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LAG-3 IMMUNOTHERAPY

A soluble LAG-3 protein (eftilagimod alpha) with an anti-PD-1 antibody (pembrolizumab): results of a phase II study in NSCLC and HNSCC

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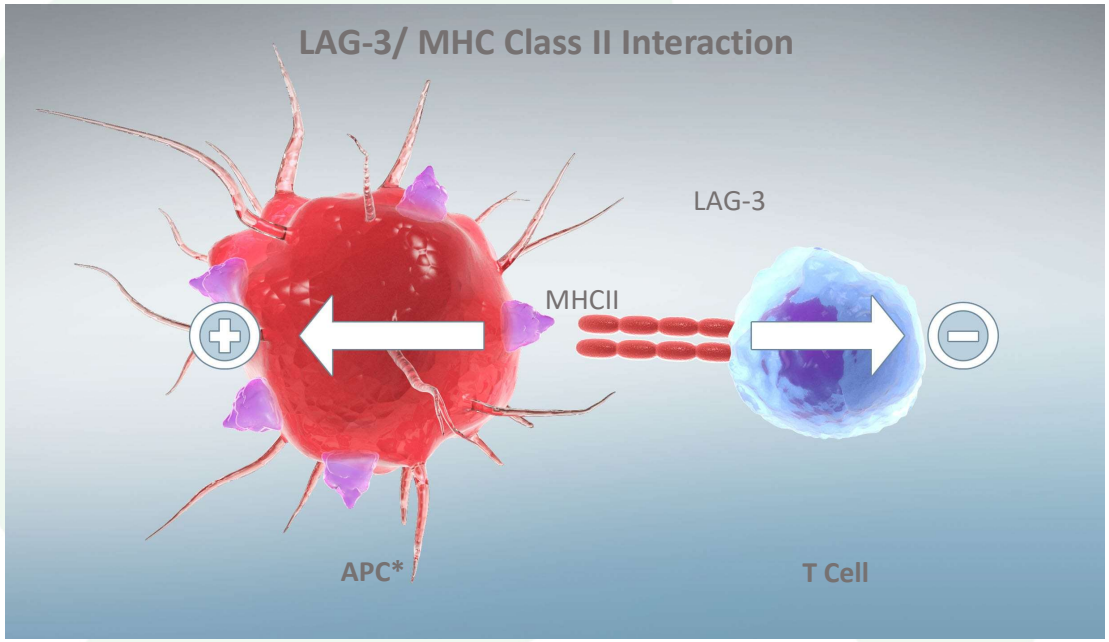
LAG-3 as a Therapeutic Target

LAG-3 is widely expressed on tumor infiltrating lymphocytes (TILs) and cytotoxic T cells →
Prime target for an immune checkpoint blocker

