2021 ASCO ANNUAL MEETING

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Results from a Phase II study of eftilagimod alpha (soluble LAG-3 protein) and pembrolizumab in patients with PD-L1 unselected metastatic non-small cell lung carcinoma

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Study Identifiers:
Sponsor: IMP321-P015; MSD: Keynote-PN798; EudraCT: 2018-001994-25; Clinicaltrials.gov: NCT03625323

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DISCLOSURE

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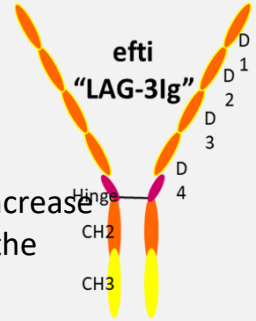
T Clay: *Honoraria - AstraZeneca; Novartis; Roche, Speakers' Bureau - AstraZeneca; Novartis; Novartis, Research Funding - Bayer (Inst); Bayer (Inst); BeyondSpring Pharmaceuticals (Inst); Clovis Oncology (Inst); Exelixis (Inst); Immutep (Inst); Merck Sharp & Dohme (Inst), Travel, Accommodations, Expenses - Astellas Pharma; Astra Zeneca; Bristol-Myers Squibb; Foundation Medicine; Roche/Genentech.*

Eftilagimod alpha (efti) MoA

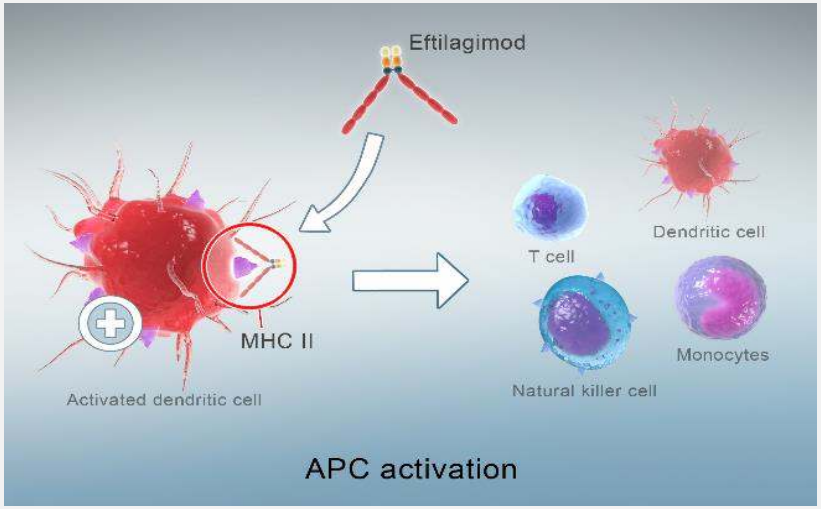
TACTI-002
TRIAL DESIGN & INTRODUCTION

MoA: Efti is a soluble LAG-3 protein targeting a subset of MHC class II molecules to mediate antigen presenting cells (APCs) and CD8 T-cell activation.

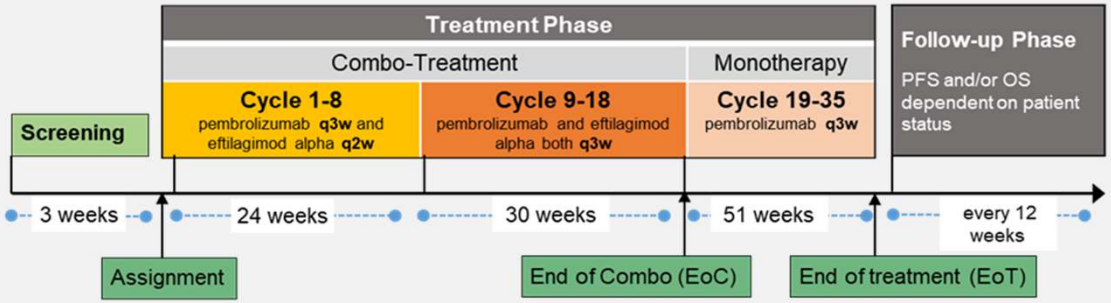
Rationale: Efti activates APCs, leading to an increase in activated T cells, thus potentially reducing the number of non-responders to PD-1/PD-L1 antagonists (e.g. pembrolizumab).



