Results from a Phase II study of eftilagimod alpha (soluble LAG-3 protein) and pembrolizumab in patients with PD-L1 unselected metastatic 2nd line head and neck squamous cell carcinoma (HNSCC)

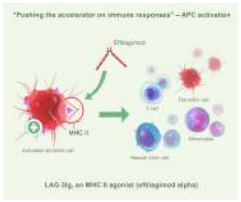
Abstract # 359

López Pousa[1], E Felip[2], M Forster[3], B Doger[4], P Roxburgh[5], P Bajaj[6], J A Peguero[7], E Carcereny[8], M Krebs[9], C Mueller[10], F Triebel[11]

[1]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [2]Vall d' Hebron Institute of Oncology, Barcelona, Spain; [3]UCL Cancer Institute / University College London Hospitals NHS Foundation, London, UK; [4] START Madrid- Fundacion Jimenez Díaz, Madrid, Spain; [5]Institute of Cancer Sciences, University of Glasgow and The Beatson West of Scotland Cancer Centre, Glasgow, UK; [6]Tasman Oncology, Southport, Australia; [7]Oncology Consultants, P.A., Houston, Texas; [8]Catalan Institute of Oncology Badalona-Hospital Germans Trias i Pujol, B-ARGO group, Badalona, Spain; [9]Division of Cancer Sciences, The University of Manchester and The Christie NHS Foundation Trust, Manchester, UK; [10] Clinical Development, Immutep GmbH, Berlin, Germany; [11]Research & Development, Immutep S.A.S., Orsay, France

BACKGROUND

Figure 1. efti's mechanism of action



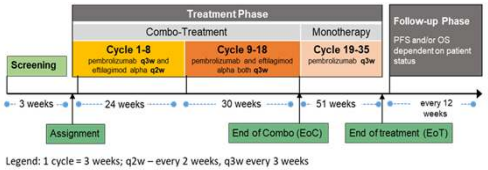
Eftilagimod alpha (efti) is a soluble LAG-3 protein binding to a subset of MHC class II molecules, thus mediating antigen presenting cell (APC) and CD8 T-cell activation (**Figure 1**). Such stimulation of the dendritic cell network and resulting T cell recruitment may lead to stronger anti-tumor responses in combination with pembrolizumab than observed with pembrolizumab alone. We report results from the 2nd line metastatic head and neck squamous cell carcinoma (HNSCC) cohort (Part C) of the TACTI-002 study (NCT03625323).

METHODS

Study Design and Patients

- Non-randomized, multinational, open-label, trial for 2nd line, PD-X naive, PD-L1 all-comer HNSCC patients.
- Simon's optimal two stage designed trial, sponsored by Immutep in collaboration with Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA (MSD).
- Efti is administered as a 30 mg subcutaneous injection every 2 weeks for the first 8 cycles and every 3 weeks for the following 9 cycles. Pembrolizumab is administered at a standard dose of 200 mg intravenous infusion every 3 weeks for maximum of 2 years (**Figure 2**).

Figure 2. Study design



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

Assessments and Statistical Analyses:

- **Primary Endpoint:** Objective response rate (ORR), as per iRECIST.
- **Secondary Endpoints:** Progression free survival (PFS), overall survival (OS), safety and tolerability, PK/PD and exploratory biomarkers.
- Central assessment of tumor cell PD-L1 expression (by Dako PD-L1 immunohistochemistry (IHC) 22C3 pharmDx) after enrolment.
- Imaging performed every 9 weeks and reported according to iRECIST.
- Safety was analyzed in all patients who received at least one dose of study medication.
- Efficacy was analyzed in all patients with measurable disease at baseline, who received at least one dose of any study medication and did not die of COVID-19 prior to the first post-baseline assessment.
- Database cut-off date was April 16, 2021 (safety) and August 4, 2021 (efficacy); minimum follow up for efficacy was 8+ months.

BASELINE CHARACTERISTICS

- A total of 39 patients were enrolled and treated into this part of the study. Baseline characteristics are reported in **Table 1**.

Table 1. Baseline characteristics (N=39)

Baseline parameters, n(%)	
Age, median (years)	62 (37-84)
Female / Male	4 (10.3) / 35 (89.7)
ECOG 0 / 1	13 (33.3) / 26 (66.7)
Non-smoker / Ex- or Current smoker	6 (15.4) / 33 (84.6)
Previous chemotherapy	39 (100)
Previous cetuximab	16 (41.0)
Patients with lung / liver metastasis	19 (48.7) / 6 (17.6)
Primary tumor location, n (%)	
Oral cavity	12 (30.8)
Oropharynx	14 (35.9)
Hypopharynx	7 (17.9)
Larynx	6 (15.4)
PD-L1 CPS score, n (%)	
CPS <1	6 (15.4)
CPS 1-19	15 (38.5)
CPS ≥20	14 (35.9)
CPS not evaluable or unknown	4 (10.3)

*… evaluable set (N=31): ≥1 treatment and ≥1 post-baseline tumor staging
**… lymph node as target lesion
***… disease progression despite target lesion decrease due to new lesions
#… full analysis set (N=37): ≥1 treatment and no death due to COVID-19 prior to first post-baseline staging
¶ … not evaluable set (N=6): dropped off prior to first staging or were not evaluable post-baseline for any reason
→ … still under therapy
• … treated beyond progression

