immutep

LAG-3 IMMUNOTHERAPY

New Data from Ongoing Melanoma Study and Clinical Development Strategy Update

Webcast - 29th / 30th May 2018

(ASX: IMM, NASDAQ: IMMP)

Notice: Forward Looking Statements

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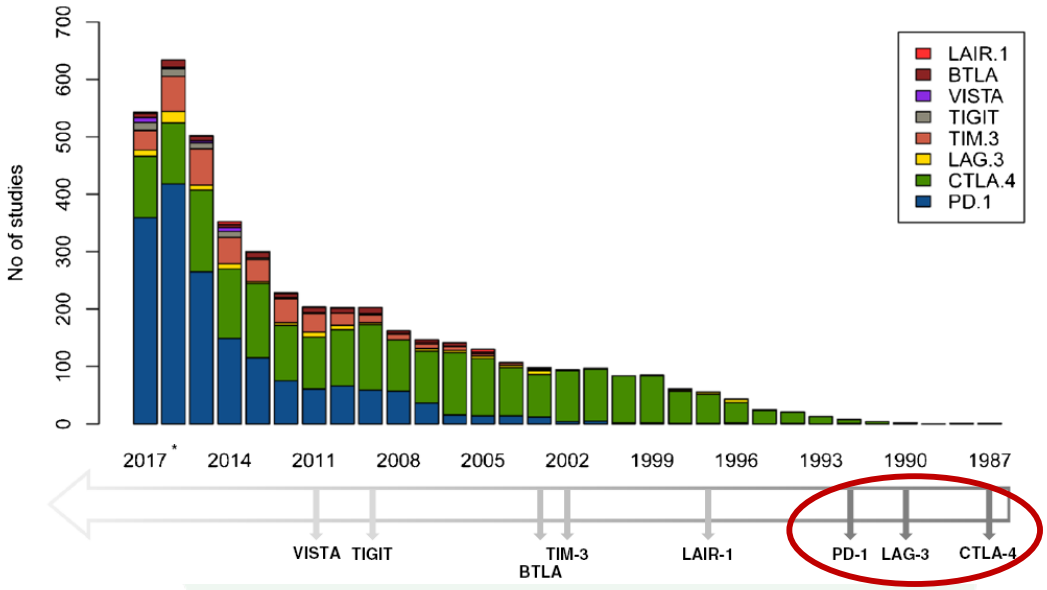
LAG-3 Overview

