2021 ASCO ANNUAL MEETING

Abstract #: 6028

Results from a Phase II study of eftilagimod alpha (soluble LAG-3 protein) and pembrolizumab in patients with PD-L1 unselected metastatic 2nd line squamous head and neck 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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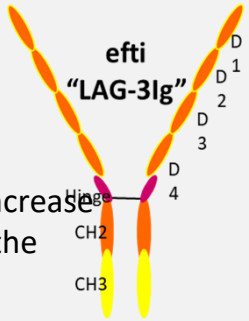
I Braña: *Consulting or Advisory Role- Merck Sharp & Dohme, Rakuten Medical, Sanofi, Achilles Therapeutics, eTheRNA Immunotherapies, Cancer Expert Now. Speakers Bureau: Bristol-Myers Squibb, Merck Serono, Roche. Research Funding: AstraZeneca, Bristol-Myers Squibb, Celgene, Gliknik, GlaxoSmithKline, Janssen Oncology, Kura, Merck Sharp & Dohme, Novartis, Orion Pharma GmbH, Pfizer, Roche, Shattuck Labs, Nanobiotix, Seattle Genetics, Immutep. Travel, Accommodations, Expenses - AstraZeneca Spain, Merck Serono.*

Eftilagimod alpha (efti) MoA

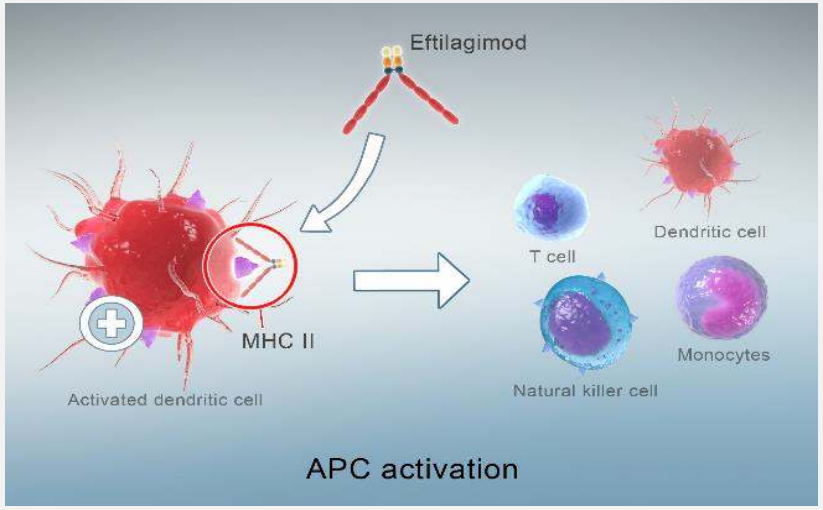
TACTI-002
TRIAL DESIGN & INTRODUCTION

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.

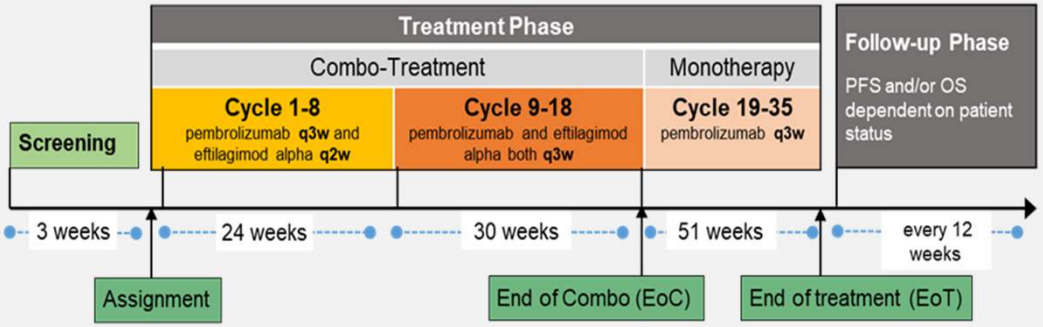
Rationale: Efti activates APCs, leading to an increase in activated T cells, thus potentially reducing the number of non-responders to PD-1/PD-L1 antagonists (e.g. pembrolizumab).



