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LAG-3 IMMUNOTHERAPY

Eftilagimod Alpha Clinical Development Update and New Data from Ongoing Melanoma Study

Date & Time: Wednesday, April 3, 2019, 7:45am Australian Eastern Standard Time
Tuesday, April 2, 2019, 4:45pm US Eastern Daylight Time

Register: Interested investors can register via a link to the webcast on the Company's website at the following link.
https://fnn.webex.com/fnn/onstage/g.php?MTID=e94df697865171ec3d04084859139fb75

Notice: Forward Looking Statements

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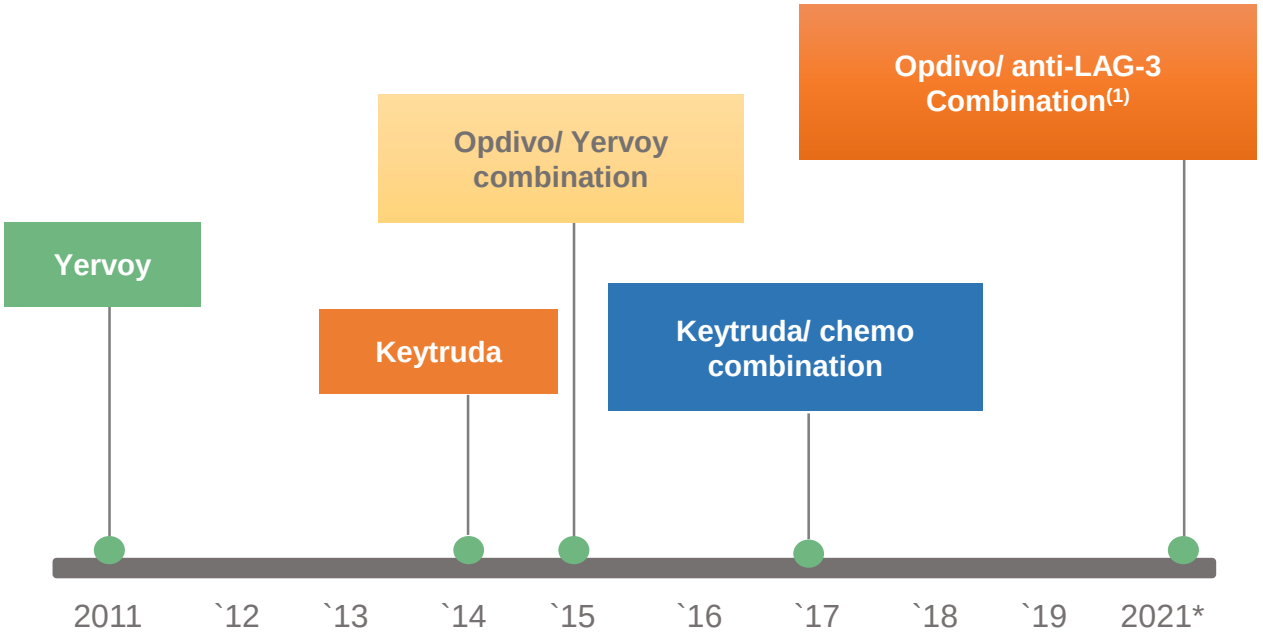
LAG-3 Overview

Evolution of Checkpoint Therapies

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

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

Program	Eftilagimod Alpha (IMP321)	LAG525 (IMP701)	GSK2831781 (IMP731)	Relatlimab
Company	immutep LAG-3 IMMUNOTHERAPY	NOVARTIS	gsk	BMS
Late stage	1 trial	3 trials	1 trial	2 trials
Phase 2	1 trial	2 trials	1 trial	12 trials
Phase 1	3 trials			10 trials
Preclinical				
Total estimated patients*	**424**	**1,017**	**347**	**7,794**

Program	MK4280	BI 754111	TSR-033	MGD013	XmAb-22841	INCAGN02385	FS-118	SYM022
Company	Merck & Co. Inc.	B.I.	Tesaro(1)	Macrogenics	Xencor	Incyte Corp.	F-Star	Symphogen A/S
Pivotal								
Phase 2	1 trial	1 trial	1 trial	1 trial	1 trial	1 trial	1 trial	1 trial
Phase 1	2 trials	3 trials						
Preclinical								
Total estimated patients*	**814**	**529**	**260**	**243**	**230**	**55**	**51**	**30**

Program	IMP761	AM003	TSR-075	IBI-110	LAG-3/ PDL1 Bi.	LAG-3 Bi.
Company	immutep LAG-3 IMMUNOTHERAPY	Armo Biosciences	Tesaro(1)	Innovent Biologics	Avacta Group	TRIGR Therapeutics
Pivotal						
Phase 2						
Phase 1						
Preclinical						

Key

Indicates one product; size indicates stage of development, green = product either developed by Immutep or under license from Immutep

Indicates No. of patients on trials

Notes:

Sources: GlobalData, company websites, clinical trials.gov, and sec.gov

Information as of March 28, 2019, includes planned and completed trials, includes trials where the company may not be the sponsor