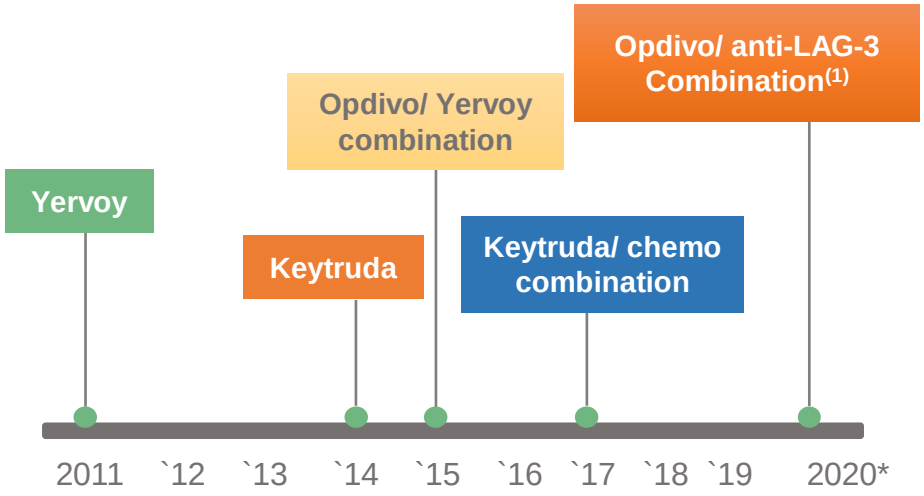
Evolution of Checkpoint Therapies

LAG-3 has the potential to be the next meaningful checkpoint target…

Timeline of Immune Checkpoint Discovery



Evolution of Immuno-Oncology Therapies

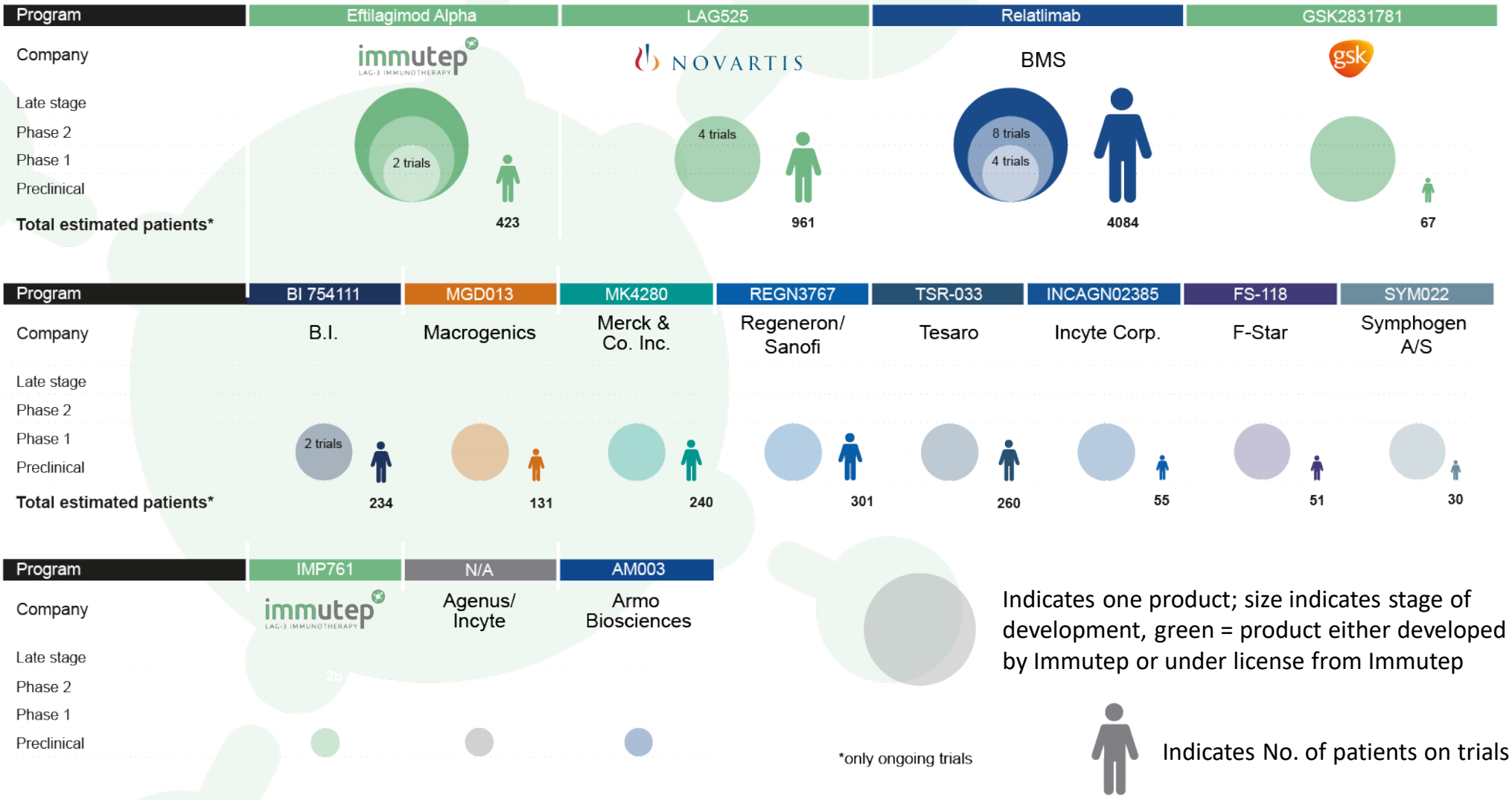


- Existing immuno-oncology therapies are CTLA-4, PD-1 and PD-L1 antagonists and are approved for many disease indications
- However, only 15 - 40% of solid tumors in patients respond to monotherapy
- Immuno-oncology market will be worth approximately US$14 billion in 2019, rising to US$34 billion by 2024, with checkpoint therapies accounting for most of the market(2)

Notes:
(1) Expected timing, actual results may differ (BMS ASCO 2017 Investor Presentation)
(2) Global Data, Immuno-Oncology Strategic Insight: Multi-Indication and Market Size Analysis (May 2016)

LAG-3 Therapeutic Landscape Overview

Immutep is the leader in developing LAG-3 modulating therapeutics

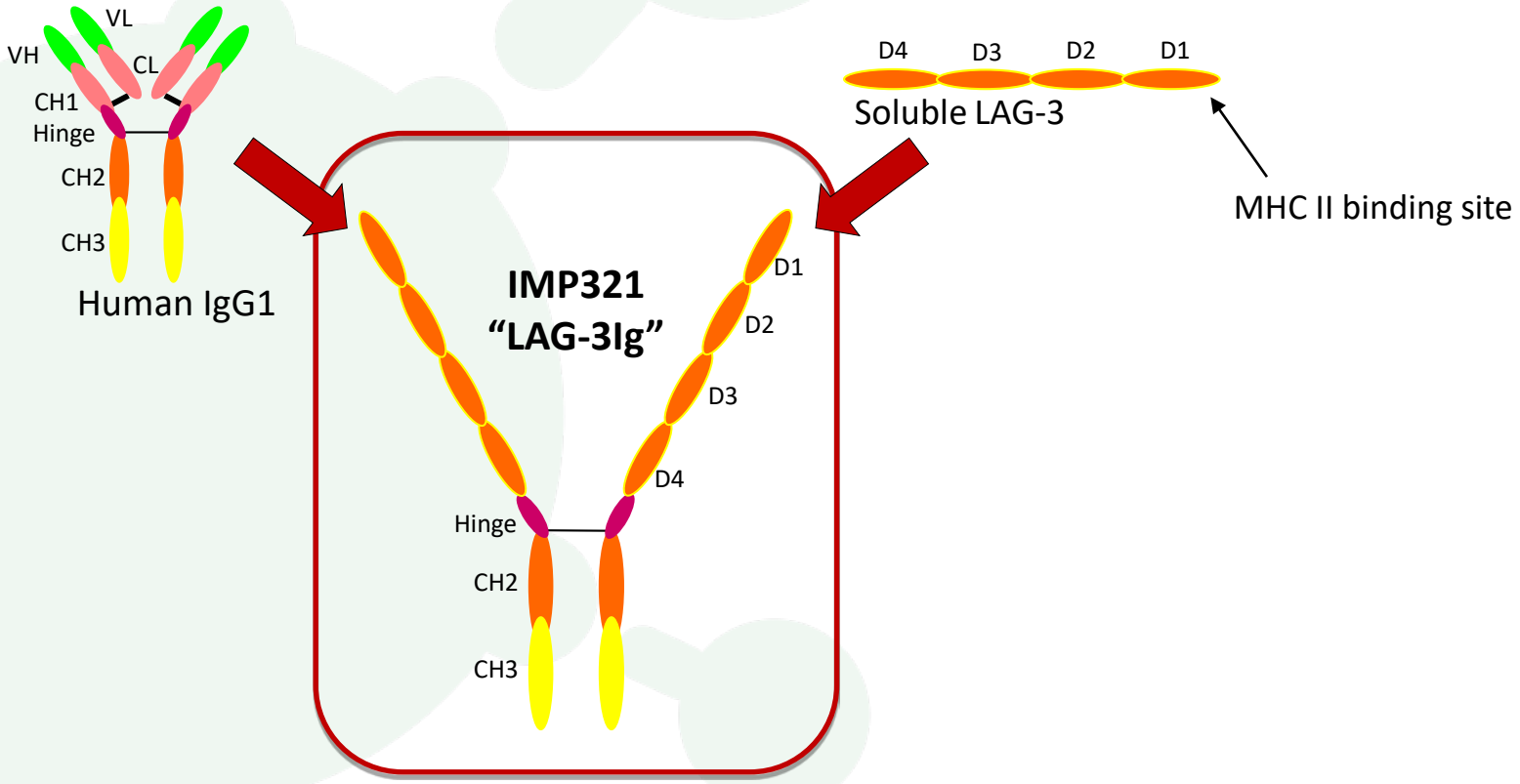


Sources: GlobalData, company websites, clinical trials.gov, and sec.gov
Information as of April 23, 2018, includes also trials which are only listed as planned, includes also trials where the company may not be the sponsor

eftilagimod alpha (efti, IMP321)

Eftilagimod alpha (IMP321)

Efti is a soluble recombinant fusion protein consisting of the Fc portion of a human antibody and the four extracellular domains of LAG-3

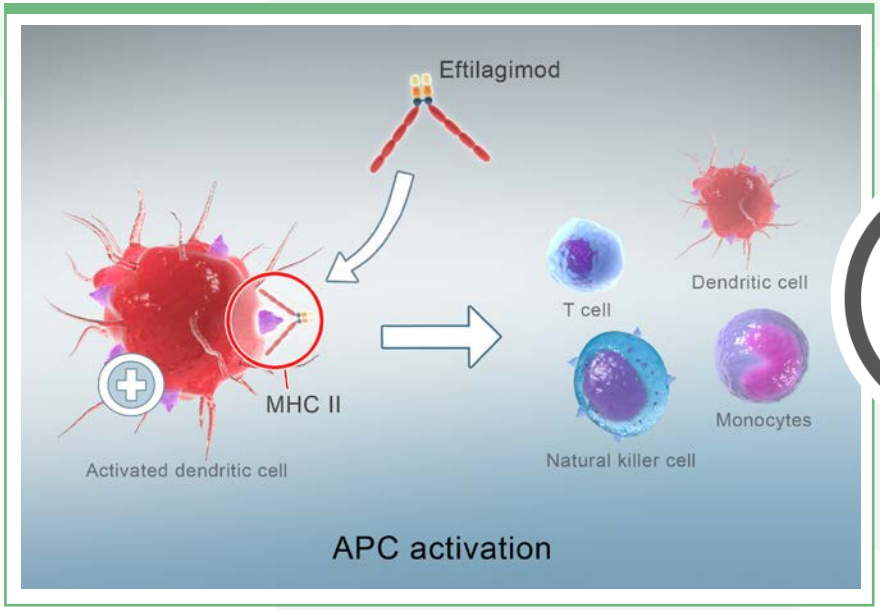


- Dimeric, very stable, high affinity for DC
- Antigen presenting cell (APC) activator
- Unique mechanism of action and potentially first-in-class

