AACR American Association for Cancer Research
ANNUAL MEETING

immutep
LAG-3 IMMUNOTHERAPY

Poster Board: 18

LB-394

Initial results from a Phase II study (TACTI-002) in Non-Small Cell Lung Cancer, or Head and Neck cancer patients receiving eftilagimod alpha (a soluble LAG-3 protein) and pembrolizumab

27th April 2020

Presenting Author: Martin Forster, *University College London Hospitals NHS Foundation, London, UK*

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).
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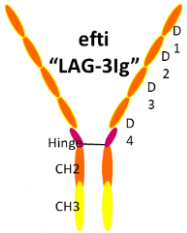
Eftilagimod alpha (efti)

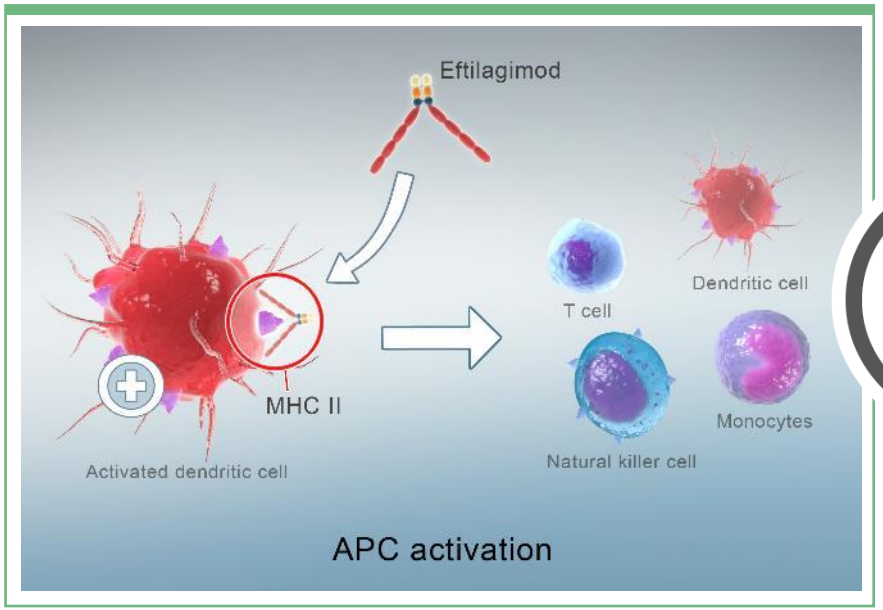
Innovative LAG-3 I-O Product Candidate



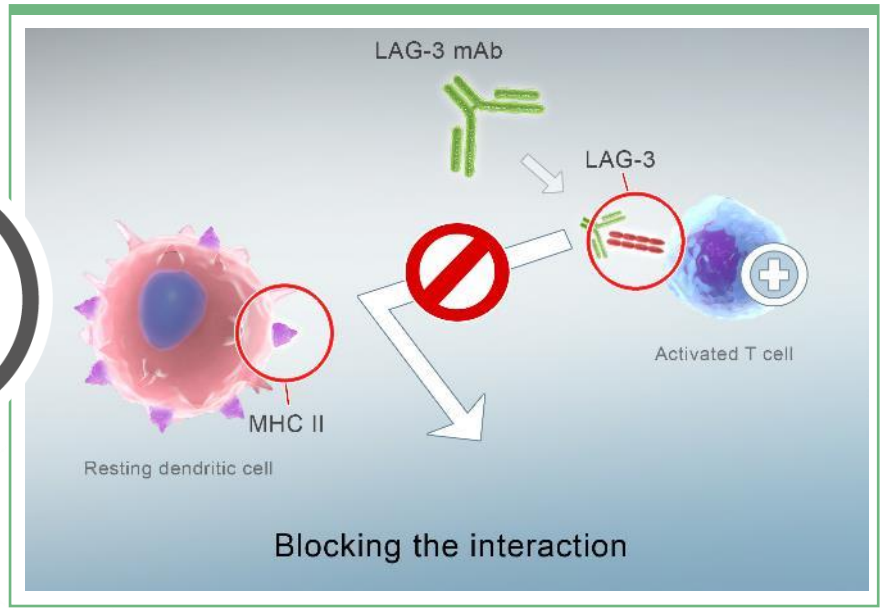
MoA: Efti is a soluble LAG-3 protein targeting a subset of MHC class II on APC to mediate antigen presenting cell (APC) and then CD8 T-cell activation.