"PUSHING THE ACCELERATOR ON IMMUNE RESPONSES"



- Phase II, multinational, open label, PD-L1 all-comer, multiple indications
- Up to 183 pts in a Simon's optimal two-stage design (NCT:NCT03625323)
- Sponsored by Immutep and in collaboration with MSD



Legend: 1 cycle = 3 weeks; q2w – every 2 weeks, q3w every 3 weeks

- Eligible patients for part A (1st line NSCLC) include:
  *patients **unselected for PD-L1** with advanced NSCLC (stage IIIB unamenable to curative treatment, or stage IV unamenable to EGFR/ALK-based therapy), treatment-naïve for advanced/ metastatic disease and immunotherapy-naïve*
- 36 patients enrolled into stage 1 + 2 (LPI: Jun 2020)
- Extension (part A) ongoing +74 patients (actively recruiting and no efficacy reported)
- **Primary objective is overall response rate acc. to iRECIST**
- Secondary objectives include PFS, OS, PK, biomarker, PD, safety and tolerability
- Data cut-off was 16th April 2021 (interim data)

APC… antigen-presenting cell
iRECIST… Immune Response Evaluation Criteria In Solid Tumors
LAG-3… Lymphocyte Activation gene-3
MHC… Major Histocompatibility Complex
MoA… Mode of Action
PD-L1, PD-L2…Programmed Death ligand-1, -2
PFS… progression-free survival

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TACTI-002: Phase II of efti and pembrolizumab in 1st line metastatic NSCLC (Part A)
SAFETY*

Table 1: Treatment-emergent adverse events occurring ≥15 %*

Adverse event by PT	Any grade N (%)	Grade 3 N (%)	Grade 4/5 N (%)
Asthenia	18 (34.6)	2 (3.8)	-
Cough	15 (28.8)	1 (1.9)	-
Dyspnoea	15 (28.8)	7 (13.5)	-
Decreased appetite	13 (25.0)	1 (1.9)	-
Fatigue	12 (23.2)	-	-
Diarrhoea	11 (21.2)	1 (1.9)	-
Pruritus	11 (21.2)	-	-
Constipation	10 (19.2)	-	-
Anaemia	10 (19.2)	2 (3.8)	-
Back pain	8 (15.4)	2 (3.8)	-
Nausea	8 (15.4)	-	-

Table 2: General overview adverse events*

Safety parameter	N (%)
Patients with any TEAE	48 (92.3)
Patients with any SAE	18 (34.6)
thereof related to efti/pembro	3 (5.8) / 3 (5.8)
Patients with any grade ≥3 TEAE	27 (51.9)
thereof related to efti/pembro	4 (7.7) / 5 (9.6)
Patients with fatal TEAEs	5 (9.6)
thereof related to efti /pembro	0
Patients with TEAEs leading to discontinuation of any study treatment	6 (11.5)
thereof related to efti /pembro	3 (5.8) / 2 (3.8)

* - Safety is displayed for all patients (n=52) recruited who received ≥1 treatment

SAE… serious adverse event
TEAE… treatment-emergent adverse event

TACTI-002: Phase II of efti and pembrolizumab in 1st line metastatic NSCLC (Part A)
BASELINE CHARACTERISTICS & EFFICACY*

Table 3: Baseline Disease Characteristics*

Baseline parameters	N (%)
Age (years), median (range)	68.5 (53-84)
Female / Male	11 (30.6) / 25 (69.4)
ECOG 0 / ECOG 1	15 (41.7) / 21 (58.3)
Current / Ex- or Non-smokers	2 (5.6) / 34 (94.4)
Squamous / Non-squamous pathology	15 (41.7) / 21 (58.3)
Patients with liver metastasis	14 (38.9)

Table 4: Tumor Response*

Best overall response, iRECIST	Local Read (investigator) N (%)	Blinded Read (BICR) N (%)
Complete Response	**2 (5.6)**	**2 (5.6)**
Partial Response	11 (30.6)	13 (36.1)
Stable Disease	11 (30.6)	10 (27.8)
Progression	8 (22.2)	6 (16.7)
Not evaluable**	4 (11.1)	5 (13.9)
Disease Control Rate	24 (66.7)	25 (69.4)
Overall Response Rate* [95 % CI interval]	**13 (36.1) [20.8-53.8]**	**15 (41.7) [25.5-59.2]**
Overall Response Rate – Evaluable pts* [95 % CI interval]**	**13 (40.6) [23.7-59.4]**	**15 (48.4) [30.1-60.9]**

** - All patients stage 1 and 2 (N=36) with* ≥ 1 treatment
*** - dropped off prior to first staging or were not evaluable post-baseline for any reason*
**** - Evaluable for efficacy meaning* ≥ 1 treatment and ≥ 1 post baseline tumor staging

ECOG… Eastern Cooperative Oncology Group
iRECIST… Immune Response Evaluation Criteria In Solid Tumors
BICR… Blinded Independent Central Review

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TACTI-002: Phase II of efti and pembrolizumab in 1st line metastatic NSCLC (Part A)
EFFICACY