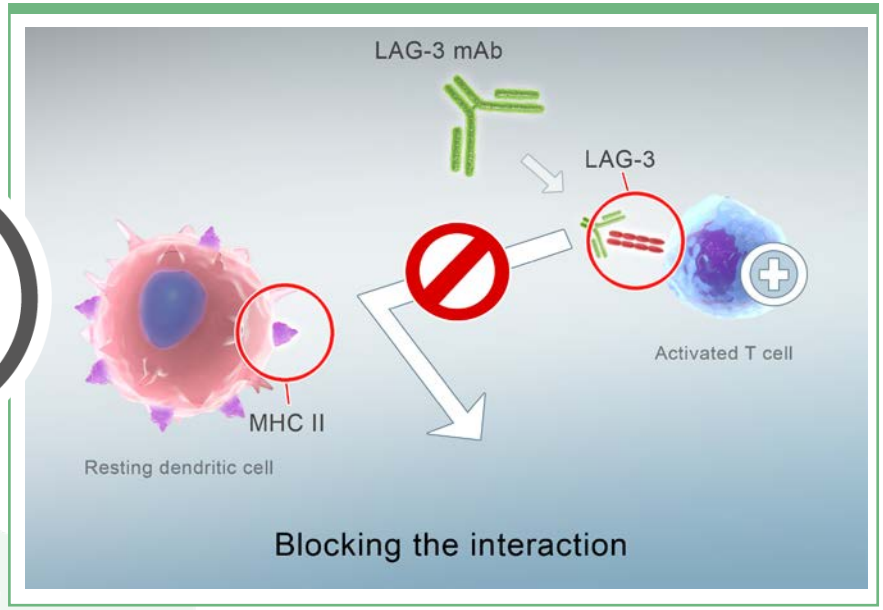
Efti - Innovative LAG-3 IO Product Candidate

- The only APC targeting LAG-3 product currently in clinical development
- A unique approach (“turning cold tumors into hot tumors” with LAG-3)
- Synergistic with other IO agents

“PUSHING THE ACCELERATOR ON IMMUNE RESPONSES”



“RELEASING THE BRAKE ON THE T CELL”



Efti, an MHC II **agonist** (eftilagimod alpha, IMP321) :

<u>APC activator</u>

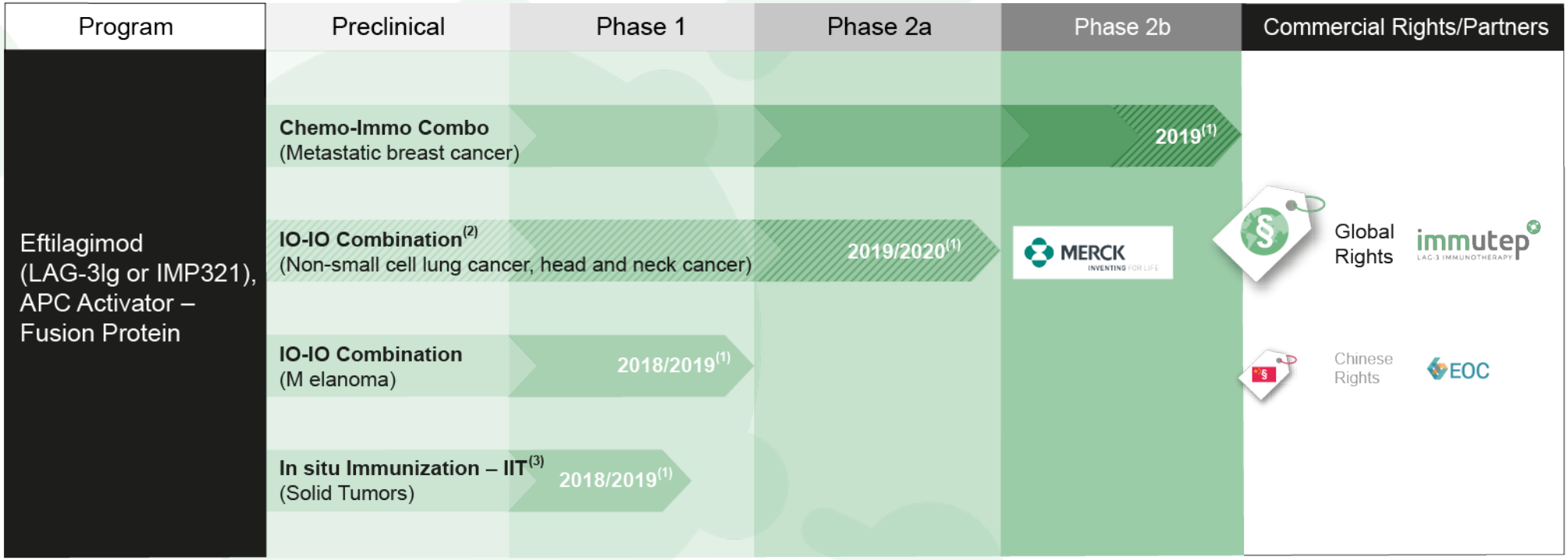
- Boost and sustain the $CD8^+$ T cell responses
- Activate multiple immune cell subsets

LAG-3 antagonist antibodies:

<u>immune checkpoint inhibitor</u>

- increase cytotoxicity of the pre-existing CD8 T cell response

Efti - Clinical Development / Description



Notes

(1) Expected timing of data readouts and actual results and timing may differ

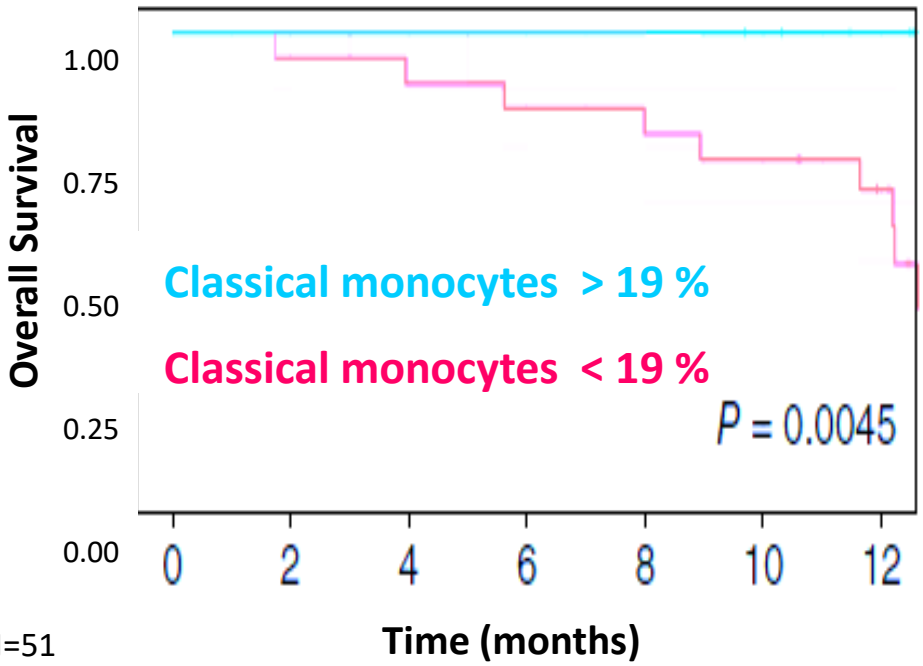
(2) In combination with KEYTRUDA® (pembrolizumab); clinical trial is currently planned and not yet active