Rationale: Efti activates APCs and leads to an increase in activated T cells which effect potentially reduces the number of non-responders to pembrolizumab.

"PUSHING THE ACCELERATOR ON IMMUNE RESPONSES"



"RELEASING THE BRAKE ON THE T CELL"



Efti is an **MHC II agonist**
APC activator

- boost and sustain the $CD8^+$ T cell responses
- activate multiple immune cell subsets

LAG-3 antagonist, or blocking, antibodies:
Immune checkpoint inhibitor

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

eftilagimod alpha
TACTI-002

Trial Design + Introduction

- → *Phase II, multi-national, open label, PD-L1 (central assessment) all comer trial*
- → *The study has a Simon's optimal two-stage design. During the first stage, N1 patients are recruited. Additional patients (N2) will be recruited for each part if the pre-specified threshold for ORR is met. In total, 109 patients planned*
- → *In collaboration with Merck Sharp & Dohme (MSD)*

Eligiiblity

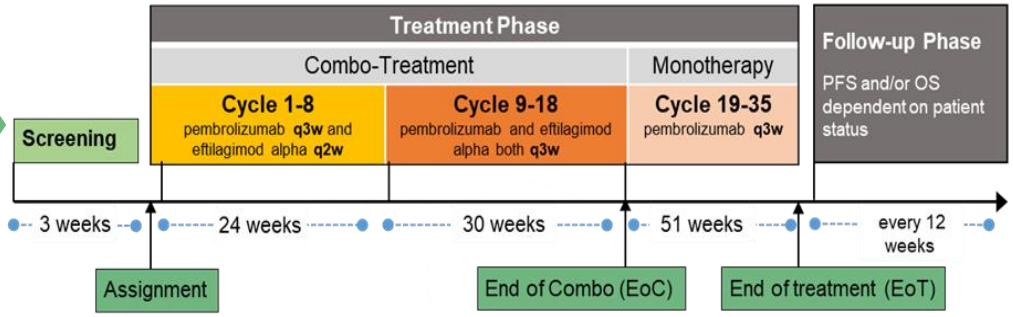
- Available tumor tissue
- ECOG 0-1
- Adequate organ functions
- **PD-L1 all comer**

Part A:
1st line NSCLC stage IIIB/IV, PD-X naïve, not eligible to EGFR/ALK therapy

Part B:
2nd line met. NSCLC, refractory for PD-1/PD-L1

Part C:
Incurable 2nd line met. HNSCC after platinum therapy

30 mg efti SC + 200 mg pembrolizumab IV for 12 months + pembrolizumab alone for another 12 months



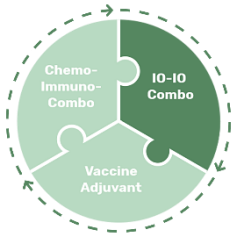
Legend: 1 cycle = 3 weeks; q2w – every 2 weeks, q3w every 3 weeks

Primary Objective: Overall Response Rate (iRECIST)

