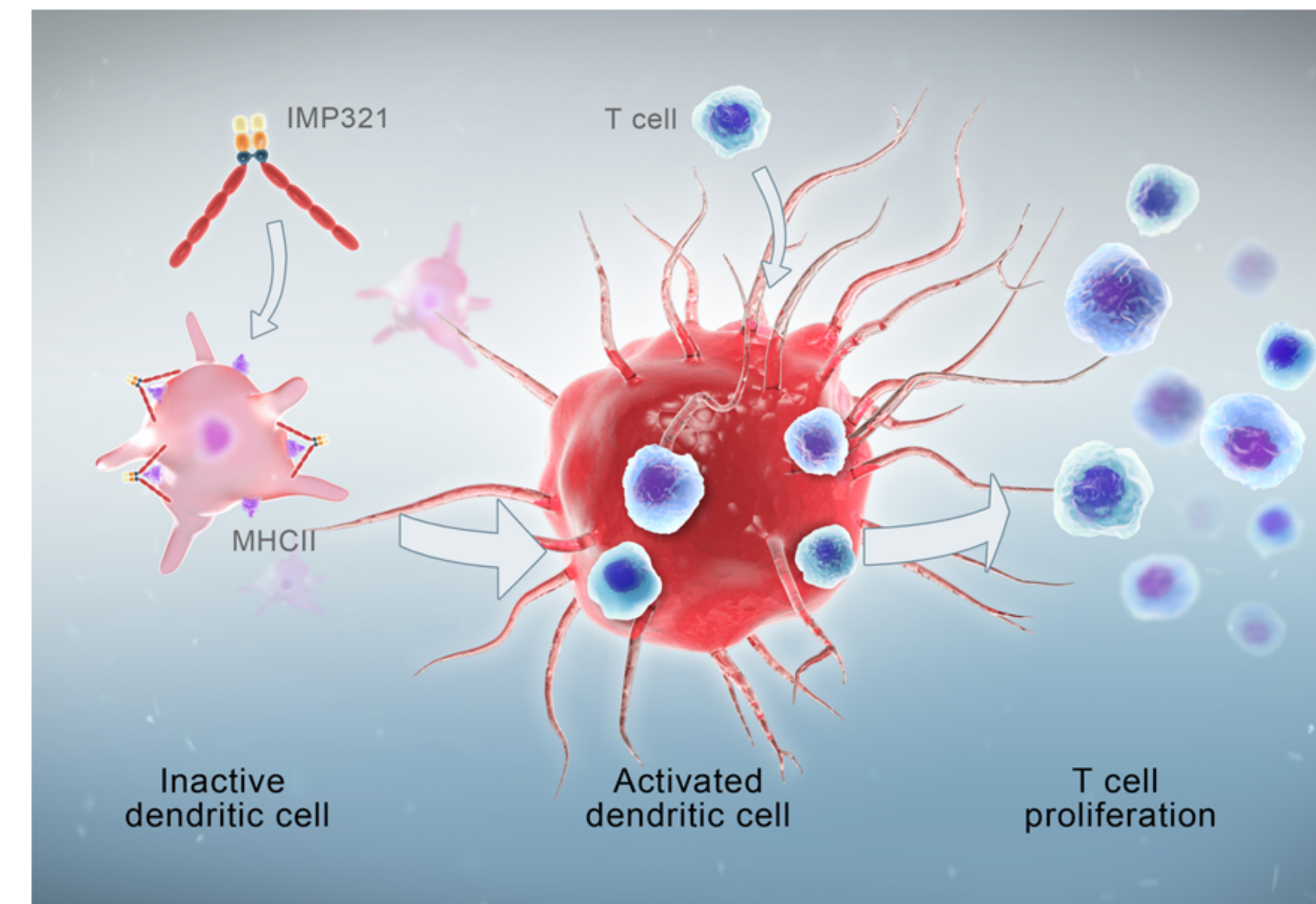


AIPAC (Active Immunotherapy PAClitaxel): A Phase IIb trial in hormone receptor-positive (HR+) metastatic breast carcinoma (MBC) patients receiving IMP321 (LAG-3Ig fusion protein) or placebo as adjunctive to a standard chemotherapy regimen of paclitaxel

¹Prima BioMed, Leipzig, Germany

²Immutep, Orsay, France

Background



IMP321 consists of the extracellular portion of the human lymphocyte activation gene 3 (LAG-3) protein fused to the Fc fraction of a human IgG1. This soluble LAG-3Ig fusion protein, like the membrane form of LAG-3 naturally expressed on human T cells, binds to major histocompatibility complex (MHC) class II molecules on the surface of antigen presenting cells (APC) and leads to their activation with enhanced presentation of tumour antigens to T cells. As a result, strong and sustained anti-tumour cytotoxic T cell responses are obtained.