(3) INSIGHT Investigator Initiated Trial (IST) is controlled by lead investigator; Immutep is not the sponsor, but supplies IMP321

Efti (IMP321)
TACTI-mel Results
(as of 9th May 2018)

New Rationale for Combining efti (IMP321) with PD-1 Antagonists (pembrolizumab)

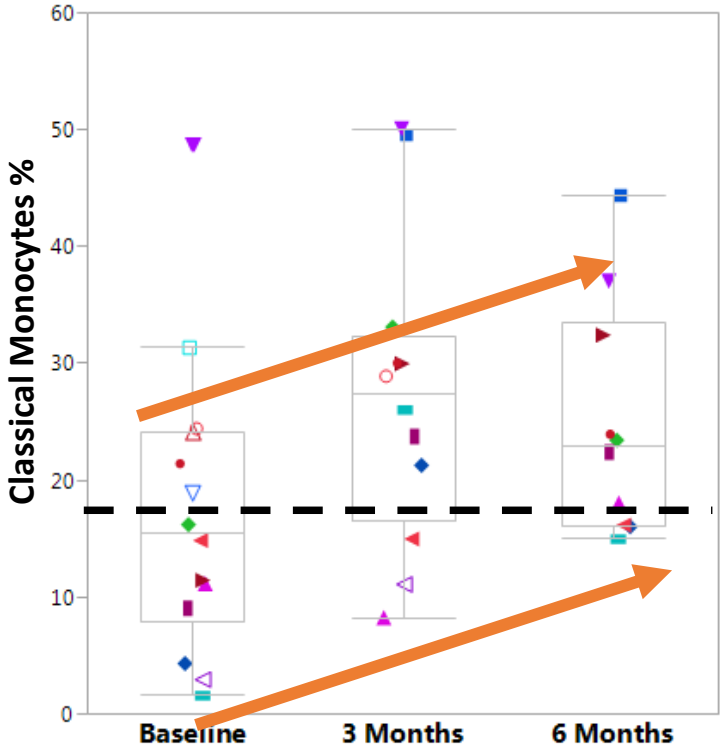
Problem: Low monocyte numbers at baseline leads to poor efficacy of anti-PD-1 therapy



N=51

Source: Krieg et al., Nat. Med. 24, 2018.

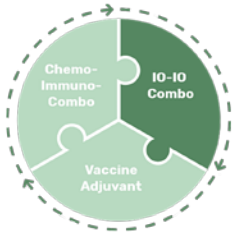
Solution: efti (IMP321) increases monocyte numbers in cancer patients



N=15

Source: AIPAC stage 1

Monocytes are important for response and survival to pembrolizumab → efti (IMP321) increases monocytes sustainably above threshold of 19 % → response to pembrolizumab more likely



Efti (IMP321) in Melanoma

TACTI-mel (IO combination) – Trial Design

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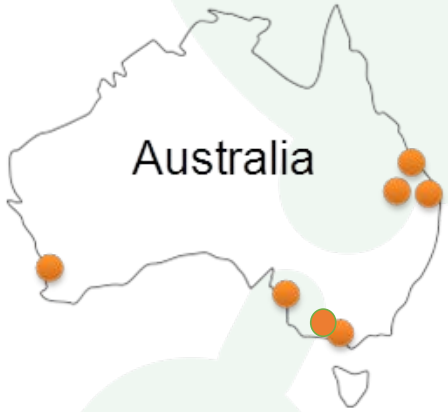
TACTI-mel = Two ACTive Immunotherapeutics in melanoma

24 patients, 4 cohorts of 6 patients → Efti (IMP321) + anti-PD-1 (Keytruda®) → Phase I, multicenter, open label, dose escalation → Recommended Phase II dose, safety and tolerability

Primary Objective	Recommended dose for Phase II with efti (IMP321) + pembrolizumab Safety + tolerability
Other Objectives	PK and PD of IMP321, response rate, time to next treatment, PFS



7 sites in Australia

- Part A: efti (IMP321) at 1, 6 and 30 mg s.c. every 2 weeks starting with cycle 5 of pembrolizumab

→ Status: recruitment completed; interim results on next slides

- Part B: efti (IMP321) at 30 mg s.c. every 2 weeks starting with cycle 1 of pembrolizumab

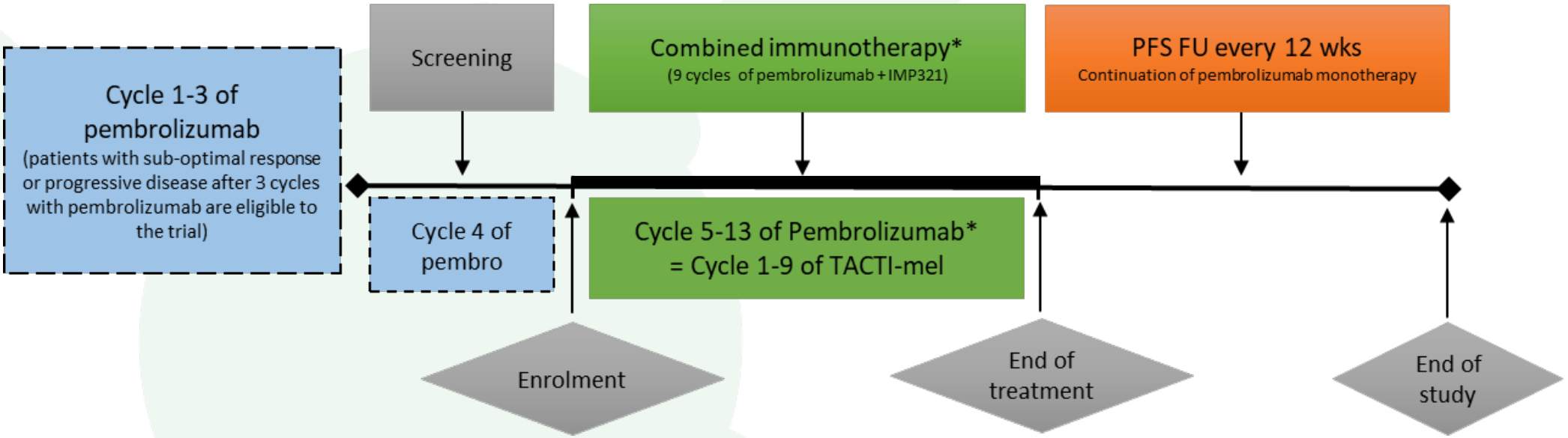
→ Status: 3 pts enrolled w/o DLTs

- Pembrolizumab (Keytruda®) 2 mg/kg every 3 weeks i.v. part A and B

preliminary data, status 9th May 2018

Efti (IMP321) in Melanoma
TACTI-mel (IO combination) – Details Part A

Study Scheme Part A:



*Tumor assessment acc to irRC

irRC…Immune-Related Response Criteria, PFS- progression free survival, FU – follow-up

Patient population Part A:

- Patients with unresectable or metastatic melanoma with **asymptomatic progression or suboptimal response** after 3 cycles of pembrolizumab

preliminary data, status 9th May 2018

Efti (IMP321) in Melanoma

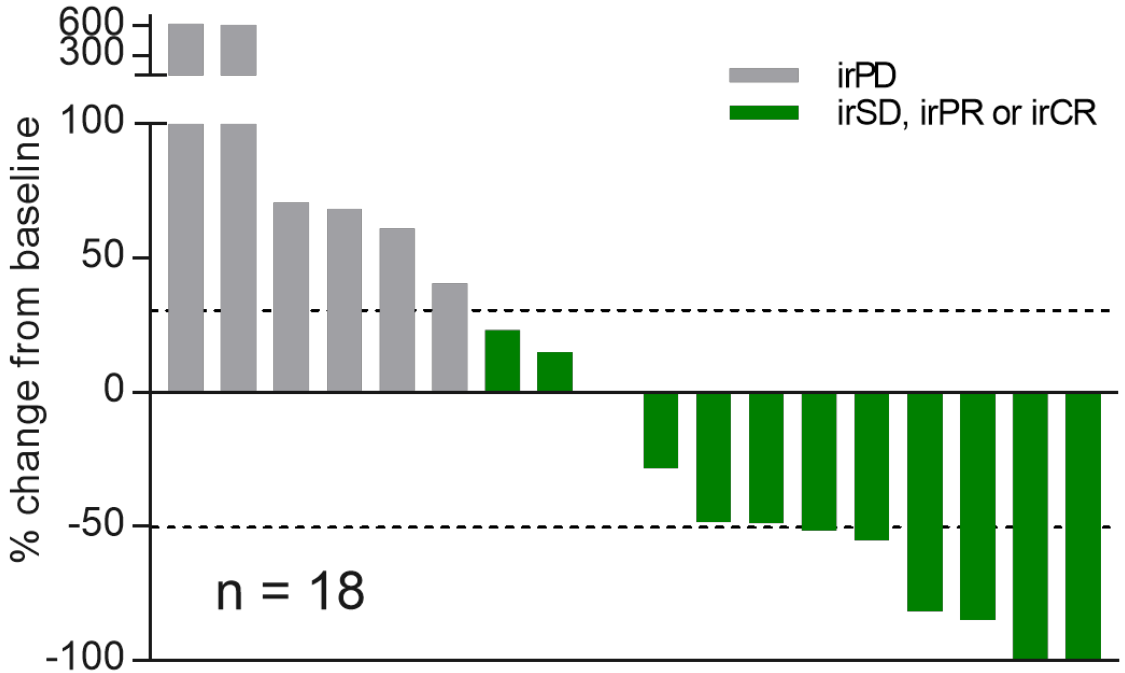
TACTI-mel (IO combination) – Results after Start of Combo (1)

Baseline Characteristics	N = 18 (%)
Elevated LDH	7 (39%)
Metastasis stage M1c	15 (83 %)
Pre-treated with BRAF/MEK/ipilimumab	4 (22 %)
irPD/irSD to pembro after 3 cycles	12 (67 %)

Best Overall Response acc. to irRC	N = 18 (%)
irCR	1 (6 %)
irPR#	5 (28 %)#
irSD	6 (33 %)
irPD	6 (33 %)
Best overall response rate (ORR)	**6 (33 %)**
Patients with tumor shrinkage	**9 (50 %)**
Disease control rate	**12 (66 %)**

- incl. 1 pt with complete disappearance of all target lesions; CR acc. to RECIST 1.1

Waterfall Plot* (starting after 4 cycles of pembrolizumab)



* - acc to irRC

- Patients very late stage of disease (M1c, elevated LDH)
- Majority not responding to pembrolizumab

→ Tumor shrinkage in 50 % of these patients incl. 2 pts with complete disappearance of all target lesions

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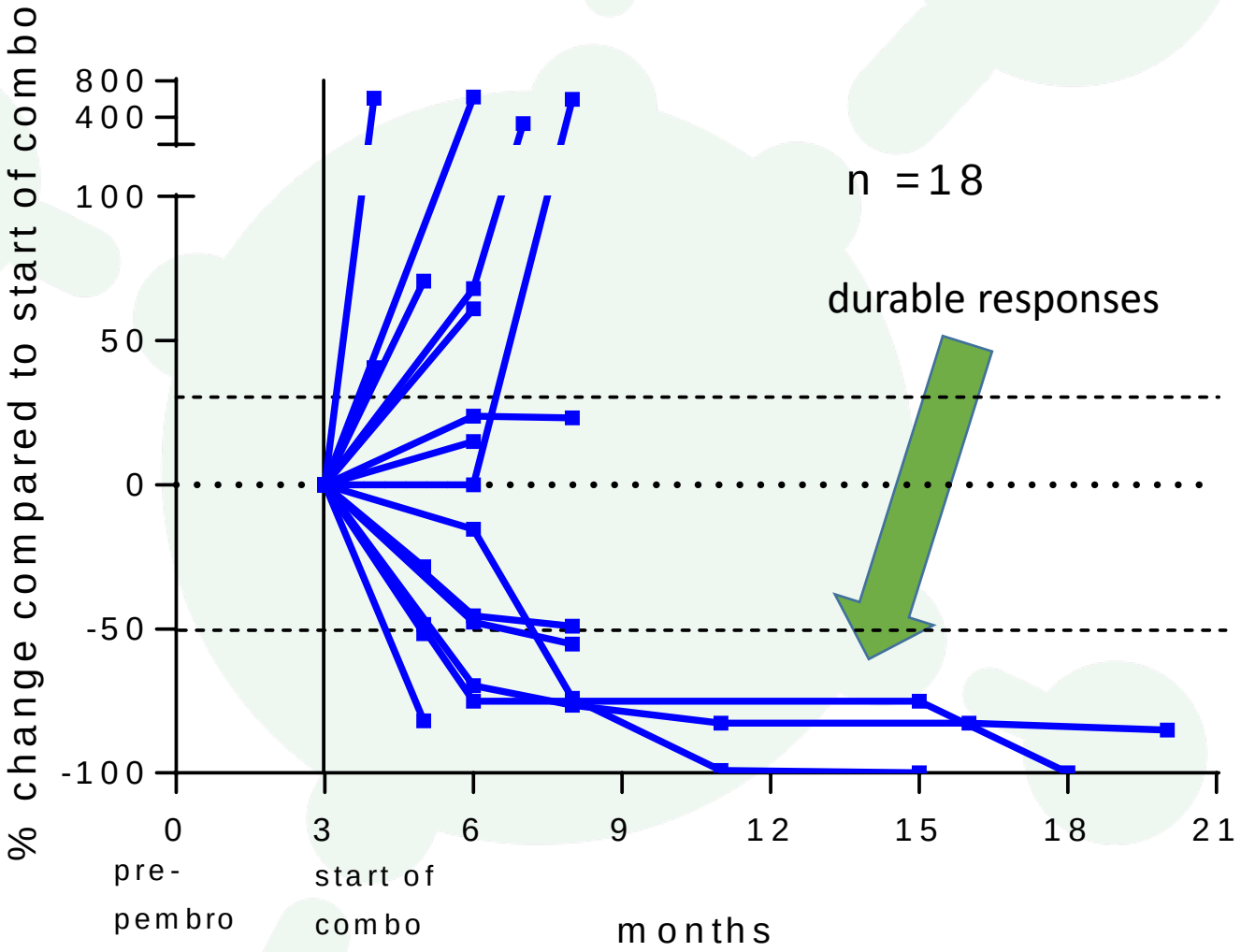
Efti (IMP321) in Melanoma