"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 (NCT03625323)
- Sponsored by Immutep and in collaboration with MSD



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

- Following patients are eligible to part C (2nd line HNSCC):

  *patients **unselected for PD-L1** with recurrent HNSCC disease unamenable to curative treatment with local or systemic therapy, or metastatic (disseminated) disease incurable by local therapies, who progressed on or after 1st line platinum-based therapy*
- 39 patients were enrolled to stage 1 + 2 (LPI in Jan 2021)
- **Primary objective: Overall Response Rate acc. to iRECIST**
- Secondary objectives include PFS, OS, PK, biomarker, PD, safety and tolerability
- Data cut-off: 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

TACTI-002: Phase II of efti and pembrolizumab in 2nd line HNSCC (Part C) SAFETY*

Table 1: Treatment-emergent adverse events occurring ≥10%*

Adverse event (PT)	Any grade N (%)	Grade 3 N (%)	Grade 4/5 N (%)
Hypothyroidism	8 (20.5)	1 (2.6)	-
Cough	7 (17.9)	-	-
Asthenia	6 (15.4)	-	-
Fatigue	5 (12.8)	-	-
Anaemia	5 (12.8)	4 (10.3)	
Diarrhoea	5 (12.8)	-	-
Weight decreased	5 (12.8)	-	-
URTI	4 (10.3)	-	-
Back pain	4 (10.3)	-	-
Pain in extremity	4 (10.3)	2 (5.1)	-

Table 2: General overview of adverse events*

Safety parameter	N (%)
Patients with any TEAE	35 (89.7)
Patients with any SAE	18 (46.2)
thereof related to efti/pembro	2 (5.1) / 2 (5.1)
Patients with any grade ≥3 TEAE	24 (61.5)
thereof related to efti/pembro	4 (10.3) / 3 (7.7)
Patients with fatal TEAEs	7 (17.9)
thereof related to efti/pembro	0 / 0
Patients with TEAEs leading to discontinuation of any study treatment	7 (17.9)
thereof related to efti/pembro	1 (2.6)

* - Safety is displayed for all patients (N=39) recruited who received ≥1 treatment

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

TACTI-002: Phase II of efti and pembrolizumab in 2nd line HNSCC (Part C)
BASELINE CHARACTERISTICS & EFFICACY*

Table 3: Baseline disease characteristics

Baseline parameters (N=39)	N (%)
Age, median (years)	62 (37-84)
Female / Male	4 (10.3) / 35 (89.7)
ECOG 0 / ECOG 1	13 (33.3) / 26 (66.7)
Current / Ex- or Non-smokers	6 (15.4) / 33 (84.6)
Previous chemotherapy	39 (100)
Previous cetuximab	16 (41.0)
Lung lesions Liver lesions	19 (48.7) / 6 (17.6)

Table 4: Primary tumor location

Primary tumour location (N=39)	N (%)
Oral cavity	12 (30.8)
Oropharynx	14 (35.9)
Hypopharynx	7 (17.9)
Larynx	6 (15.4)

Table 5: Tumor response*

Best overall response*, iRECIST	Investigator assessment N (%)
Complete Response	**5 (13.5)**
Partial Response	**6 (16.2)**
Stable Disease	3 (8.1)
Progression	17 (45.9)
Not evaluable**	6 (16.2)
Disease Control Rate	14 (37.8)
Overall Response Rate [95 % CI interval]	**11 (29.7) [15.9 – 47.0]**
Overall Response Rate – Evaluable pts* [95 % CI interval]**	**11 (35.5) [19.2 – 54.6]**

** - All patients (N=37) with* ≥ 1 treatment and no death due to COVID-19 prior to first post-baseline staging
*** - dropped off prior to first staging or were not evaluable post-baseline for any reason*
**** - evaluable patients (N=31):* ≥ 1 treatment and ≥ 1 post baseline tumor staging

ECOG… Eastern Cooperative Oncology Group
iRECIST… Immune Response Evaluation Criteria In Solid Tumors

TACTI-002: Phase II of efti and pembrolizumab in 2nd line HNSCC (Part C)
EFFICACY*

*Figure 1: Waterfall plot***

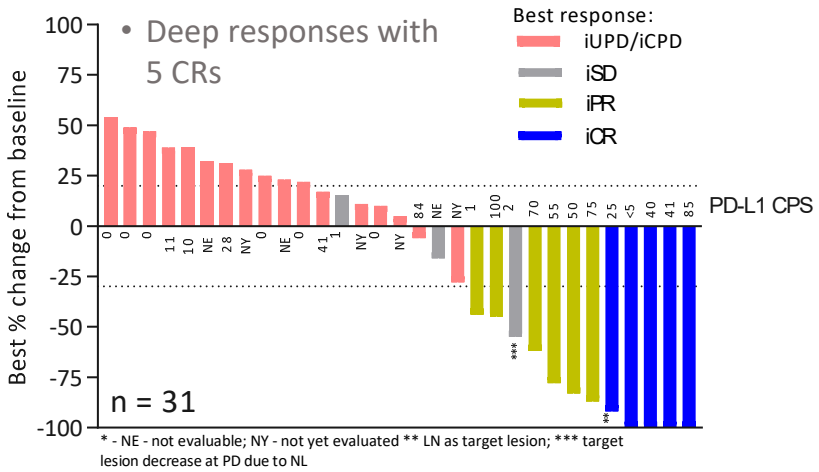
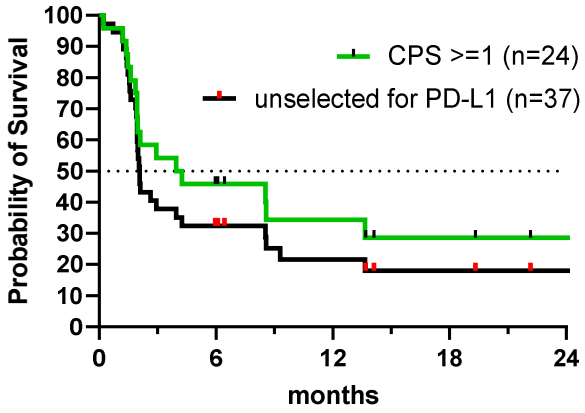


