

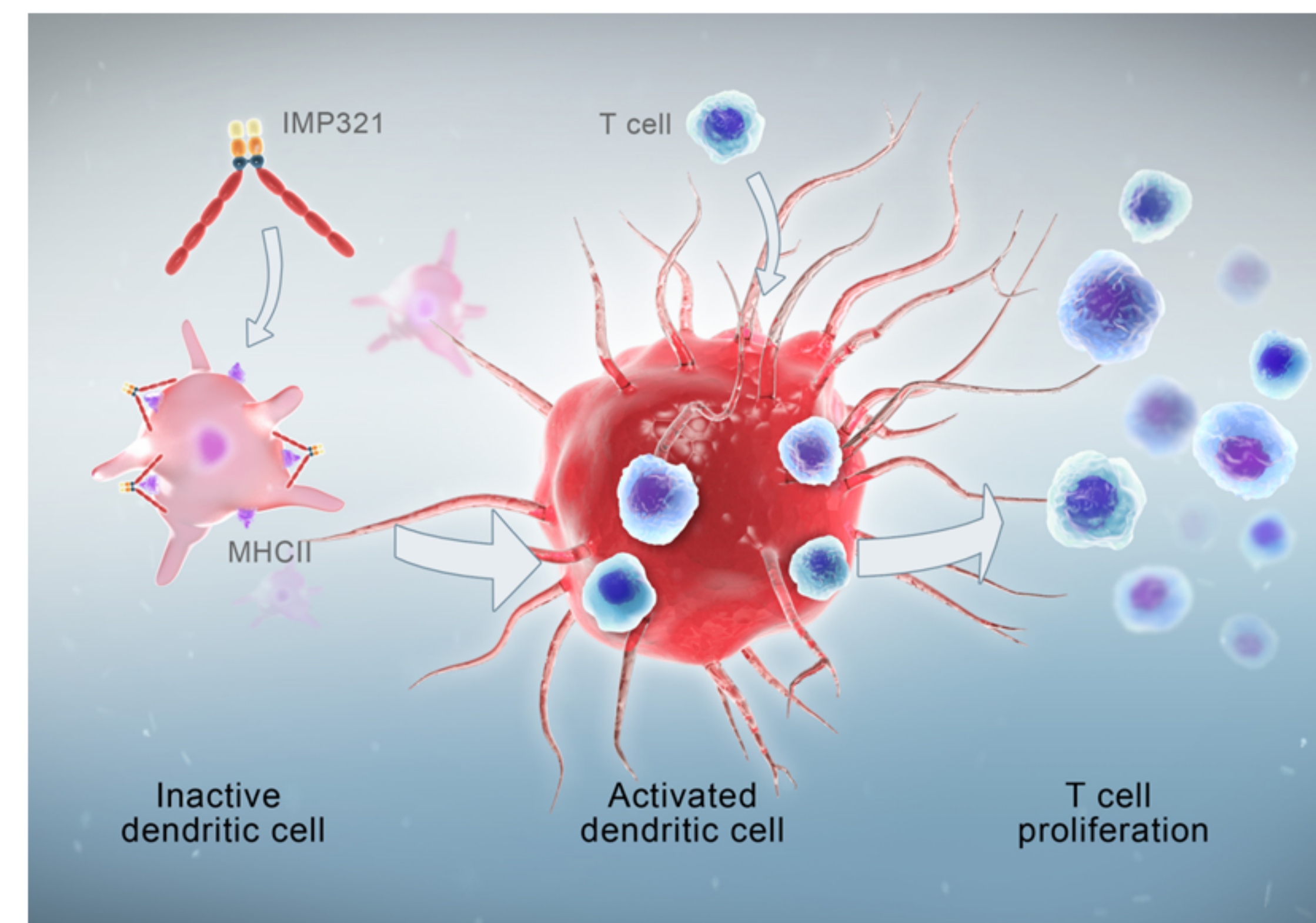


TACTI-mel (Two ACTIVE Immunotherapeutics in melanoma): A Phase 1 trial in patients with unresectable or metastatic melanoma receiving IMP321 (LAG-3Ig fusion protein) as an adjunctive therapy to anti-PD-1 therapy with pembrolizumab

¹Prima BioMed, Leipzig, Germany

² ImmuteP, 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-P012 (sponsor code) and NCT02676869 (ClinicalTrials.gov).
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Study rationale

Pembrolizumab resulted in an ORR of 26-38 %. Three types of patients (based on IFN- γ signature) have been identified:

- A- Inflamed responders – respond to anti-PD-1
- B- Inflamed non-responders (some infiltrates in the tumor margins but no response)
- C- Non inflamed. “Cold tumor” with no response