TACTI-mel (IO combination) – Results after Start of Combo (2)

Spiderplot* Cohort 1-3 – May 2018



* - acc to irRC

Conclusion

- Complete responses of target lesions occurred after 11 and 18 months --> **combination takes time to act**
- 3 (out of 12 = 25 %) durable responses in first 2 dose levels → treatment and FU ongoing
- **Treatment and follow-up of 3 patients in 3rd cohort (30 mg) ongoing**

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Efti (IMP321) in Melanoma

TACTI-mel (IO combination) – Single Case at 1 mg efti

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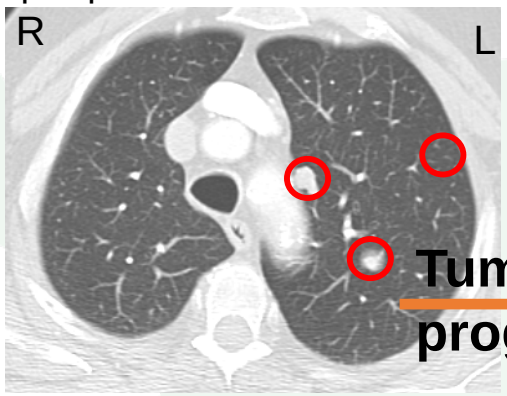
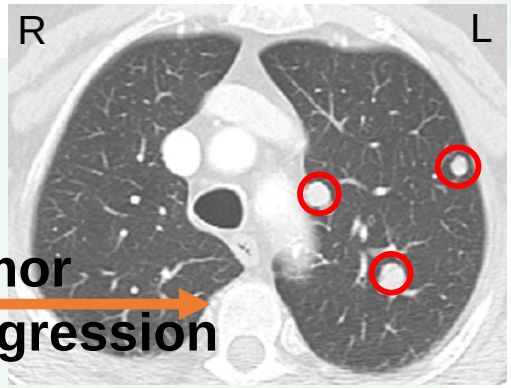
Efficacy: Metastatic Melanoma

pre-pembro

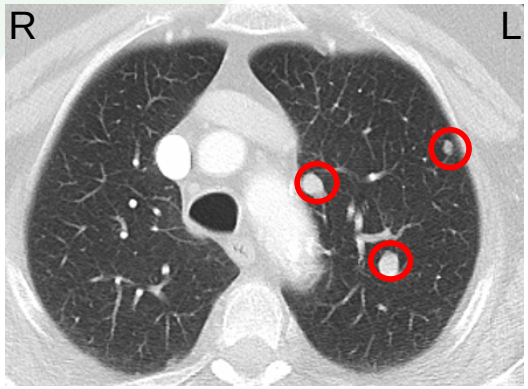


week 9 (pembro)

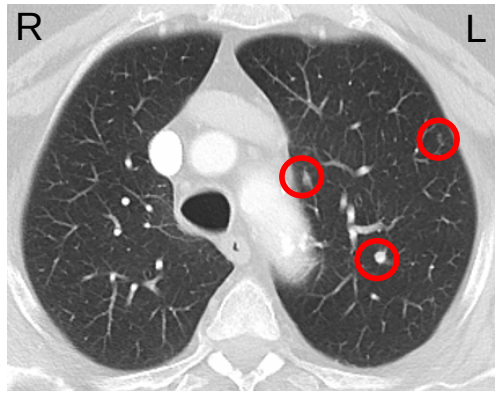


Tumor progression

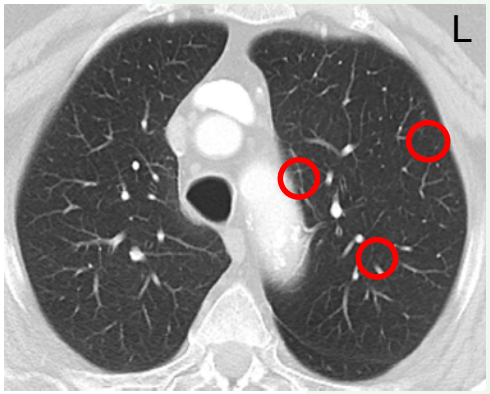
week 25 (combo)



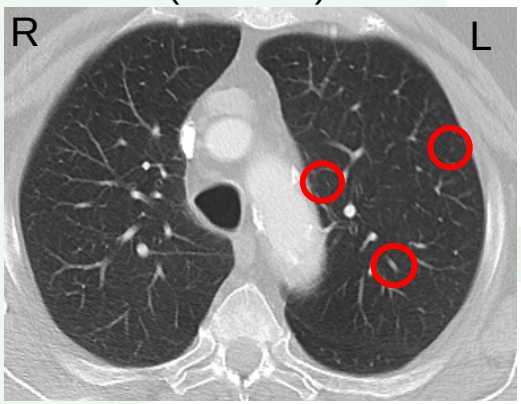
week 37 (combo)

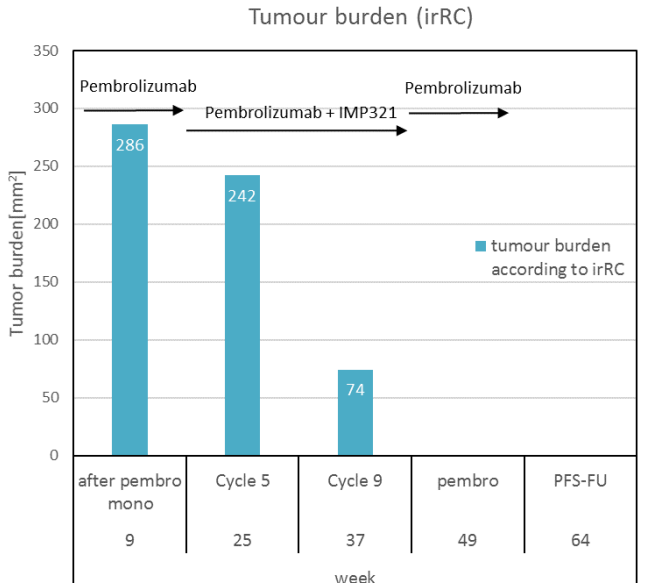


week 49 (Pembro mono)



week 64 (PFS-FU)