For more information, please visit:

<http://primabiomed.com.au/products/LAG-3.php>



1 - Brignone et al. Clin Cancer Res 2009;15(19) October 1, 2009; 2 - Brignone et al. Journal of Translational Medicine 2010, 8:71
The trial identifiers are IMP321-P011 (sponsor code), 2015-002541-63 (EudraCT) and NCT02614833 (ClinicalTrials.gov).
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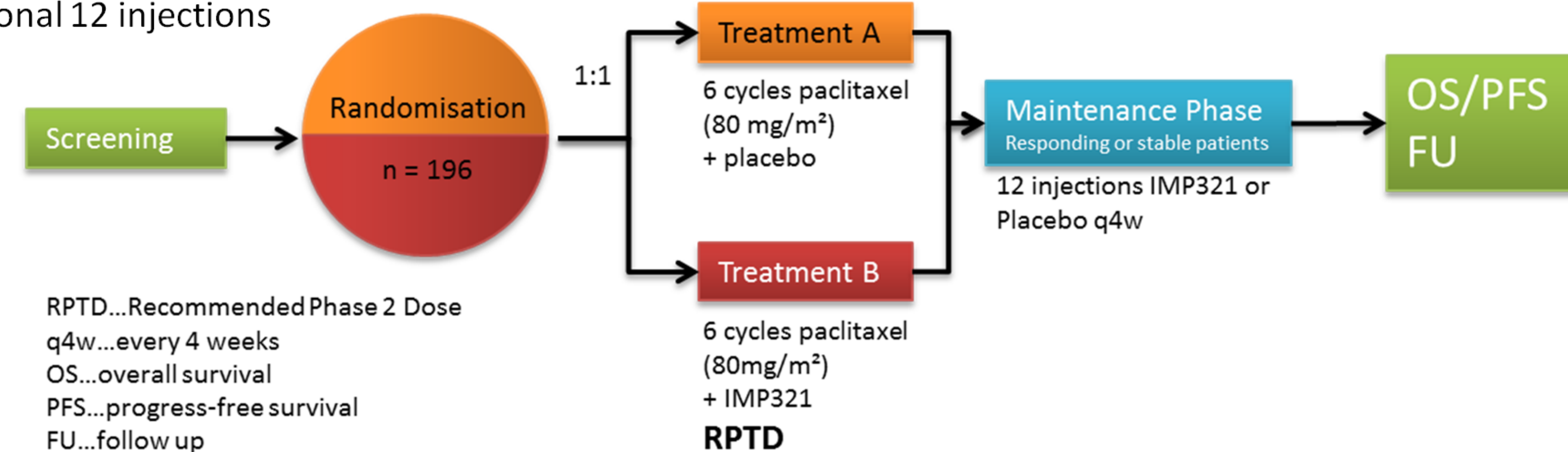
Trial design

Multinational, multicenter, placebo-controlled, double blind, 1:1 randomized Phase IIb trial consisting of 2 stages:

- **Safety run-in stage (n=15)**: open-label, determining recommended phase two dose (RPTD) of IMP321 in combination with paclitaxel for the randomized phase
- **Randomization stage (n=196)**: randomized (1:1), placebo-controlled, double-blind: IMP321 + paclitaxel vs. paclitaxel + placebo

In both stages, treatment consists of a chemo-immunotherapy phase followed by a maintenance phase:

- **chemo-immunotherapy phase**: 6 cycles with weekly paclitaxel (80 mg/m²) at days 1, 8 and 15 + either IMP321 or placebo, on Days 2 and 16 of each 4-week cycle.
- **maintenance phase**: responding or stable patients will receive study agent (IMP321 or placebo) every 4 weeks for additional 12 injections



Objectives

Primary:

- To determine the efficacy (as assessed by PFS) of IMP321 compared to placebo as adjunctive to a standard chemotherapy of paclitaxel in HR+ MBC patients

Secondary:

- To assess overall survival (OS)
- To determine safety and tolerability
- To assess objective response rate, time to and duration of response and time to next treatment
- To characterize the pharmacokinetic properties and immunogenic profile of IMP321
- To assess quality of life of IMP321 compared to placebo

Exploratory:

- To evaluate the immune response patients in relation to the treatment with IMP321
- To identify biomarkers that correlate with clinical outcome and treatment response

Statistics

Based on the statistical assumptions (not disclosed), projected recruitment and treatment timelines **196 patients will be randomized.**