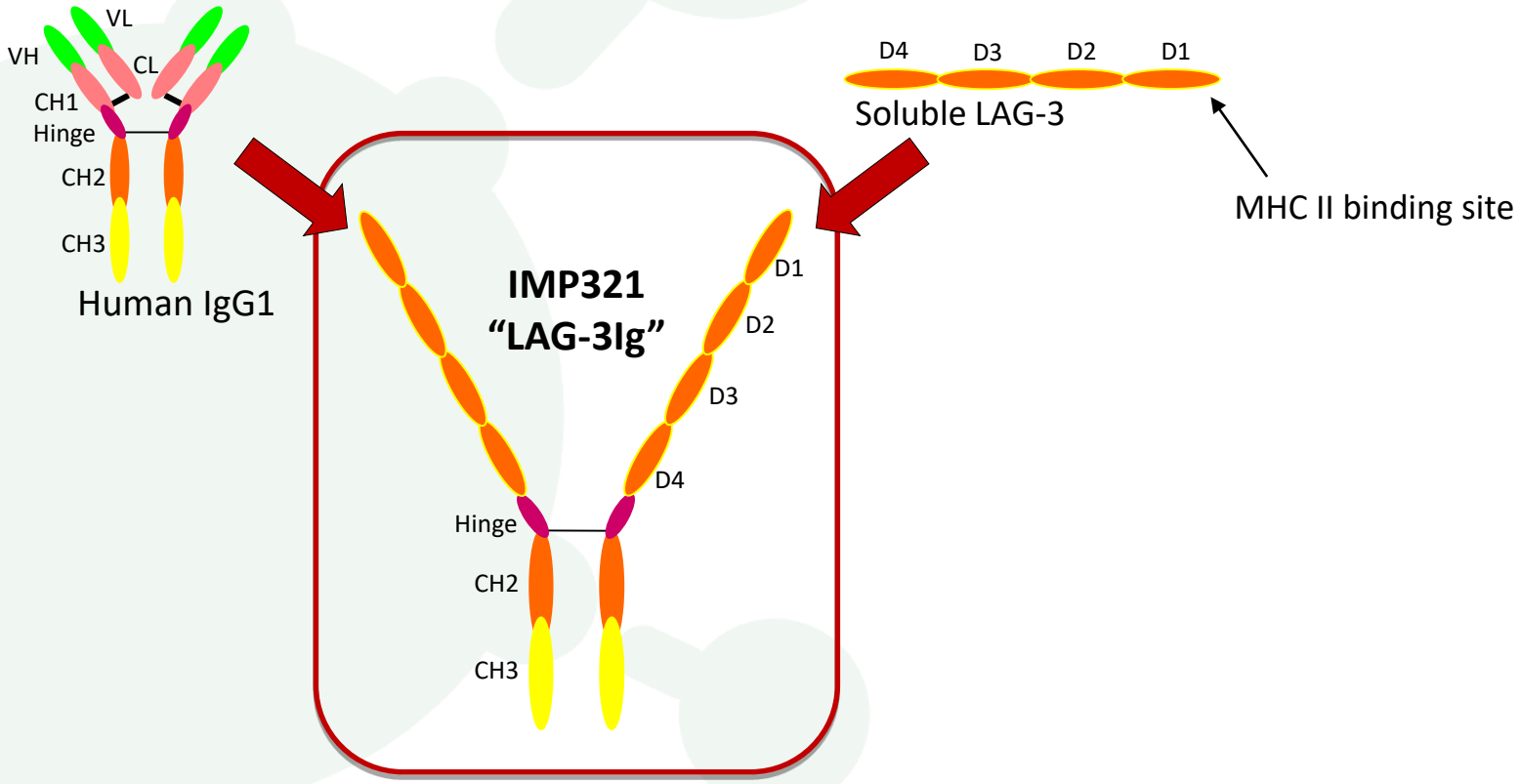
(1) Tesaro was acquired by and is now part of GSK

Eftilagimod Alpha

(Efti, IMP321)

Eftilagimod Alpha

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

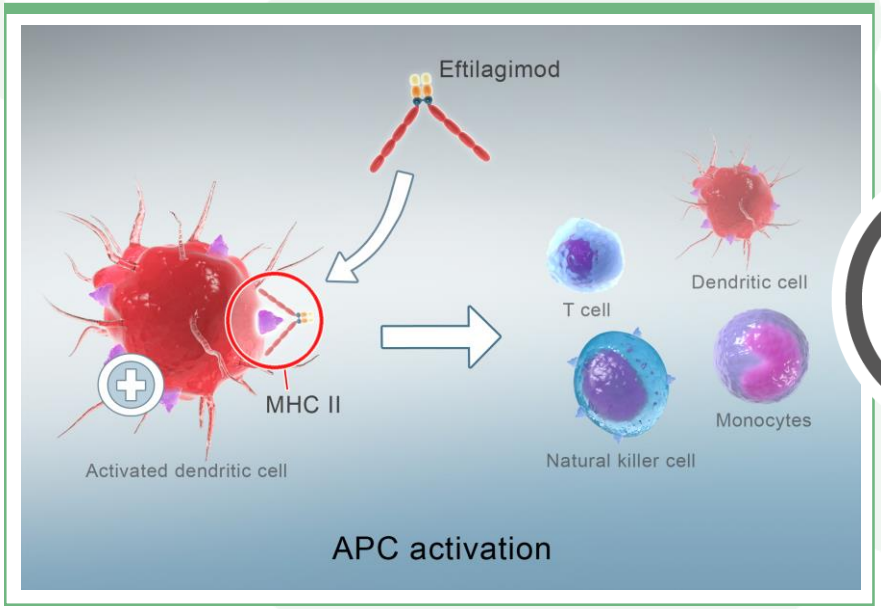


- Dimeric, very stable, high affinity for DC
- Antigen presenting cell (APC) activator
- Unique mechanism of action and potentially first-in-class

Efti - Innovative LAG-3 IO Product Candidate

- Only APC targeting LAG-3 product candidate currently in clinical development
- A unique approach (“turning cold tumors into hot tumors” with LAG-3)
- Synergistic with other therapeutic agents and modalities e.g. IO agents, chemotherapy

“PUSHING THE ACCELERATOR ON IMMUNE RESPONSES”

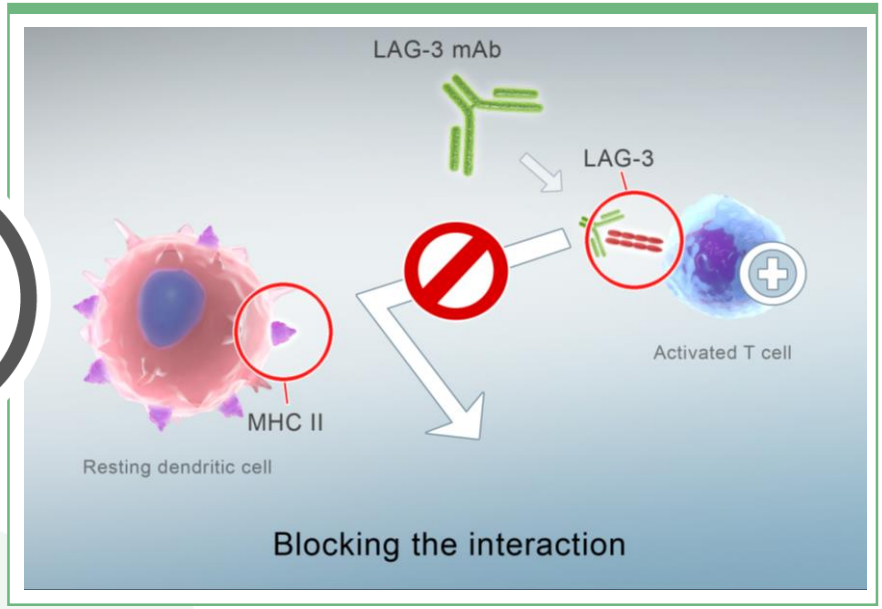


Efti is a MHC II **agonist**

APC activator

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

“RELEASING THE BRAKE ON THE T CELL”