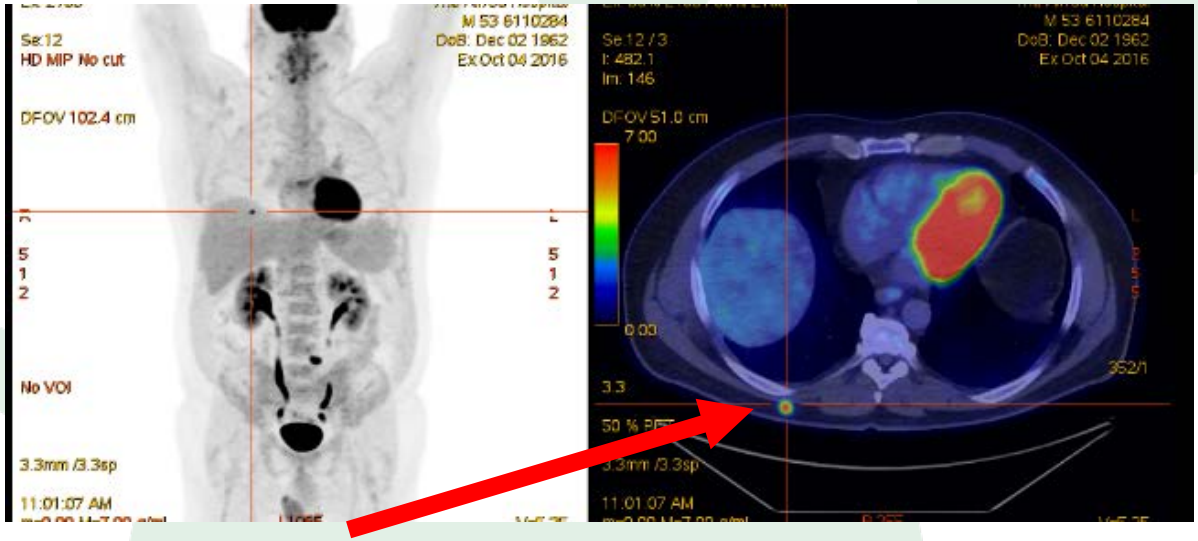
All lesions disappeared → CR (confirmed)
patient without treatment and disease free

preliminary data, status 9th May 2018

Efti (IMP321) in Melanoma

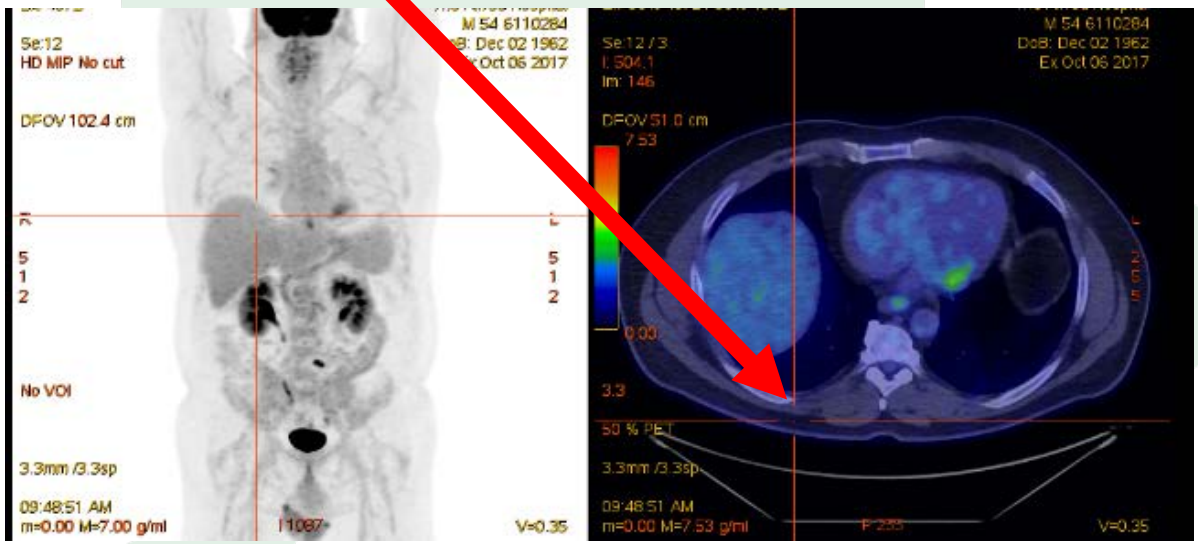
TACTI-mel (IO combination) – Single Case at 6 mg efti

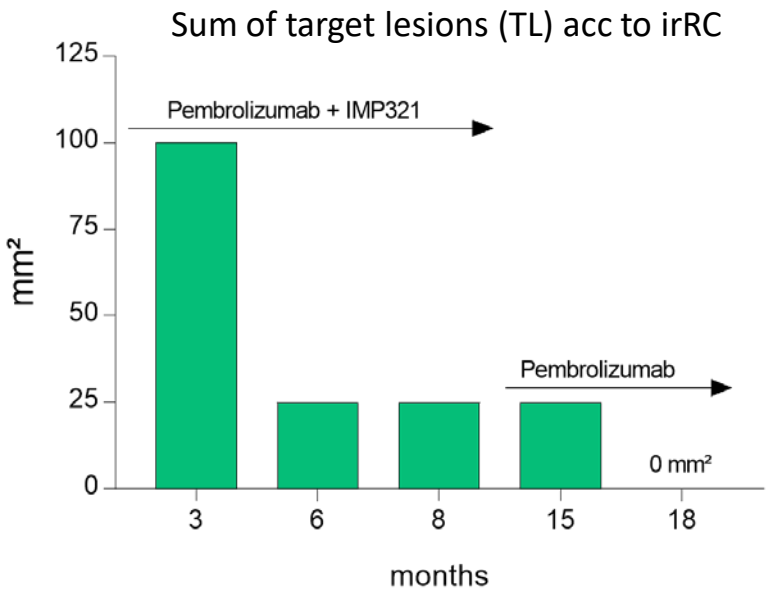
Pre pembro



Target lesion: chest wall; Non-target lesion: Left common iliac LN

9 months after start of combo

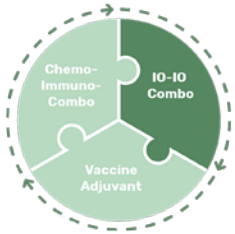




Σ TL (irRC)	100 mm²	25 mm²	25 mm²	25 mm²	0 mm²
In %	0 %	-75 %	-75 %	-75 %	-100 %
Response	NA	irPR	irPR	irPR	irPR

- **Complete disappearance of target lesions → CR acc. to RECIST 1.1**
- **Patient still on pembrolizumab**

preliminary data, status 9th May 2018



Efti (IMP321) in Melanoma

Response Analysis Starting Cycle 1 Day 1 Pembrolizumab

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Trial Design TACTI-mel: Combination treatment of efti and pembrolizumab starts at cycle 5 in patients not responding well or progressing on pembrolizumab → difficult to compare to any historical control

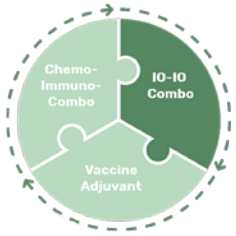
How does the efficacy looks from the start of pembrolizumab?
→ Performed analysis of read-outs starting from cycle 1 day 1 of pembrolizumab, including the 4 cycles pembrolizumab monotherapy ("C1/D1 Analysis")

- Overall response rate is 61% and 66% of patients are progression free 6 months after start of pembrolizumab (1)
- 7/12 (58 %) patients with progression (irPD) or stable disease (irSD) have a benefit by adding IMP321(1)

Best Overall Response acc. to irRC (C1/D1 analysis)(1)	N = 18 (%)
irCR	1 (6%)(1)
irPR#	10 (56%)(1),(2)
irSD	5 (28%)(1)
irPD	2 (11%)(1)
Best overall response rate (ORR)	**11 (61%)(1)**
Progression free at 6 months	**12 (66%)(1)**

Notes
(1) Response rates determined by C1/D1 Analysis
(2) Includes 1 patient with complete disappearance of all target lesions, CR acc to RECIST1.1

preliminary data, status 9th May 2018



Efti (IMP321) in Melanoma

Comparison to historical controls

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How does the data fit in the treatment landscape and in comparison to pembro monotherapy?