EFFICACY

Figure 3. Spider plot (N=31)*

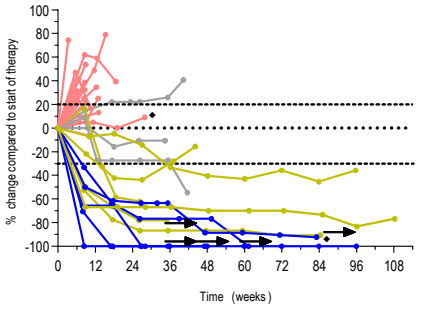


Figure 4. Waterfall plot (N=31)*

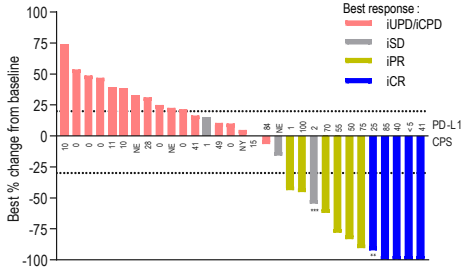


Table 2. Best overall response (iRECIST), all comer N=37#

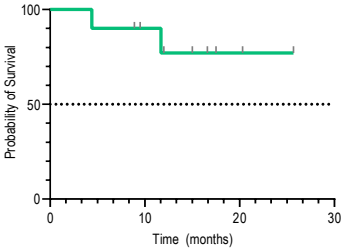
Best overall response, iRECIST	Investigator assessment N (%)
Complete Response	**5 (13.5)**
Partial Response	**6 (16.2)**
Stable Disease	3 (8.1)
Progression	17 (45.9)
Not evaluable¶	6 (16.2)
Disease Control Rate	14 (37.8)
Overall Response Rate [95% CI]	**11 (29.7) [15.9 – 47.0]**
Overall Response Rate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

Table 3. Response according to PD-L1 subgroup

CPS score	All comer (N=37)	≥1 (N=27)	≥20 (n=14)
ORR (iRECIST)			
ORR, %	29.7	40.7	64.3
Overall survival			
No. of events	23	17	7
6-month OS, %	54.7	55.5	71.4
12-month OS, %	48.4	48.2	64.3
Progression-free survival			
No. of events	30	17	8
3-month PFS, %	37.8	48.2	64.3
6-month PFS, %	32.4	40.7	57.1

- ORR (IRECIST) of 35.5% in evaluable patients (**Table 2**).
- 5 patients (13.5%) with complete responses (**Table 2**).
- 5 patients still under therapy and 1 patient completed 2 years of therapy (**Figure 3**).
- Responses seen in PD-L1 low and high expressors (**Figure 4**).
- 91% of responses confirmed.
- Median duration of response not reached; all ongoing responses lasting 9+ months (**Figure 5**).
- ORR, 6-month PFS and 12-month OS rates for PD-L1 CPS ≥1 patients are 40.7%, 41% and 48% respectively (**Table 3**).
- ORR, 6-month PFS and 12-month OS rates for PD-L1 CPS ≥20 patients are 64.3%, 57.1% and 64.3%, respectively (**Table 3**).

Figure 5. Duration of response for confirmed responders (N=10)



EXPOSURE AND SAFETY

Table 4. General overview of adverse events (N=39)

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 efti	6 (15.4)
thereof related to efti/pembro	0 / 0
Patients with TEAEs leading to discontinuation of pembro	7 (17.9)
thereof related to efti/pembro	1 / 2.6

Table 5. Treatment-emergent adverse events occurring ≥10% (N=39)

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)	-

- The most common TEAEs were hypothyroidism (20.5%), cough (17.9%) and asthenia (15.4%) (**Table 5**).
- No treatment-related deaths occurred (**Table 4**).

CONCLUSION

- Encouraging ORR (30% according to iRECIST) in patients unselected for PD-L1.
- 13.5% complete responses observed.
- Durable, deep responses with median DoR not yet reached and min. duration of 9+ months.
- Trends compare favorably to KEYNOTE-040 (ORR ~15%)[1] in a comparable patient population.
- The combination of efti plus pembrolizumab is well-tolerated with no new safety signals.
- Majority of most frequent adverse events are mild to moderate.
- Data has led to fast-track designation by the US FDA for 1st line HNSCC, resulting in a phase IIb study comparing efti and pembrolizumab to pembrolizumab alone in PD-L1-positive 1st line HNSCC patients (NCT04811027).

APC…antigen-presenting cell
CI…confidence interval
ECOG…Eastern Cooperative Oncology Group
HNSCC…head & neck squamous cell cancer
iRECIST…Immune Response Evaluation Criteria In Solid Tumors
LAG-3…Lymphocyte Activation gene-3
MHC…Major Histocompatibility Complex
NSCLC…non-small cell lung cancer
PD…pharmacodynamics
PD-L1…Programmed Death ligand-1
PD-X…PD-1 or PD-L1 targeted therapy
PFS…progression-free survival
PK…pharmacokinetics
PT…preferred term
ORR…objective response rate
SAE…serious adverse event
TEAE…treatment-emergent adverse event
TRAE…treatment-related adverse event

1. Cohen E, et al. Lancet 2019; 393: 156-167. (KN-040)

Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA provided pembrolizumab for the study.
The trial identifiers are IMP321-P015 (Sponsor code), Keynote-PN798 (MSD code), 2018-001994-25 (EudraCT) and NCT03625323 (ClinicalTrials.gov).
Corresponding author: Frederic Triebel, frederic.triebel@immutep.com