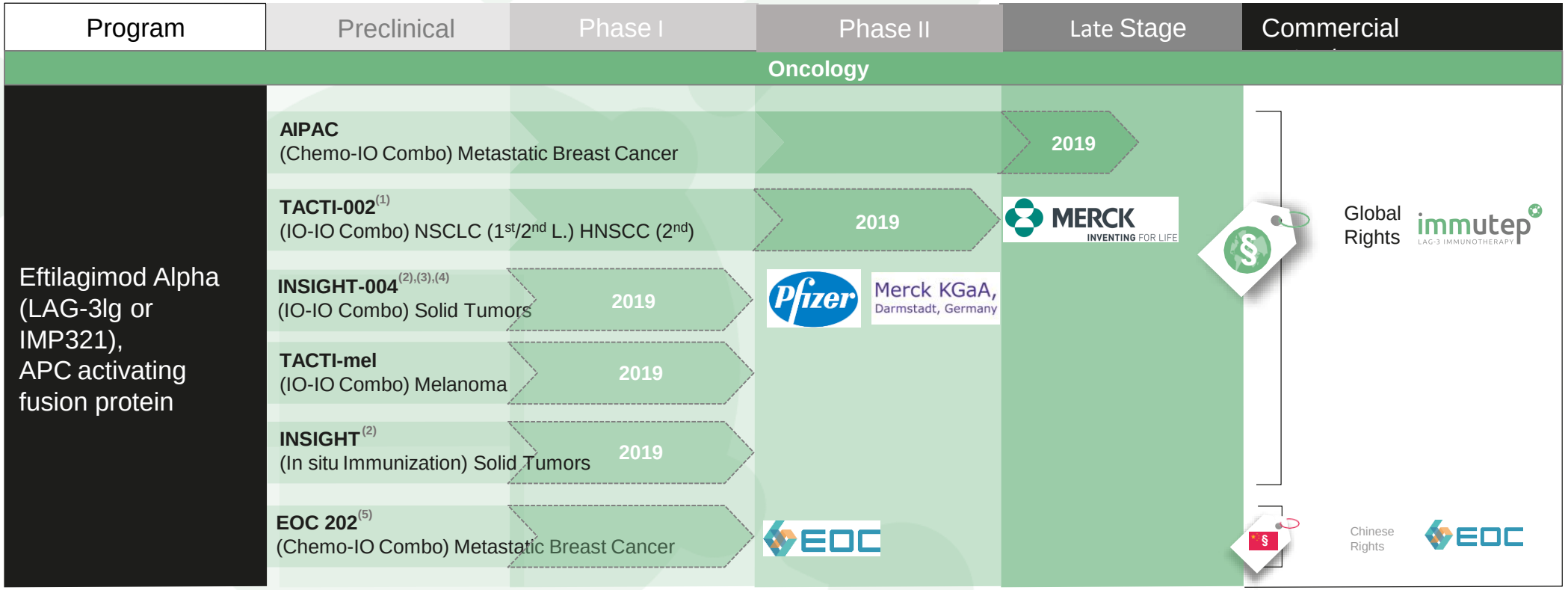
LAG-3 antagonist, or blocking, antibodies:

Immune checkpoint inhibitor

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

Eftilagimod Alpha Clinical Trials*

*Expecting multiple data readouts throughout H2 2019**



Notes

* Actual timing of data readouts may differ from expected timing shown above. Information in pipeline chart current as at 12 February 2019.

(1) In combination with KEYTRUDA® (pembrolizumab) in non-small cell lung carcinoma ("NSCLC") or head and neck carcinoma ("HNSCC"); clinical trial is currently planned and not active

(2) INSIGHT Investigator Initiated Trial ("IIT") is controlled by lead investigator and therefore Immutep has no control over this clinical trial

(3) In combination with BAVENCIO® (avelumab)

(4) Clinical trial is currently planned and not active

(5) EOC Phama is the sponsor of the EOC 202 clinical trial which is being conducted in the People's Republic of China

Efti Clinical Development Overview

Efti - Areas of Development Multiple Strategies

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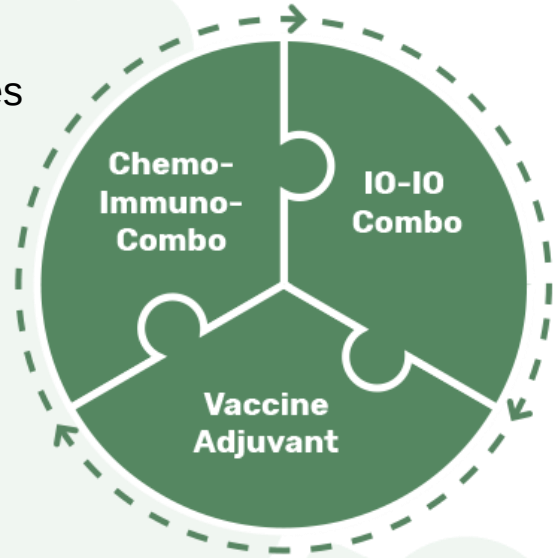
Efti has multiple shots on goal in different indications and in different combinations

Chemo-immunotherapy

- Exploit the antigen debris from chemotherapy with an APC activator → combination with agents such as taxanes (e.g. paclitaxel)

• *European Phase IIb AIPAC (Immutep)*
• *Chinese Phase I Chemo Combo in MBC pts (EOC)*



IO-IO combination

- Increase response rates and durability, overcoming resistance in combination with IO agents with complementary mechanisms (e.g. pembrolizumab, avelumab)

• *Phase I TACTI-mel (Immutep)*
• *Phase II TACTI-002 (Immutep[1])*
• *Phase I INSIGHT – Stratum D (Immutep[2])*

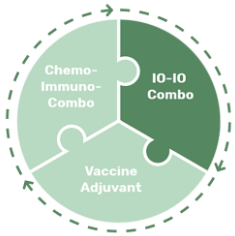
Cancer vaccine or in situ vaccination

- Stimulate the immune system locally → intratumoral or in vaccination studies

• *Phase I Solid Tumors (Cytlimic)*
• *Phase I INSIGHT - Stratum A+B (IKF[3])*

Notes
(1) In collaboration with Merck & Co., Inc., Kenilworth, NJ, USA (known as MSD outside the United States and Canada) and in combination with KEYTRUDA® (pembrolizumab)
(2) In collaboration with Merck KGaA, Darmstadt, Germany and Pfizer Inc. and in combination with BAVENCIO® (avelumab)
(3) INSIGHT Investigator Initiated Trial ("IIT") is controlled by lead investigator and therefore Immutep has no control over this clinical trial

Efti TACTI-mel results



Efti in Melanoma
TACTI-mel – 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

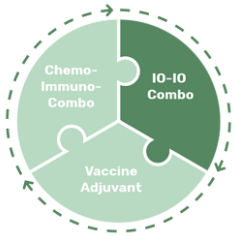
Other objectives	PK and PD of efti, response rate, PFS
Patient Population	Metastatic melanoma

7 sites in Australia

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

→ Status: recruitment completed; interim results on following slides

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



Efti in Melanoma
TACTI-mel – Safety Part A + B

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Efti has a favorable safety profile in combination with pembrolizumab - No DLTs or MTDs and no new safety signals observed

Frequent TEAE (selected if ≥ 15 % of pts)