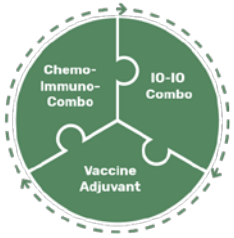
TACTI-Mel enrolled ipilimumab (ipi) naive and ipi pre-treated patients → Keynote-002 (pre-treated) and Keynote-006 (naive) used for comparison

Baseline Characteristics	Tacti-Mel (C1/D1 response analysis) Pembro 2 mg/kg N=18 in %	KN-006 (ipi naive) Pembro 10 mg/kg n=277 In %	KN-002 (ipi pre-treated) Pembro 2 mg/kg n=180 In %
Metastasis stage M1c	83%	68%	82%
ECOG 1 / 0	22% / 78%	32% / 68%	45% / 55%
irCR	6%(1)	6%(2)	2%(2)
ORR	**61%(1)**	**33%**(2)	**21%**(2)
Progression free at 6 months	**66%(1)**	**46%**(2)	**34%**(2)

61 % response rate(1, 2) and **66 % progression free at 6 months** (1, 2) with the PD-1 antagonist **pembrolizumab** and APC activator **eftilagimod alpha** in very late stage **melanoma**

preliminary data, status 9th May 2018

Notes
(1) Response rates determined by C1/D1 Analysis
(2) TACTImel used irRC and KN-002 and KN-006 RECIStT1.1



Efti (IMP321) – Clinical Overview

Exposure and Safety

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Exposure[2] in cancer patients

- 87 cancer patients in different indications and combinations (see table)
- Subcutaneous injection every two weeks
- 52 (~60%) received 6-30 mg efti (IMP321)

Combination partner / indication	Cancer patients N = 87[2]
Efti (IMP321) alone / renal cell cancer	21
with paclitaxel / met. Breast cancer	48
with pembrolizumab / met. melanoma	18

Safety profile in cancer patients

- No efti (IMP321) related deaths
- In total 24 SAEs (29%) thereof 4 (5%) (possibly) related to efti[1]
- No MTD in any combination
- Most common adverse events: local erythema and any type of injection site reaction up to NCI-CTC grade 2

✓ Efti (IMP321) has very favorable safety profile up to 30 mg given s.c. every 2 weeks

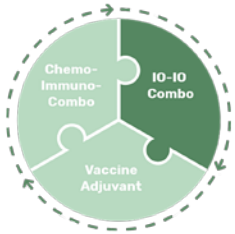
✓ Combination with chemotherapy or PD-1 antagonists is feasible without reaching MTD

Notes *preliminary data, status 9th May 2018*

(1) None of them related to combination of IMP321 + pembrolizumab, all in trials in combination with paclitaxel

(2) Ongoing trials like randomized part of AIPAC (226 patients), IITs (n=38) or new trials (N=120) not included here

Efti (IMP321)
TACTI-002 - Design



Efti (IMP321) – Clinical Development

Collaboration and Supply Agreement

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MERCK
INVENTING FOR LIFE

- In **March 2018** Immutep entered into a clinical trial collaboration and supply agreement with Merck & Co., Inc., Kenilworth, NJ, USA (known as MSD outside the United States and Canada) to evaluate the combination of **efti (IMP321**) with MSD's anti-PD-1 therapy **KEYTRUDA® (pembrolizumab)** in a **new Phase II clinical trial**

Efti (IMP321) – Clinical Development

TACTI-002 Trial Design

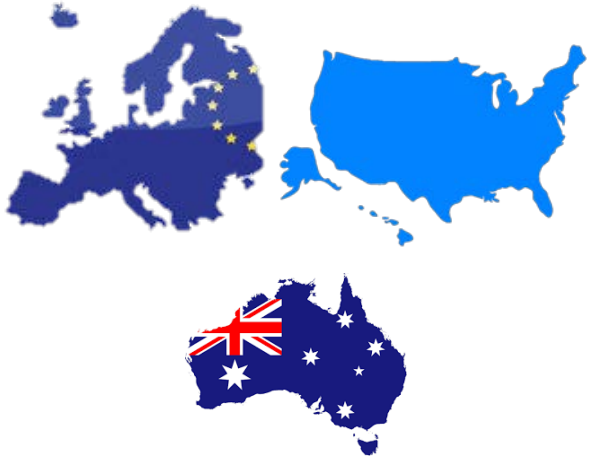
TACTI-002; a basket trial: Two ACTive Immunotherapeutics in different indications

Simons 2 stage; 3 indications; up to 120 pts → Efti (IMP321) + Pembrolizumab (Keytruda®) for 12 months + max. of 12 months pembrolizumab monotherapy → Phase II, multi-national (EU + US + AUS), open label → Response rate; PFS, OS, PK, Biomarker; Safety and tolerability

Primary Objective	Response rate (iRECIST)
Other Objectives	Safety, PFS+OS, PK, exploratory biomarker analysis
Patient Population	Part A: 1st line NSCLC PD-X naive Part B: 2nd line NSCLC, PD-X refractory Part C: 2nd line HNSCC, PD-X naive
Treatment	30 mg Efti (IMP321) s.c. 200 mg Pembrolizumab i.v.

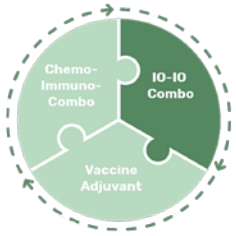
Status Report

- Protocol Development + IND preparation ongoing
- Study start expected Q.4 ‘18
- First DMC meeting planned mid ’19
- First data expected mid ‘19



12-15 sites in Europe / US / Australia

Notes
NSCLC – non-small-cell lung cancer, HNSCC – head and neck squamous cell cancer, DMC – data monitoring comittee, PFS – progression free survival, OS – overall survival, PK – pharmacokinetics, PD-X – any PD-1 or PDL-1 treatment



Efti (IMP321) Summary

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- ✓ Very favorable safety profile → no DLT/MTD reached with pembrolizumab → combination feasible and safe
- ✓ Able to induce a IFN-γ type response in patients
- ✓ ***Response rate of 61 %*** and ***progressions free survival rate at 6 months of 66 %*** in late stage mostly ***visceral (M1C) melanoma*** if combined with pembrolizumab(1)
- ➢ Will be investigated in combination with pembrolizumab in 3 new indications starting 2018

preliminary data, status 9th May 2018

Notes
(1) Response rates determined by C1/D1 Analysis

Thank you!