AIPAC (Active Immunotherapy PAClitaxel): A randomized, double blind, placebo-controlled, multinational Phase IIb trial evaluating the efficacy of eftilagimod alpha (a soluble LAG-3 fusion protein) in combination with paclitaxel in hormone receptor positive metastatic breast cancer.

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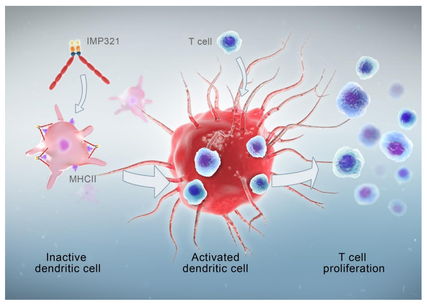
Background



Eftilagimod alpha (efti, previously IMP321) is a recombinant LAG-3Ig fusion protein that binds to MHC class II and mediates antigen-presenting cell (APC) activation followed by CD8 T-cell activation. The activation of the dendritic cell network with efti injected s.c. the day after chemotherapy at a time when these APC are loaded with tumor antigens may lead to stronger anti-tumor CD8 T cell responses. This is approached in the present AIPAC trial (Active Immunotherapy PAClitaxel) in hormone receptor-positive stage IV metastatic breast carcinoma patients receiving eftilagimod alpha or placebo as adjunctive to weekly paclitaxel as a first-line chemotherapy. The safety run-in stage (stage 1) is completed, whereas the randomized part (stage 2) is actively recruiting.

For more information, please visit http://www.immutep.com/investors-media/presentations.html or use the following:

The AIPAC trial protocol has been released on 28 August 2015. The trial identifiers are IMP321-P011 (sponsor code), 2015-002541-63 (EudraCT) and NCT02614833 (ClinicalTrials.gov).

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Objectives (randomisation stage)

- To determine the efficacy of efti combined with weekly paclitaxel versus weekly paclitaxel plus placebo in hormone receptor positive metastatic breast cancer patients
- To characterise the anti-tumour activity of efti, safety, tolerability, immunogenic properties, quality of life, immune responses and biomarker of efti + paclitaxel versus placebo.

Trial design

A multicentre, placebo-controlled, double blind, 1:1 randomised Phase IIb clinical trial in 2 stages:

- **Safety run-in stage (n=15)*:** open-label, determing recommended Phase 2 dose of efti in combination with paclitaxel for randomized phase
- **Randomisation stage (n=226):** placebo-controlled, double-blind, treatment: efti + paclitaxel vs. paclitaxel + placebo

Treatment design

The treatment consists of a chemo-immunotherapy phase followed by a maintenance phase:

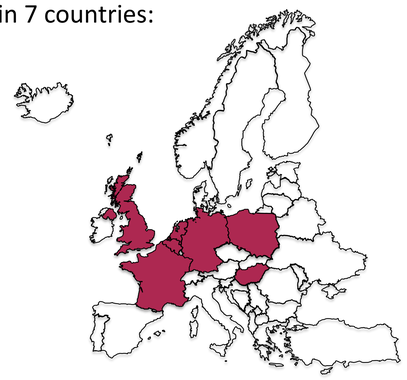
- **chemo-immunotherapy phase**: 6 cycles of 4 weeks with weekly paclitaxel (80 mg/m², corticoid premedication allowed) at Days 1, 8 and 15 + either efti or placebo, on Days 2 and 16 of each 4-week cycle.
- **maintenance phase**: responding or stable patients will receive afterwards study agent (efti or placebo) every 4 weeks for additional 12 injections

Study duration

- Study start: First patient first visit (stage 1) by January 2016
- Start of the randomisation stage: first patient first visit (stage) by January 2017
- Estimated last patient first visit: H2 2018
- Estimated study end: 36 months after last patient first visit (stage 2)

Involved countries

- The AIPAC trial was submitted and approved in 7 countries:
  - Belgium
  - The Netherlands
  - France
  - Hungary
  - Poland
  - United Kingdom
  - Germany
- Number of sites: 34



***Please note, the safety run-in stage is completed and is not part of this poster. Details and results are shown on poster #131 (abstract 1050).**

Main Exclusion criteria

Patients are to be excluded from the study at the time of screening for any of the following reasons:

- Prior chemotherapy for metastatic breast adenocarcinoma
- Disease-free interval of less than twelve months from the last dose of adjuvant chemotherapy
- Candidate for treatment with trastuzumab (or other Her2/neu targeted agents)
- Systemic chemotherapy, endocrine therapy, or any other investigational agent within 4 weeks prior to first dose of study treatment and until completion of study treatment
- Known cerebral or leptomeningeal metastases
- Active acute or chronic infection
- Active autoimmune disease requiring immunosuppressive therapy
- Known HIV positivity, history of Hepatitis B or C exposure, currently controlled by antiviral therapy
- Any condition requiring continuous systemic treatment with either corticosteroids (>10 mg daily prednisone equivalents) or other immunosuppressive medications within 4 weeks prior to first dose of study treatment. Inhaled or topical steroids and physiological replacement doses of up to 10 mg daily prednisone equivalent are permitted in the absence of active autoimmune disease

Main Inclusion criteria

- Able to give written informed consent and to comply with the protocol
- Stage IV oestrogen receptor positive and/or progesterone receptor positive breast adenocarcinoma, histologically proven
- Female of age 18 years or above
- Patients who are indicated to received first line chemotherapy with weekly paclitaxel
- Effective contraception or postmenopausal or permanently sterilized or otherwise be incapable of pregnancy
- ECOG performance status 0-1
- Expected survival longer than three months
- Resolution of toxicity of prior therapy to grade < 2 (except for alopecia and transaminases in case of liver metastases)
- Evidence of measurable disease as defined by RECIST version 1.1
- Adequate laboratory criteria

Statistical analysis (randomisation stage)

- N = 226 patients
- Minimum of 152 PFS events

Endpoints:

- Progression-free survival and overall survival
- Assessment of adverse events according to National Cancer Institute common terminology criteria for adverse events and other safety parameter
- Time to next treatment, objective response rate according to RECIST 1.1, time to and duration of response and duration of stable disease
- Plasma concentration time profile of efti and derived PK parameters
- Development of anti-drug (efti) antibodies
- Assessment of TH1 biomarker of interest as pharmacodynamics markers in the same subset of patients monitored for blood cell phenotype
- Determination of autoantibodies
- Assessment of serum tumour markers

APC…antigen-presenting cell
ECOG…Eastern Cooperative Oncology Group
efti…Eftilagimod alpha
MHC…Major Histocompatibility Complex
PFS…Progression-free survival