Adverse Event*	Any grade N (%)	≥ Grade 3 N (%)
Abdominal pain (various terms)	5 (21)	-
Arthralgia	5 (21)	1 (4)
Cough	4 (17)	-
Diarrhea / Colitis	6 (25)	1 (4)
Fatigue	12 (50)	-
Headache	4 (17)	-
Injection site reaction	6 (25)	-
Nausea	7 (29)	-
Rash##	12 (50)	1 (4)

* - Adverse events occurred in > 15 % of pts
- any kind of rash

- 10 SAEs in 9 pts; one related to pembrolizumab, none to efti
- 6 pts (25 %) with ≥ 1 AE ≥ grade 3 (no grade 5)

Grade 3 / 4 TEAEs and rel. to study treatment

Reported term	Grade 3 N (%)	Grade 4 N (%)	Rel to efti / pembro
Maculo-papular rash	1 (4 %)	-	No / Yes
Decreased renal function	1 (4 %)	-	Yes / No
Colitis	1 (4 %)	-	No / Yes
Altered liver functions	1 (4 %)	-	No / Yes
Arthralgia	1 (4%)	-	No / Yes

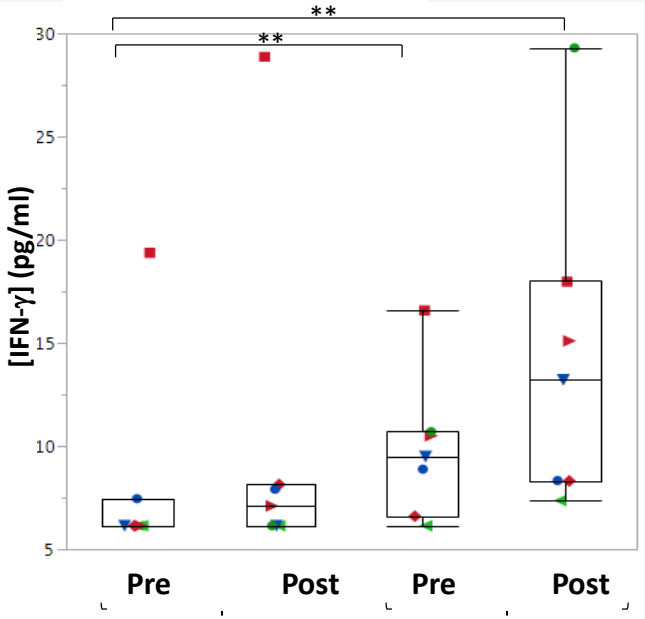
- 2 pts died due to AE (grade 4 intracranial hemorrhage, not related to treatment; grade 4 Sepsis, not related to treatment)
- 1 pt disc. due to an AE (anaemia; not related to treatment)
- 6 pts experienced treatment delays due to AEs

preliminary data, cut-off February 2019

Efti in Melanoma
TACTI-mel – Blood Pharmacodynamics

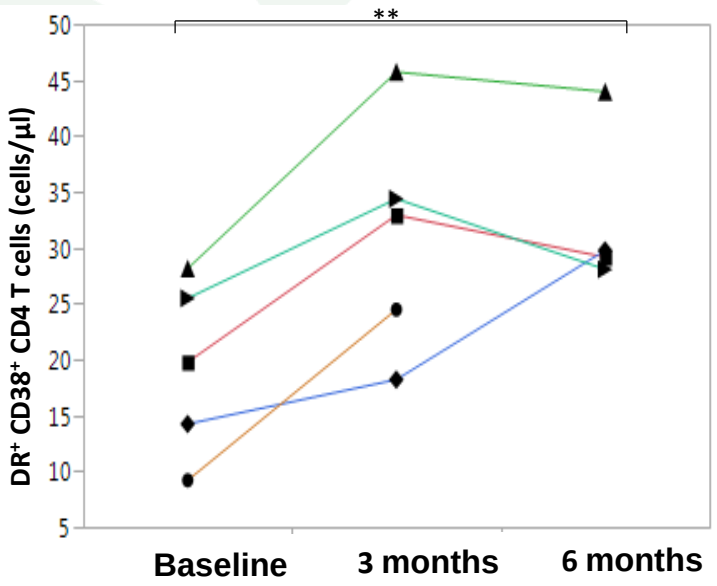
Sustained markers of immune response observed

Part A
IFN-g (not yet available for Part B)

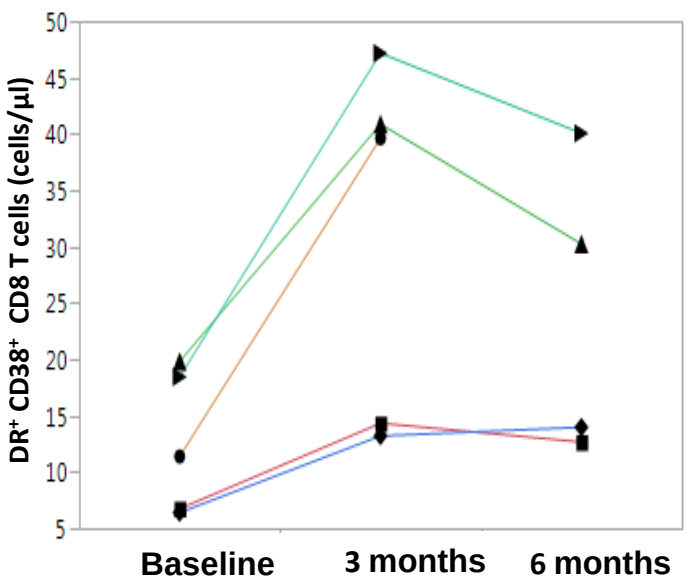


1st application **6 months**

Part B
Activated CD4 T cells

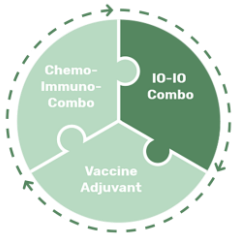


Part B
Activated CD8 T cells



- ✓ At 6 months, pre-dose (i.e. 14 days after last injection) serum IFN-γ is elevated: sustained increase of systemic Th1 status (i.e. not at the tumor site only, but in the whole organism)
- ✓ Also increased absolute numbers of activated CD4 and CD8 cells for all patients in part B
- ✓ Improved Th1 status and increased activated T cells numbers have also been reported for efti + chemo (AIPAC)

preliminary data, cut-off February 2019



Efti in Melanoma
TACTI-mel – Baseline Characteristics

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Patients in very late stage of disease (M1c, elevated LDH, liver metastasis)