Safety run-in stage - dose escalation

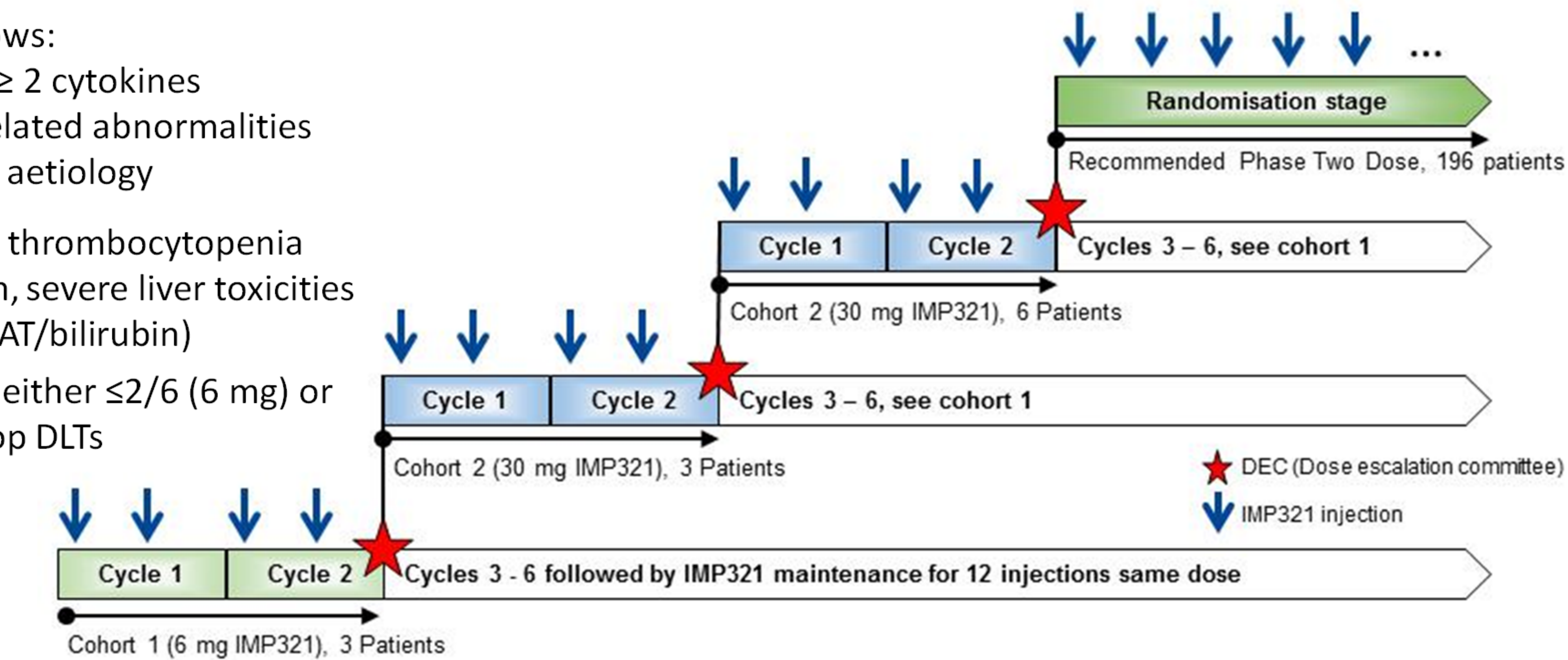
Dose levels of 6 mg and 30 mg IMP321 have been selected based on previous trials with IMP321 in renal cell cancer¹ and metastatic breast cancer².

DLTs are defined as follows:

- > 50fold increase of ≥ 2 cytokines
- ≥ grade 3 immune related abnormalities
- ≥ grade 4 ARs or any aetiology

- Febrile neutropenia, thrombocytopenia requiring transfusion, severe liver toxicities (defined by ALAT/ASAT/bilirubin)

Dose considered safe if either ≤2/6 (6 mg) or ≤2/9 pts (30 mg) develop DLTs



Main inclusion criteria

- Stage IV oestrogen receptor positive and/or progesterone receptor positive breast adenocarcinoma
- Female of age 18 years or above
- Patients who are indicated to receive first line chemotherapy with weekly paclitaxel
- ECOG performance status 0-1
- Evidence of measurable disease as defined by RECIST version 1.1
- Adequate laboratory criteria e.g. total white blood cell count ≥ 3 * 10⁹/L; platelet count ≥ 100 * 10⁹/L; ANC ≥ 1.5 * 10⁹/l; serum creatinine ≤ 1.5 x ULN; haemoglobin > 9g/dL or 5.58 mmol/L

Main exclusion criteria

- Prior chemotherapy for metastatic breast adenocarcinoma
- Disease-free interval of < 12 months
- Candidate for treatment Her2/neu targeted therapy
- Systemic therapy, or any other investigational agent within 4 weeks
- Known cerebral or leptomeningeal metastases
- Active acute or chronic infection
- HIV positivity, hepatitis B or C
- Active autoimmune disease requiring immunosuppressive therapy
- Any condition requiring continuous systemic treatment with either corticosteroids (>10 mg daily prednisone equivalents) or other immunosuppressive medications within 4 weeks

Status:

- Recruiting for safety run-in has been finished
- Recruitment start for stage 2 is expected in early 2017