Table 5. ORR by PD-L1 subgroup*

PD-L1	ORR iRECIST* (%)
≥ 50 % TPS	53.8
< 50 % TPS	31.6
≥ 1 % TPS	44.0

** according to investigator read, evaluable pts only*

Table 6. Overall PFS estimates by PD-L1 subgroup**

PD-L1	Median PFS iRECIST* (months)
Unselected	8.2
≥ 50 % TPS	11.8
< 1 % TPS	4.1

*** according to investigator read, minimum follow-up of 8.3 months, all patients stage 1 and 2 with* ≥ 1 treatment

Figure 1. Waterfall plot

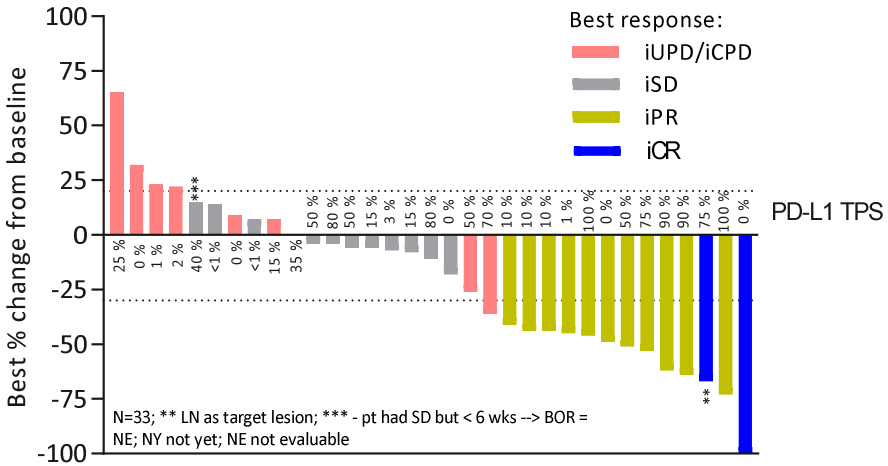
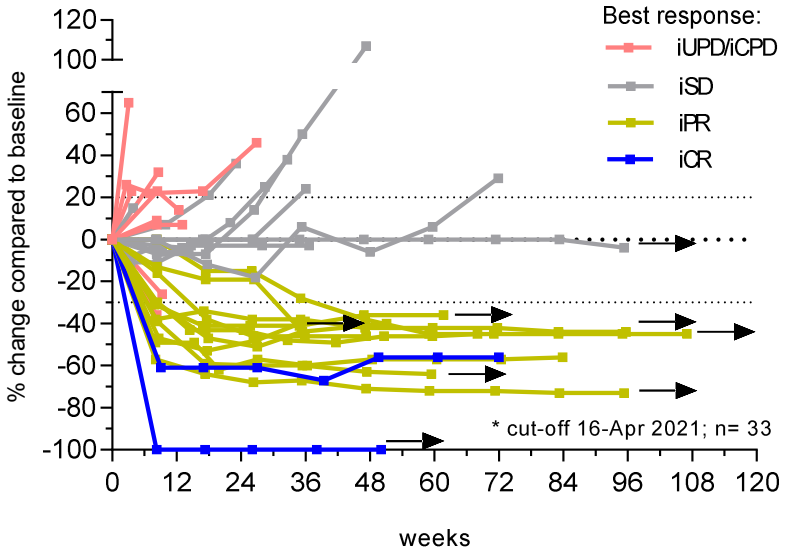


Figure 2. Spider plot



Duration of response (DOR)

- 92 % responses confirmed
- 58 % confirmed responses ongoing with 6+ months
- Responses progressed after 6.5-13.8 months
- Median DOR estimated 13+ months

- At data cut-off, 7 pts still under therapy and 1 pt completed the 2 yrs of therapy

iRECIST… Immune Response Evaluation Criteria In Solid Tumors
PD-L1, PD-L2…Programmed Death ligand-1, -2
PFS… progression-free survival

ORR… objective response rate
→ *… patients still under therapy*

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TACTI-002: Phase II of efti and pembrolizumab in 1st line metastatic NSCLC (Part A)
CONCLUSION

SAFETY

- Treatment with efti plus pembrolizumab is well-tolerated with no new safety signals
- 4 % of patients discontinued treatment due to AEs related to efti/pembrolizumab
- Most frequent AEs include general symptoms frequently occurring in a NSCLC patient population
- Majority of most frequent adverse events are mild to moderate
- Safety profile is similar to KN-042 (pembrolizumab monotherapy)

EFFICACY

- Encouraging ORR (41.7 % by BICR) in patients unselected for PD-L1
- Median PFS (8.2 months) in patients unselected for PD-L1 is encouraging for a chemo-free 1st line regimen
- Responses observed in all PD-L1 subgroups and responses are durable
- ORR in each PD-L1 subgroup report favorable compared to KN-042 (pembrolizumab monotherapy, PIII randomized trial)

The combination of efti plus pembrolizumab is well-tolerated, showing encouraging signs of activity supporting further clinical investigation. An extension of the study is ongoing.

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