Secondary:
PFS, OS, PK, biomarker, PD, safety and tolerability

Reported here: Safety all parts, initial efficacy Part A and part C stage 1

Notes:
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



eftilagimod alpha - TACTI-002 Results[1] – all parts stage 1

Exposure and Safety

Summary

- In total 63 pts were enrolled until data cut-off[1]. Recruitment is ongoing.
- Pts received median 6 (range 1-22) efti injections and median of 5 (range 1-19) pembrolizumab infusions
- 20 pts (31.7%) had ≥ 1 TESAE
- 24 pts (38.1 %) had 1 TEAE ≥ grade 3 (thereof 5 pts (7.9 %) drug related)
- 5 fatal TEAEs (hemoptysis G5; bronchospasm G5, respiratory failure G4, respiratory failure G5, malignant neoplasm progress G5) were reported – all unrelated to both study drugs
- 3 TEAEs (hepatitis drug induced G4; ALT and AST elevation G3; syncopal event G3) lead to discontinuation both study drugs - first 2 were assessed as related to both study drugs

TEAEs occured in ≥10 % of pts (N=63 in total)

Adverse event (PT)	Any Grade N (%)	Grade 3 N (%)	Grade 4 N (%)
Cough	20 (31.7)	-	-
Asthenia	13 (20.6)	-	-
Decreased appetite	11 (17.5)	-	-
Dyspnoe	11 (17.5)	3 (4.8)	1 (1.6)
Fatigue	10 (15.9)	1 (1.6)	-
Diarrhoea	9 (14.3)	1 (1.6)	-
Upper respiratory tract infection	8 (12.7)	-	-
Constipation	7 (11.1)	1 (1.6)	-
Nausea	7 (11.1)	-	-

- Injection site reactions all were reported related to efti
- No new safety signals observed thus far

Notes:

(1) Preliminary data, cut-off 20-Mar 2020; TEAE – treatment emergent adverse events regardless of causality; TESAE – treatment emergent serious adverse events regardless of causality

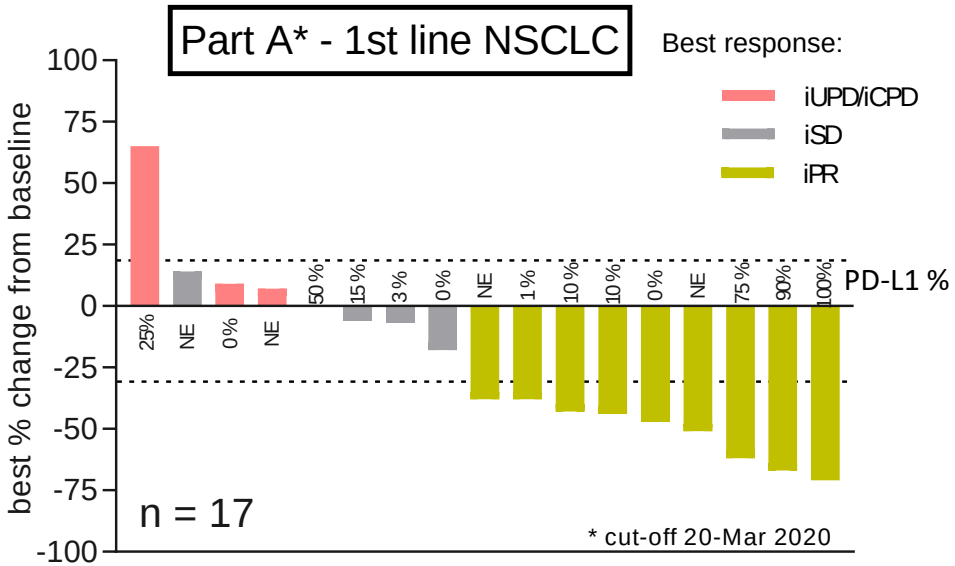
eftilagimod alpha - TACTI-002 Results[1] - 1st line NSCLC (part A, stage 1)