Baseline Characteristics	Part A N = 18 (%)	Part B N = 6 (%)	Overall N =24 (%)
Median Age	67 yrs	61 yrs	62 yrs
Sex (f/m)	6 % / 94 %	17 % / 83 %	8 % / 92 %
ECOG 1 / 0	22 % / 78 %	50 % / 50 %	29 % / 71 %
Pre-treated with BRAF/MEK/ipilimumab	5 (28 %)	0 (0 %)	5 (21 %)
Poor prognostic marker at study entry			
Elevated LDH (>ULN)	7 (39%)	5 (83%)	12 (50 %)
Liver metastasis	10 (56 %)	2 (33 %)	12 (50 %)
Lung metastasis	11 (61 %)	5 (83 %)	16 (67 %)
Metastatic stage M1c	14 (78 %)	6 (100 %)	20 (83 %)

preliminary data, cut-off February 2019

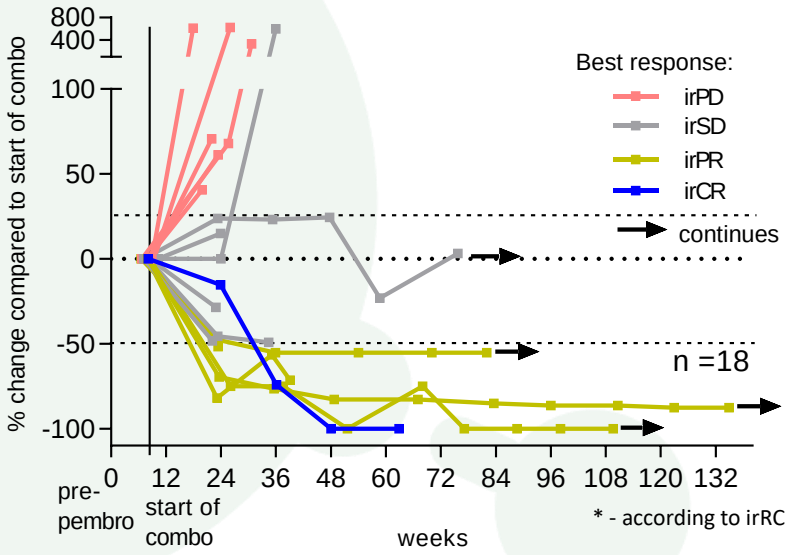
Efti in Melanoma
TACTI-mel – Results Part A

Majority not responding to pembrolizumab monotherapy
→ Tumor shrinkage in 56 % incl. 2 pts with disappearance of all target lesions

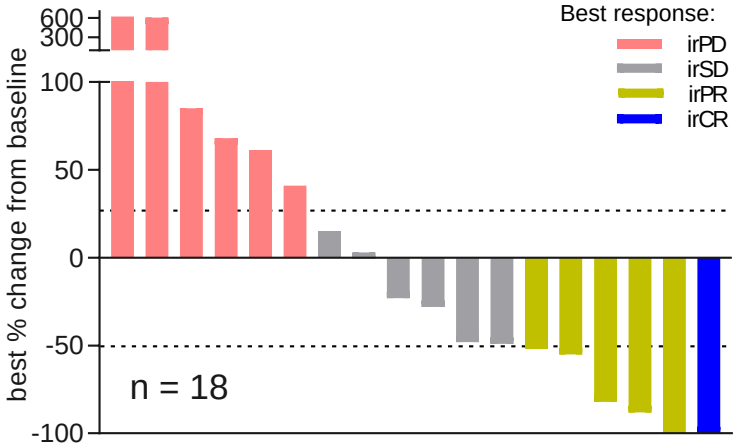
Best Overall Response acc. to irRC	N = 18 (%)
irCR	1 (6 %)
irPR#	5 (28 %)#
irSD	6 (33 %)
irPD	6 (33 %)
Best overall response rate (ORR)	**6 (33 %)**
Patients with tumor shrinkage	**10 (56 %)**
Disease control rate	**12 (66 %)**

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

Spider plot* (part A)
(starting with cycle 5 of pembrolizumab)



Waterfall plot* (part A)
(starting with cycle 5 of pembrolizumab)



Exploratory analysis
(C1D1 pembrolizumab):
ORR of 61 %

preliminary data, cut-off February 2019

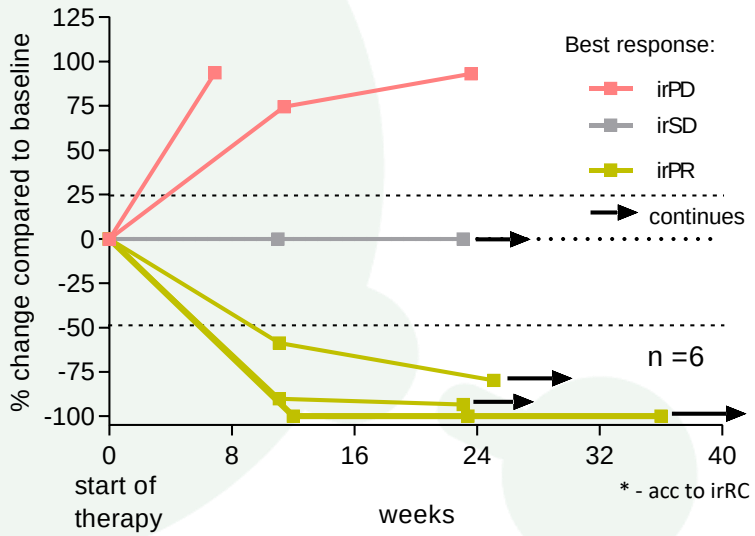
Efti in Melanoma
TACTI-mel – Results Part B

Confirmed deep partial responses in 3 (50%) of the pts
Treatment of 4 pts ongoing, all over 6 months

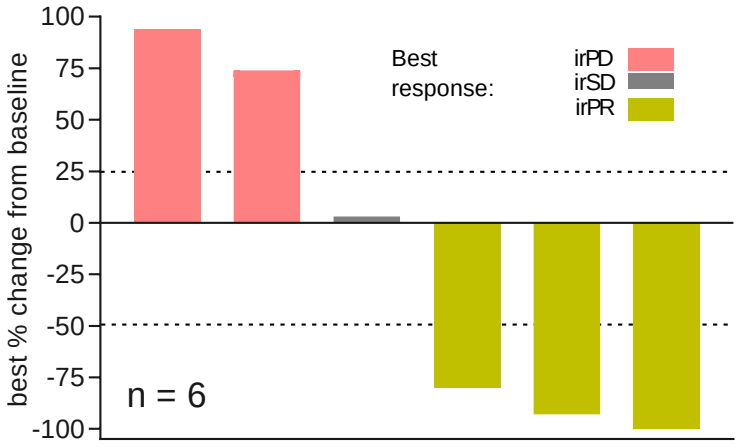
Best Overall Response acc. to irRC	N = 6 (%)
irCR	0 (0 %)
irPR#	3 (50 %)#
irSD	1 (13 %)
irPD	2 (25 %)
Best overall response rate (ORR)	**3 (50 %)**
Patients with tumor shrinkage	**3 (50 %)**
Disease control rate	**4 (66 %)**