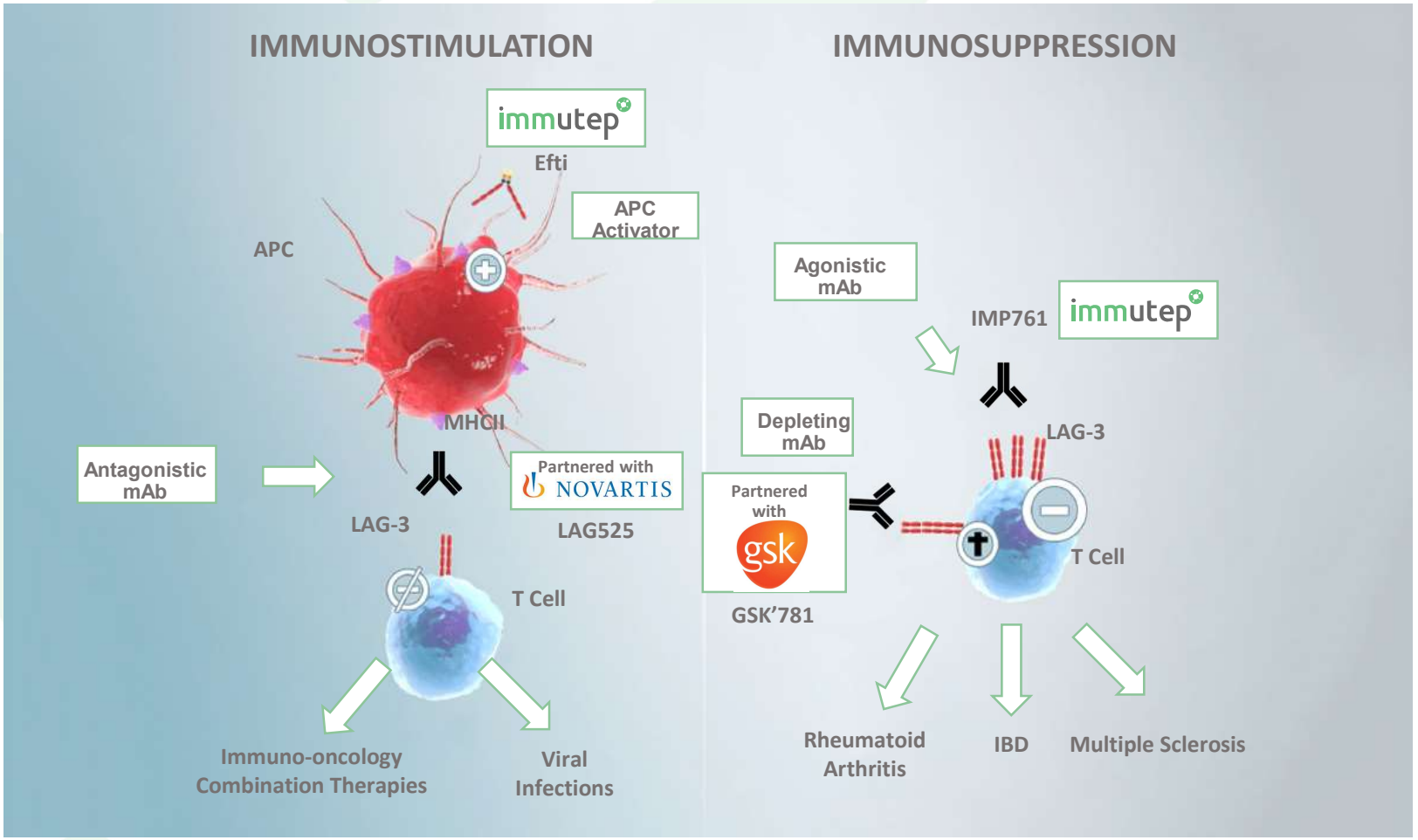


→ **Positive regulation** of antigen presenting cells (APC) → increase in antigen presentation to cytotoxic $CD8^+$ T cells

→ **Negative regulation** of $LAG\text{-}3^+$ T Cells

Notes:
* APC: antigen presenting cell

Targeting LAG-3/MHC II May Lead to Multiple Therapeutics in Numerous Indications



Opportunity for Eftilagimod Alpha

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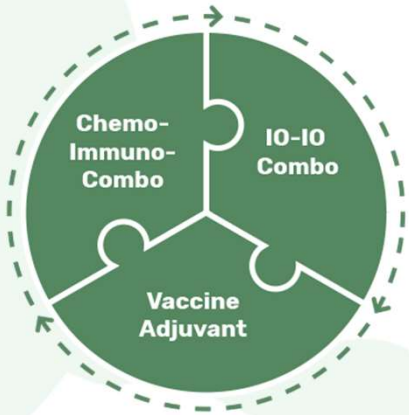
Efti has multiple shots on goal in different indications and in different combinations

- **Best-and-First-In-Class** MHCII agonist
- Good safety profile and encouraging efficacy data thus far
- Estimated favorable (low) cost of goods, current flat dosing and manufacturing process
- Potential for use in various combination settings – **potential pipeline in a product**



• Late Stage European Phase IIb AIPAC (Immutep)

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

• 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). This extension of INSIGHT is also referred to as INSIGHT-004
(3) INSIGHT Investigator Initiated Trial ("IIT") is controlled by lead investigator and therefore Immutep has no control over this clinical trial

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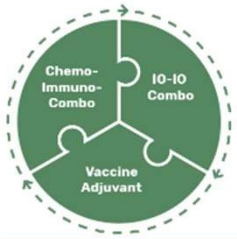
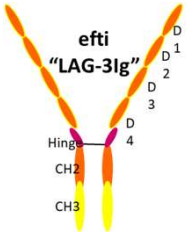
TACTI trials: Two ACTive Immunotherapies

“Pushing the gas on the APC while releasing the brake on the T cell”



Eftilagimod alpha (efti)