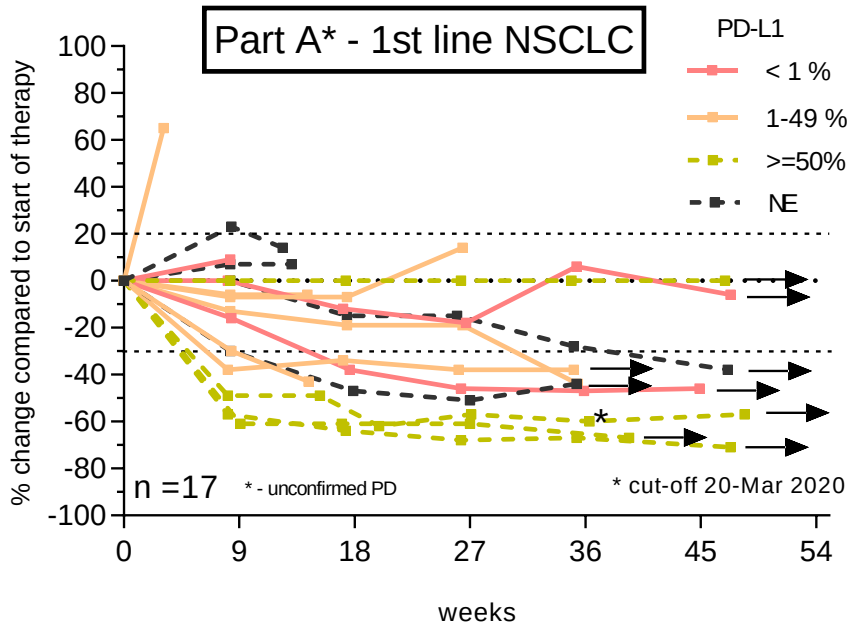
Baseline Characteristics + efficacy

- PD-L1 distribution as historically expected with 31 % of evaluable pts ≥ 50 % → PD-L1 all comer trial
- 65 % male, 71 % ECOG 0, median age 65 yrs, 94 % smokers, 59 % Squamous + 41 non-squamous → typical NSCLC 1st line pts

Tumor response - iBOR as per iRECIST	N (%) Total (N=17)
Complete Response (iCR)	0 (0.0)
Partial Response (iPR)	9 (52.9)
Stable Disease (iSD)	5 (29.4)
Progressive Disease (iPD)	3 (17.7)
Objective Response Rate (iORR)	**9 (52.9)**
Disease Control Rate (iDCR)	**14 (82.4)**

- 12/17 (71 %) patients with target lesion decrease
- Responses in all PD-L1 subgroups (3/9 iPRs in ≥ 50 % subgroup)
- 6/9 iPRs confirmed and treatment ongoing in 7/9
- At data cut-off 9 pts (53 %) were still under treatment (8+ months) → median not yet reached
- Two late responders after 8 and 10 months





Notes:
(1) Preliminary data, cut-off March 20 2020
(2) % in reference to evaluable samples; 4 specimens not evaluable by central lab using standard IHC kit
(3) Garon et al N Engl J Med 2015;372:2018-28

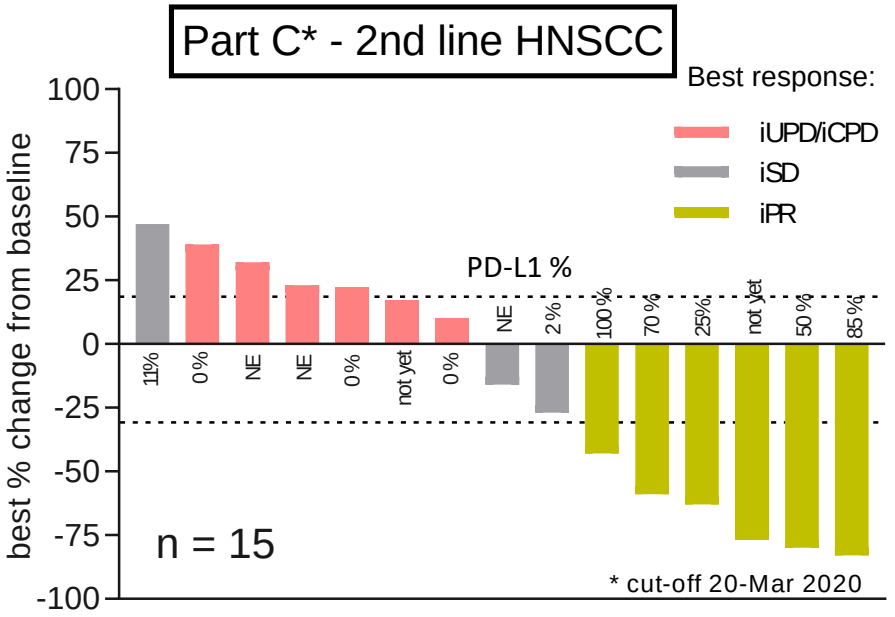
eftilagimod alpha - TACTI-002 Results[1] – 2nd line HNSCC (part C, stage 1)