- incl. 1 pt with complete disappearance of all target lesions

Spider plot* (part B)



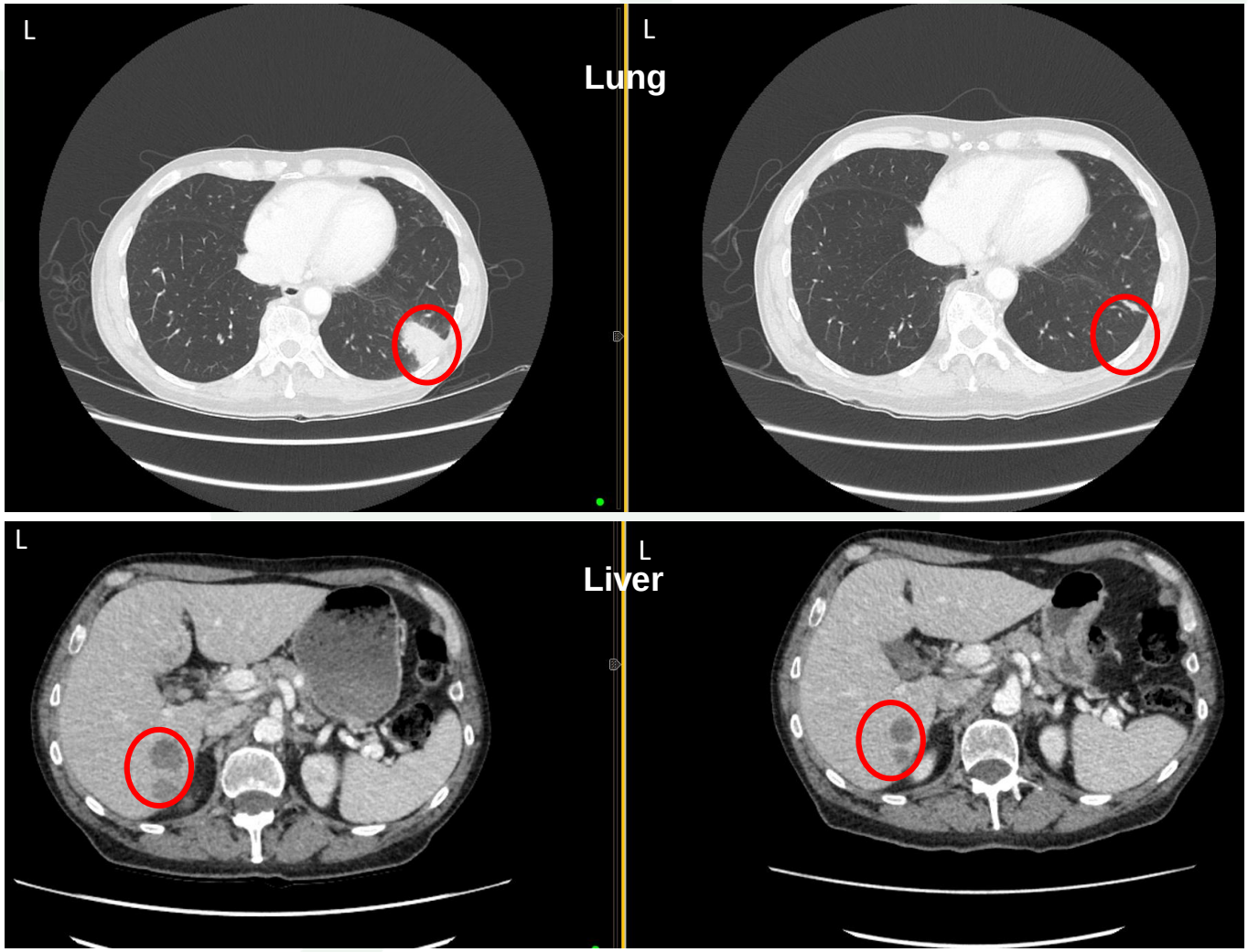
Waterfall plot* (part B)



preliminary data, cut-off February 2019

Efti (IMP321) in Melanoma
TACTI-mel – Results Part B – Single Case

July 2018 (baseline) | **January 2019 (6 months)**



- 69 year old male
- Multiple lung, bone, liver and lymph node metastases from melanoma → **M1C stage**
- BRAF wild type
- ECOG 1

→ clear regression of lung and liver metastases → treatment continues (6+ months)

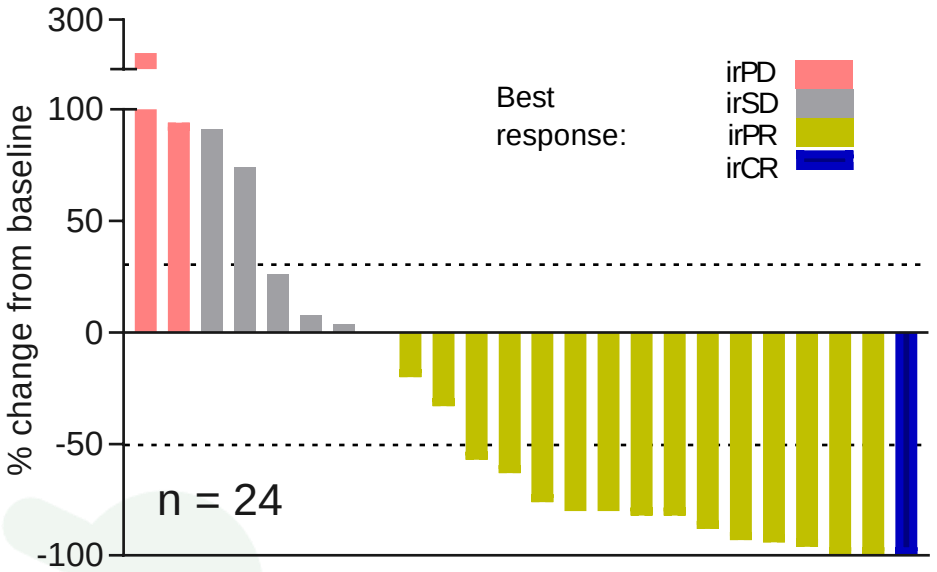
preliminary data, cut-off February 2019

Efti in Melanoma
TACTI-mel – Analysis Parts A+B (1)

Overall response rate is 58% and 58% of patients are progression-free 6 months after start of pembrolizumab (1)

ORR acc. to irRC (C1/D1 analysis)[1]	N = 24 (%)
irCR	1 (4%)[1]
irPR#	13 (54%)[1],[2]
irSD	6 (25%)[1]
irPD	4 (17%)[1]
Overall response rate (ORR)	**14 (58%)[1]**
Progression-free at 6 months	**14 (58%)[1]**