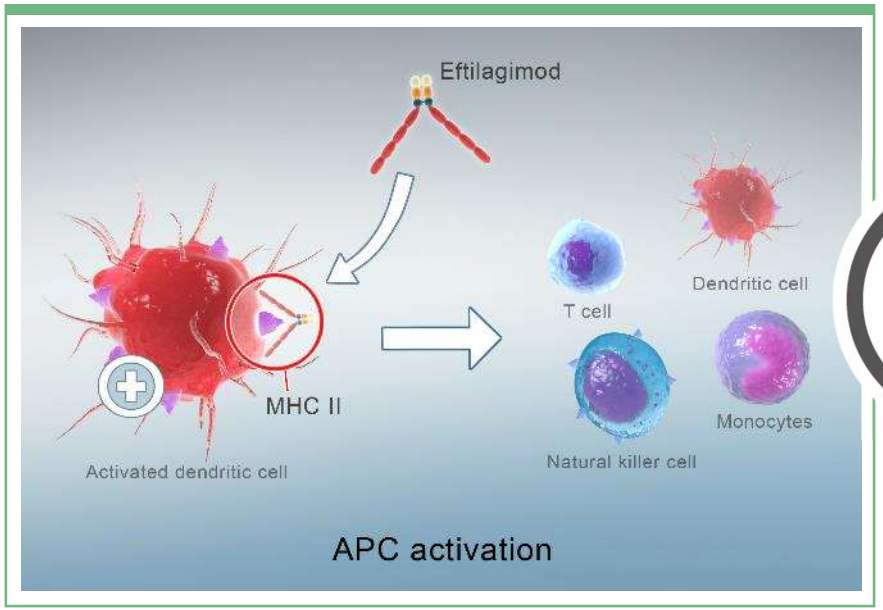
Innovative LAG-3 I-O Product Candidate



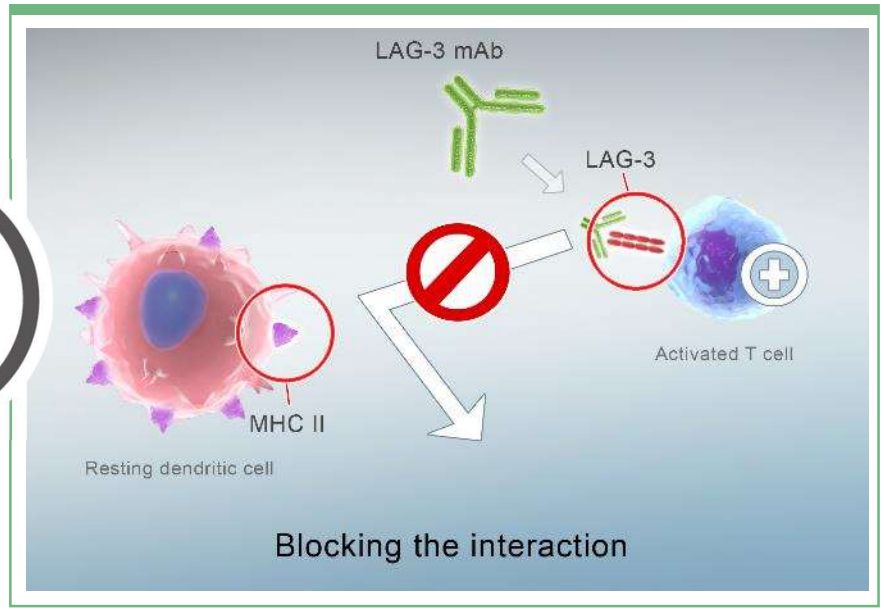
MoA: Efti is a soluble LAG-3 protein targeting a subset of MHC class II on APC to mediate antigen presenting cell (APC) and then CD8 T-cell activation.

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

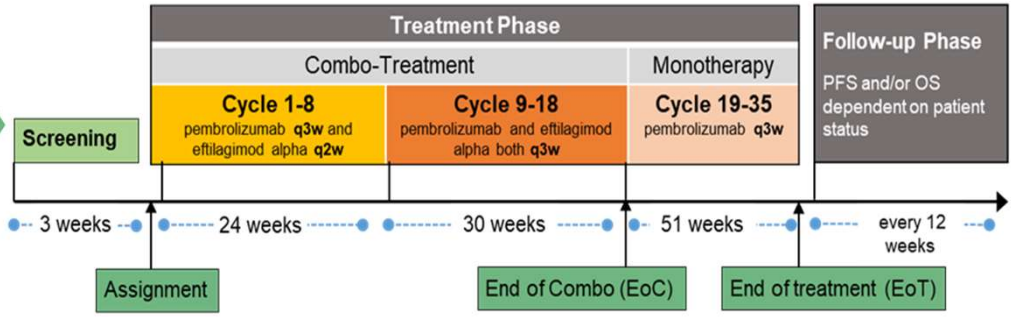
- Available tumor tissue
- ECOG 0-1
- Adequate organ functions
- **PD-L1 all comer***

