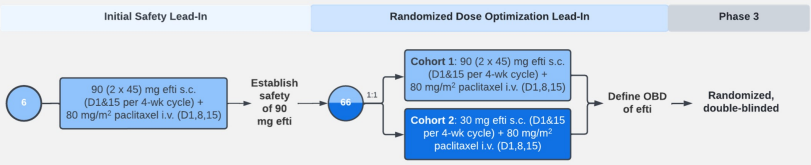
TRIAL DESIGN

AIPAC-003 has multiple components including an **initial safety lead-in** component followed by a Phase 2 **open-label dose optimization lead-in** and **Phase 3** component (**Figure 2**).

- **Safety lead-in (n=6):** evaluate safety of a higher dose of efti (90 mg).
- **Dose optimization lead-in (n=66):** determine optimal biological dose (OBD) based on safety, tolerability, efficacy & pharmacodynamic data. Evaluation comprises data from the safety lead-in and the randomized dose optimization lead-in.
- **Phase 3:** randomized, double-blinded; to be initiated after OBD determination.

Treatment will consist of a chemo-immunotherapy (chemo-IO) phase followed by an immunotherapy (IO)-phase (**Figure 3**).

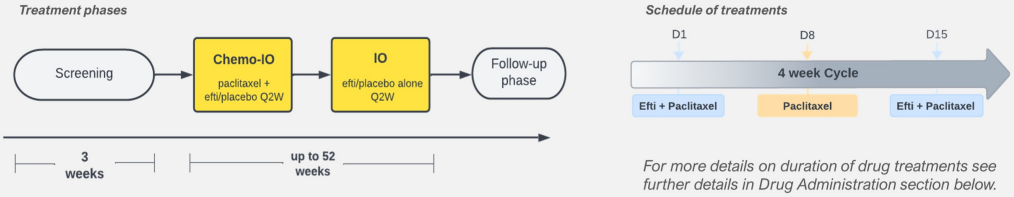
Figure 2: Trial flow chart



Objectives of the dose optimization lead-in:

PRIMARY OBJECTIVES	SECONDARY OBJECTIVES
• Safety and tolerability of 90 mg efti plus paclitaxel, compared to 30 mg efti plus paclitaxel. • Define OBD of efti when combined with weekly paclitaxel.	• ORR by RECIST 1.1; PFS and OS of 30 and 90 mg efti plus paclitaxel. • Quality of life at both doses. • Pharmacokinetic profile of efti at 30 and 90 mg.

Figure 3: Treatment phases and schedule of treatments



For more details on duration of drug treatments see further details in Drug Administration section below.

KEY ELIGIBILITY CRITERIA

Key inclusion criteria

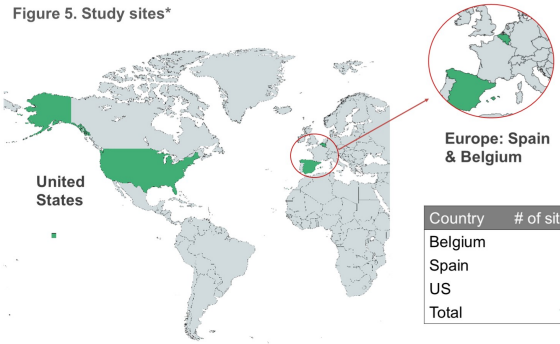
- Patients with HR+ HER2-neg/low MBC or mTNBC.
- HR⁺ MBC patients with proven resistance to endocrine-based therapy and are indicated to receive chemotherapy for metastatic disease.
- mTNBC patients who are ineligible for anti-PD-X-based therapy and are indicated to receive paclitaxel for metastatic disease in 1st line setting.
- Measurable disease as defined by RECIST 1.1 for the dose optimization lead-in.
- ECOG performance status 0-1.
- Expected survival longer than 3 months.

Key exclusion criteria

- Prior chemotherapy for MBC.
- Disease-free interval less than 12 mo from last dose of adjuvant chemotherapy.

TRIAL SITES & RECRUITMENT

Figure 5. Study sites*



Country	# of sites
Belgium	4
Spain	9
US	5
Total	18

*The study will expand to other sites/countries in the Phase 3 component.

RECRUITMENT

Recruitment is ongoing. For more info, please visit: https://www.clinicaltrials.gov/ct2/show/NCT05747794

DRUG ADMINISTRATION

Paclitaxel:

80 mg/m² as I.V. infusion over 1-hr as part of a 4-week cycle.

6 planned cycles with extension possibility at discretion of investigator as per patient's tolerability. If paclitaxel is stopped due to toxicity, patient may move on to efti/placebo alone if 4 cycles with paclitaxel were completed.

Eftilagimod alpha:

30 or 90 mg injected s.c. in the anterior face of thigh on same day ≥30 min after paclitaxel infusion.

Maximum of 26 injections.

ABBREVIATIONS

AIPAC… Active Immunotherapy PAClitaxel
DOL… Dose optimization lead-in
ECOG… Eastern Cooperative Oncology Group)
HR… hormone receptor
IO… immuno-oncology therapy
(i)RECIST… (Immune) Response Evaluation Criteria In Solid Tumors
I.V… intravenous
LAG-3… Lymphocyte Activation gene-3
MHC… Major Histocompatibility Complex
NK… natural killer
OBD… Optimal biological dose
ORR… objective response rate
OS… overall survival
PD-L1…Programmed death-ligand 1
PD-1… Programmed cell death protein 1
PFS… progression-free survival
PK… Pharmacokinetic
QoL… Quality of life
s.c… Subcutaneous
Th1… T helper type 1

REFERENCES

[1] Wildiers, H. 2024. Paclitaxel plus Eftilagimod Alpha, a Soluble LAG-3 Protein, in Metastatic, HR+ Breast Cancer: Results from AIPAC, a Randomized, Placebo Controlled Phase IIb Trial. Clin Cancer Res.

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