Waterfall Plot* (part A+B)
(starting cycle 1 day 1 pembrolizumab)



Note Trial Design TACTI-mel part A: 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

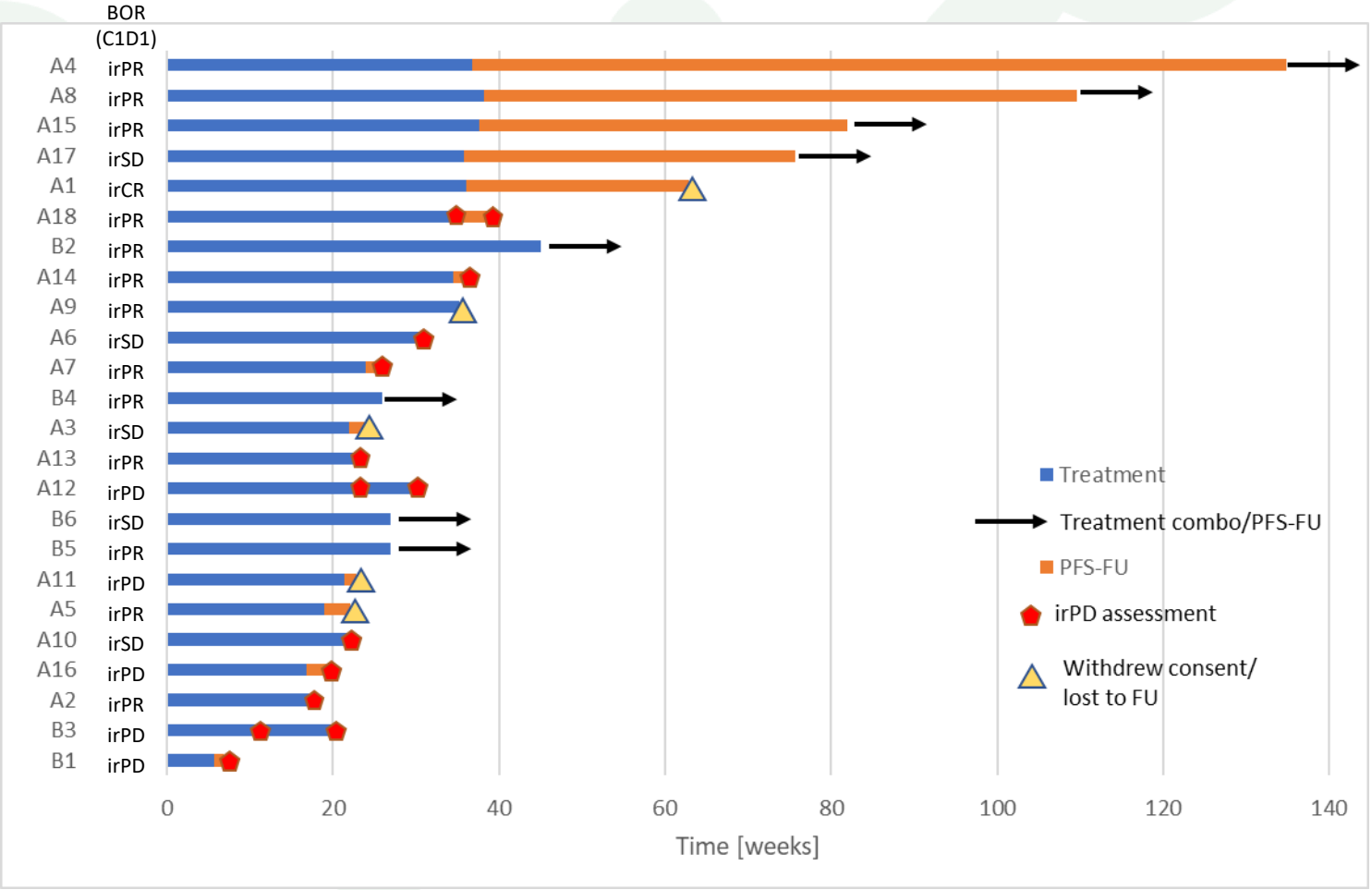
How does the efficacy looks from the start of pembrolizumab?
→ Performed exploratory analysis starting from cycle 1 day 1 of pembrolizumab, including the 4 cycles pembrolizumab monotherapy ("C1/D1 Analysis") and include pts from part B

preliminary data, cut-off February 2019

Notes
(1) Response rates determined by C1/D1 Analysis for part A
(2) Includes 2 patients with complete disappearance of all target lesions, but with remaining non-target lesions or lymph nodes

Efti in Melanoma
TACTI-mel – Analysis Parts A+B (2)

Swimmerplot parts A + B
(starting cycle 1 day 1 pembrolizumab)

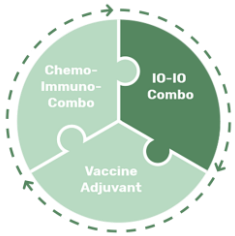


Note: BOR – best overall response per patient with start of pembrolizumab as baseline

Conclusion

- No treatment termination due to safety issues of the combination
- 5+ pts on treatment for > 12 months → durable responses
- 8 (4 part A) and (4 part B) patients still progression free and under treatment

preliminary data, cut-off February 2019



Efti 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

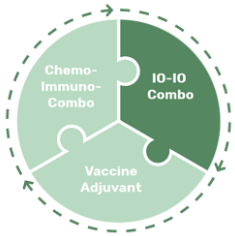
Baseline Characteristics	Tacti-Mel (C1/D1 response analysis) Pembro 2 mg/kg N=24 in %	KN-006 (ipi naive) Pembro 10 mg/kg n=277 in %	KN-002 (ipi pre-treated) Pembro 2 mg/kg n=180 in %
Metastatic stage M1c	83%	68%	82%
ECOG 1 / 0	29% / 71%	32% / 68%	45% / 55%
irCR	4%(1)	6%(2)	2%(2)
ORR	**58%(1)**	**33%**(2)	**21%**(2)
Progression-free at 6 months	**58%(1)**	**46%**(2)	**34%**(2)

58 % response rate(1, 2) and **58 % progression free at 6 months** (1, 2) with the PD-1 antagonist **pembrolizumab** and APC activator **eftilagimod alpha** in **very late stage partly pre-treated metastatic melanoma patients**

preliminary data, cut-off February 2019

Notes
(1) Response rates determined by C1/D1 Analysis
(2) TACTImel used irRC and KN-002 and KN-006 ECIStT1.1
(3) Source of the figure: 7th edition (2010) of the AJCC cancer staging manual

Efti
Clinical Development Updates
TACTI-002 / INSIGHT-004 /AIPAC



Efti - Clinical Development TACTI-002 (Phase II)