Optimal checkpoint inhibitor combos will target groups B and C and help them to:

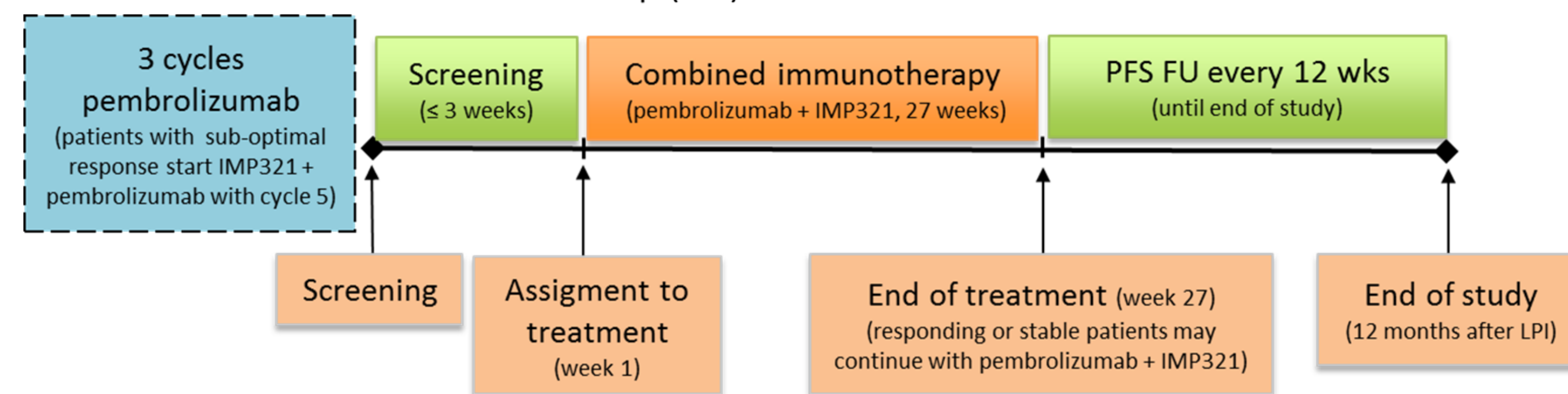
- Promote cross presentation of tumor antigens
- Induce T cell recruitment into tumor microenvironment

IMP321 has been shown to elicit sustained monocyte and CD8 T cell increase and activation

Trial design

Phase I, multi-centre (6 sites in Australia), open-label, dose escalation

- Up to 24 patients with asymptomatic irPD or suboptimal response (irSD, irPR) to pembrolizumab after 3 cycles will be enrolled
- Combination with IMP321 starts in parallel to cycle 5 of pembrolizumab
- Subcutaneous IMP321 injections will be administered every 2 weeks at dose levels of 1 mg (cohort 1), 6 mg (cohort 2), 30 mg (cohort 3) for a total of 13 injections
- Thereafter patients are observed for PFS follow-up (FU)



Objectives

Primary Objective:

- To evaluate the safety, tolerability and recommended phase 2 dose of IMP321 when combined with anti-PD-1 treatment in patients with unresectable or metastatic melanoma

Secondary Objectives:

- To assess the pharmacokinetics and pharmacodynamics of different doses of IMP321 when combined with anti-PD-1 treatment in patients with unresectable or metastatic melanoma
- To assess response to treatment by immune related response criteria (irRC) and response evaluation criteria in solid tumours (RECIST) version 1.1
- To assess the objective response rate (ORR)
- To assess time to and duration of response
- To assess the time to next treatment (TTNT)
- To assess progression free survival (PFS)