*Figure 2: Kaplan-Meier Plot PFS**



Overall:
- Median PFS 2.1 mts
- 30+ % progression free at 6 mts

Figure 3: Duration of response (DOR) for confirmed responders

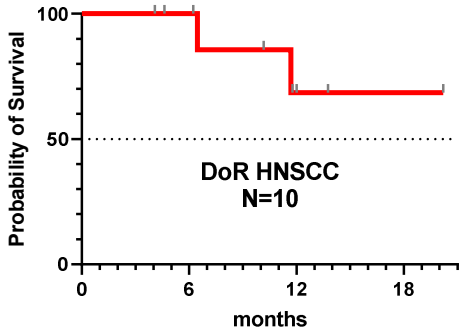


*Figure 4: Spider plot***

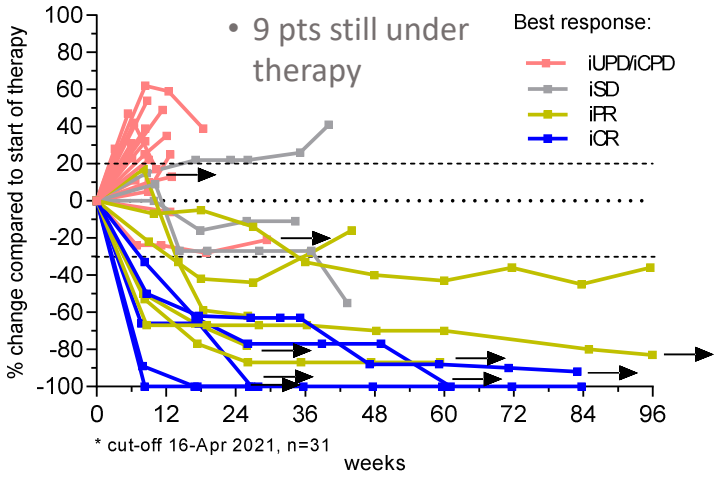


Table 6. ORR, PFS, DoR, OS for pts with CPS ≥ 1 (N=24)*

OS (58 % events)	PFS (71 % events)	ORR iRECIST (95 % CI)
• Median 12.6 mts • 54 % alive at 12 mts	• Median 4.1 mts • 45 % PFS free at 6 mts	***45.8 %*** *(25.6-67.2)*

Duration of response
- 91 % confirmed responses
  - *80 % confirmed responses ongoing (censoring at 4-20 months → Figure 3)*
  - *No progression prior to 6 months DOR*
- Median duration of response cannot be estimated yet

* ≥ 1 treatment and no death due to COVID-19 prior to first post-baseline staging (N=37)
** >= 1 post baseline tumor staging (N=31)

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
NL… new lesion
DOR… Duration of Response
→ *…. patients still under therapy*

TACTI-002: Phase II of efti and pembrolizumab in 2nd line HNSCC (Part C)
CONCLUSION

SAFETY

- Treatment with efti plus pembrolizumab is well-tolerated with no new safety signals
- Majority of most frequent adverse events are mild to moderate
- Safety profile compares well to KN-040 (pembrolizumab monotherapy)

EFFICACY

- Encouraging ORR (30 % acc. to iRECIST) in patients unselected for PD-L1
- 13.5 % complete responses observed
- Responses were durable with median DOR not yet reached
- In pts with PD-L1 CPS ≥1, ORR was 45.8 % (95 % CI 25.6-67.2), median PFS of 4.1 months and median OS of 12.6 months
- Efficacy in PD-L1 CPS ≥1 encouraging compared to KN-040 (PIII, randomized trial)

The combination of efti plus pembrolizumab is well-tolerated and shows encouraging signs of activity supporting further clinical investigation. A study in 1st line HNSCC patients has been initiated (NCT04811027).

AE… adverse event
PD-L1, PD-L2…Programmed Death ligand-1, -2
PFS… progression-free survival
ORR… objective response rate

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