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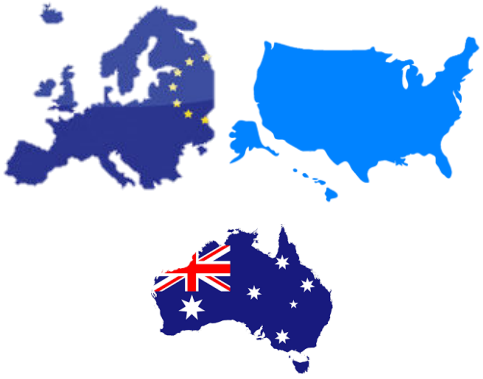
TACTI-002: Two ACTive Immunotherapeutics in different indications

Simon's 2 stage design; 3 indications; 109 pts → Efti (IMP321) + Pembrolizumab (Keytruda®) for 12 months + 12 months pembrolizumab mono → Phase II, multi-national (EU + US + AU), open label → **ORR,** PFS, OS, PK, Biomarker; Safety and tolerability

Patient Population	A: 1st line NSCLC PD-X naive B: 2nd line NSCLC, PD-X refractory C: 2nd line HNSCC, PD-X naïve
Treatment	30 mg Efti (IMP321) s.c. 200 mg Pembrolizumab i.v.

Status Report (Apr 2019)

- ✓ Fully approved in all countries (ES, GB, US, AU)
- ✓ >10 patients enrolled
- • First data expected mid 2019



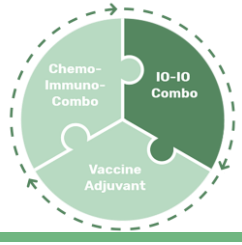
13 sites in Europe / US / Australia

In collaboration with

MERCK INVENTING FOR LIFE

Key features: PD-X refractory patients (part B), chemo-free option for NSCLC, first FDA IND

NSCLC – non-small-cell lung cancer, HNSCC – head and neck squamous cell cancer, ORR – overall response rate, PFS – progression free survival, OS – overall survival, PK – pharmacokinetics, PD-X – any PD-1 or PD-L1 treatment



Efti - Clinical Development
INSIGHT-004 (Phase I)

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INSIGHT-004 – Dose escalation of efti in combination with avelumab

Dose escalation, solid tumors, 2 cohorts of 6 pts each → Efti (IMP321) + Avelumab (Bavenico®) for 6 months + 6 months avelumab monotherapy → Phase I, monocenter DE, open label, IIT → **RP2D, Safety,** ORR, PFS, PK, PD

Patient Population	Solid tumors after failure of standard therapy
Treatment	6/30 mg Efti (IMP321) s.c. 800 mg avelumab i.v.; Both every 2 weeks

In collaboration with

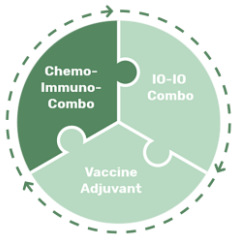
Pfizer, Merck KGaA & I.K.F.

Status Report (Apr 2019)

- ✓ 1 site in Germany
- ✓ Protocol approved by CA/ ED
- • First patient expected in Q2 2019

Key features: safety with a PD-L1 antagonist avelumab

R2PD – recommended phase 2 dose, ORR – overall response rate, PFS – progression free survival, OS – overall survival, PK –pharmacokinetics



Efti - Clinical Development AIPAC

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AIPAC: Active Immunotherapy PAClitaxel in MBC

Safety-run in, 15 (6+9) patients, 2 cohorts → Stage 2 → Arm 1, *113* patients: paclitaxel + IMP321; Arm 2, *113* patients: paclitaxel + placebo → Phase IIb, multinational, randomized, double-blind → Run-in: RP2D; Stage 2: Efficacy (PFS)

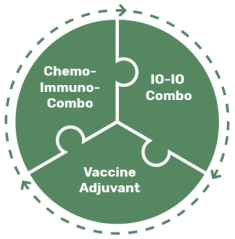
Other Objectives	Anti-tumor activity, safety and tolerability, PK, immunogenicity, quality of life
Patient Population	Advanced MBC indicated to receive 1st line weekly paclitaxel
Treatment	Run-in: Paclitaxel + IMP321 (6 or 30 mg) Arm 1: Paclitaxel + IMP321 (30 mg) Arm 2: Paclitaxel + Placebo
Location	>30 sites in 7 (GB, DE, PL, HU, FR, BE, NL) EU countries

Status Report (Apr 2019)

- ✓ To-date, efficacy and safety data (ASCO 2018) in-line with historical control group / prior clinical trials (Brignone et al J Trans Med 2010, 8:71)
- ✓ Regulatory approval in 7 EU countries
- ✓ >200 patients recruited in Stage 2 → LPI expected May/Jun 2019
- Primary read out expected within 12 months dependent on the number of events, but not before Q.4 2019

Key features: double blinded, potentially pivotal trial in metastatic breast cancer patients

R2PD – recommended phase 2 dose, ORR – overall response rate, PFS – progression free survival, OS – overall survival, PK –pharmacokinetics



Efti - Areas of Development Potential Target Markets

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Treatment Landscape MBC (Before AIPAC) | **Treatment Landscape (Today)**

HER2-negative / HR positive MBC (~65 % of all breast cancers)

~ 40-66 % 1-2 lines of endocrine therapy

66 %[2] endocrine therapy ± CDK 4/6 ± everolimus

Chemotherapy (paclitaxel, capecitabine and others)

MBC patients are heavier pre-treated → chemotherapy may be less effective

AIPAC randomized → no bias

MBC

- ~**800,000 new cases** p.a. worldwide with **HER$^-$HR$^+$ BC**
- Despite all changes → no improvement for patients receiving chemotherapy
- Paclitaxel one of the most widely used chemotherapies

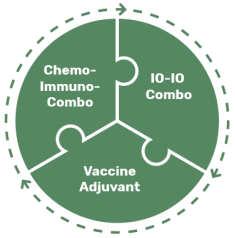
Other indications/combinations

- Efti is investigated in **melanoma** with **pembrolizumab** (2019 estimated global sales of US$9.8 billion[1])
- Efti is investigated in **head and neck** and two different treatment lines of **NSCLC with pembrolizumab**
- Efti is investigated with **avelumab** (2019 estimated sales of US$242 million[1])

Multiple shots on goal in large indications → efti not limited by indication/combination

Notes
(1) Source: GlobalData 2019
(2) Caldeira et al Oncology and therapy 2016; 4:189-197

MBC – metastatic breast cancer BC – breast Cancer
NSCLC – non-small cell lung cancer



Efti Summary

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- ✓ Favorable safety profile
- ✓ Sustained systemic immune response
- ✓ Encouraging efficacy data in different settings
- ✓ Clinical trials with industry leading collaborators
- ✓ Potentially low cost of goods
- ✓ Potential pipeline in a product
- ✓ Late stage clinical development with multiple “shots on goal”

Thank you!