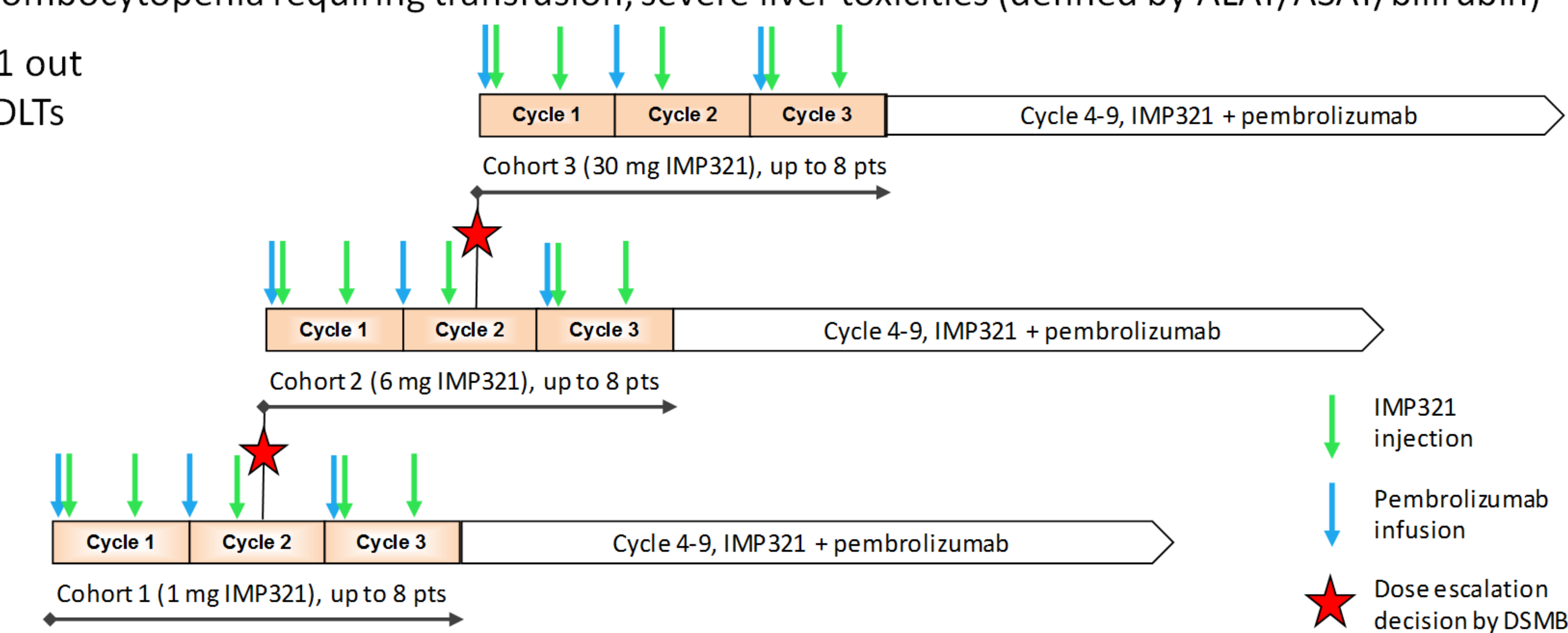
Dose escalation

Dose levels of 1, 6 mg and 30 mg IMP321 have been selected based on previous trials with IMP321 in renal cell cancer¹ and metastatic breast cancer² implementing a safety step at 1 mg IMP321.

DLTs are defined as follows:

- > 50fold increase of ≥ 2 cytokines
- $\geq$ grade 3 immune related abnormalities, $\geq$ grade 4 ARs or any aetiology
- Febrile neutropenia, thrombocytopenia requiring transfusion, severe liver toxicities (defined by ALAT/ASAT/bilirubin)

Dose is considered safe if ≤ 1 out of 8 patients (pts) develop DLTs



Main inclusion criteria

- Locally advanced (unresectable Stage III) or metastatic (Stage IV) melanoma
- Received 3 cycles of pembrolizumab and achieved asymptomatic irPD or sub-optimal response (irSD, irPR)
- Female or male 18 years of age or above
- ECOG performance status 0-1
- Resolution of toxicity associated with prior or current therapy to grade < 2
- Evidence of measurable disease as defined RECIST version 1.1
- Adequate laboratory criteria e.g. total white blood cell count $\geq 3 \times 10^9/L$; platelet count $\geq 100 \times 10^9/L$; ANC $\geq 1.5 \times 10^9/L$; serum creatinine $\leq 1.5 \times$ ULN; haemoglobin > 9g/dL or 5.58 mmol/L

Main exclusion criteria

- ≥ 4 prior lines of therapies
- Prior PD-1/PDL-1 targeted therapy
- Receiving any investigational drug, chemotherapy, targeted small molecule therapy, radiotherapy, or biological cancer therapy (other than pembrolizumab) ≤ 4 weeks
- History of irAEs from ipilimumab of CTCAE Grade 4 requiring steroid treatment
- Known cerebral or leptomeningeal metastases
- Serious intercurrent, active acute or chronic infection
- Active auto-immune disease requiring immunosuppressive therapy
- HIV positivity, active hepatitis B or hepatitis C
- Any condition requiring continuous systemic treatment with either corticosteroids (>10 mg daily prednisone equivalents) or other immunosuppressive medications ≤ 4 weeks

Status

- Recruiting for cohort 1 is ongoing
- Recruitment is expected to be finished in 2017