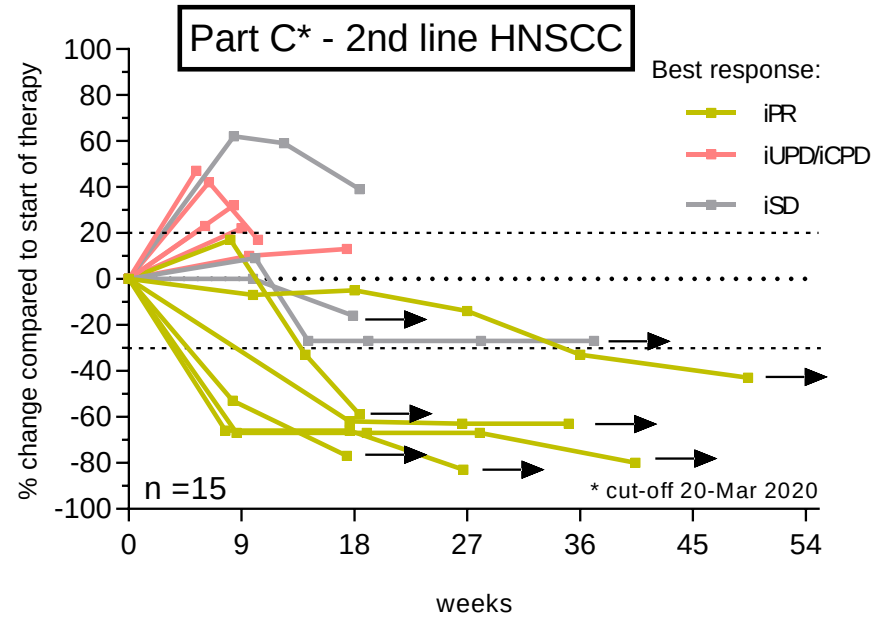
Baseline Characteristics + efficacy

- Median age 66, 94 % male, 47 % ECOG 1, different HNSCC subtypes -> typical 2nd line HNSCC population

Tumor response - iBOR as per iRECIST	N (%) Total (N=18)
Complete Response (iCR)	0 (0.0)
Partial Response (iPR)	6 (33.3)
Stable Disease (iSD)	3 (16.6)
Progressive Disease (iPD)	6 (39.9)
Not evaluable*	2 (11.1)
Not yet evaluated**	1 (5.6)
Objective Response Rate (iORR)	**6 (33.3)**
Disease Control Rate (iDCR)	**9 (50.0)**

- Initial iORR of 33.3 % in this PD-L1 all comer 2nd line HNSCC pts (1 pt with outstanding imaging)
- 5 responses confirmed; all 6 pts with PR still under therapy
- 1 iPR after pseudoprogression, 1 iPR at 8 months, responses getting deeper over time
- At cut-off 9 pts (50 %) still under therapy - HNSCC 2nd line patients





* - dropped out prior to first restaging

** - not yet staged still on therapy for > 9 weeks

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