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

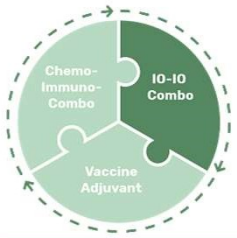
Primary Objective:
Overall Response Rate (iRECIST)

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

* - assessed centrally

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

Exposure and Safety

Summary

- In total, 88 pts were enrolled in all three parts and all stages until data cut-off1.
- Pts received median 5.5 (range 1-22) efti injections and median of 4 (range 1-25) pembrolizumab infusions
- 27 pts (30.7%) had ≥ 1 SAE
- 42 pts (47.7%) had 1 TEAE ≥ grade 3
- 12 fatal TEAEs were reported – all unrelated to both study drugs
- 3 TEARs leading to permanent discontinuation of treatment (drug induced hepatitis G4; ALT & AST elevation G3; diarrhoea G1)
- Injection site reactions (all G1) were reported related to efti

TEAEs occured in ≥10 % of pts (N=88 in total)

Adverse event (PT)	Any Grade N (%)	Grade 3 N (%)	Grade 4 N (%)
Asthenia	25 (28.4)	2 (2.3)	-
Cough	24 (27.3)	1 (1.1)	-
Decreased appetite	19 (21.6)	-	-
Dyspnoea	18 (20.5)	7 (8.0)	1 (1.1)
Fatigue	16 (18.2)	1 (1.1)	-
Diarrhoea	13 (14.8)	1 (1.1)	-
Pruritus	12 (13.6)	-	-
Constipation	11 (12.5)	1 (1.1)	-
Back pain	11 (12.5)	-	-
Anaemia	10 (11.4)	1 (1.1)	-
Musculoskeletal pain	10 (11.4)	-	-

No new safety signals observed thus far

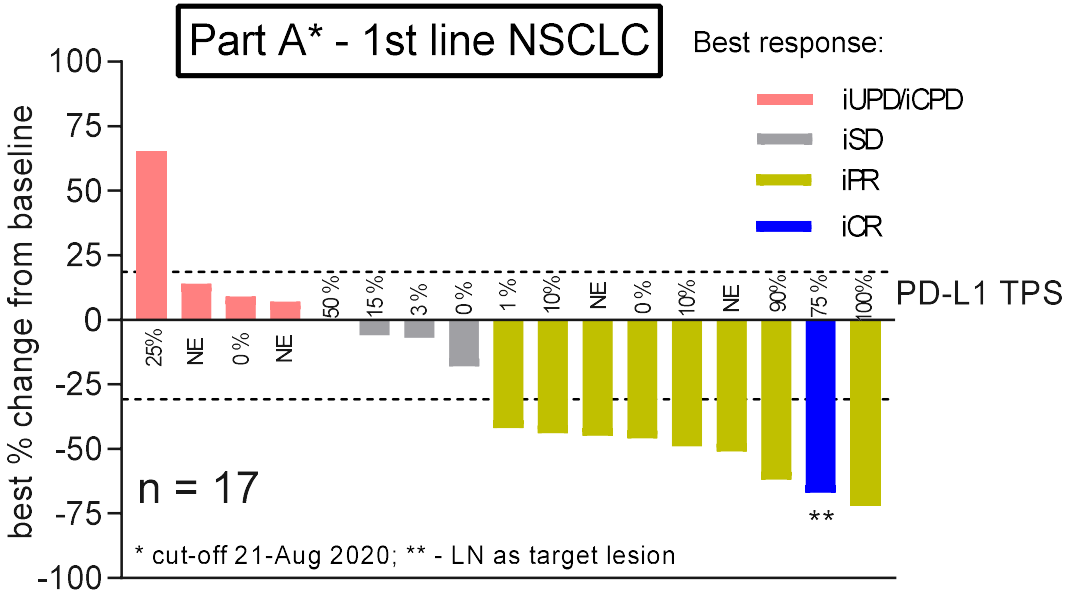
Notes:
(1) Preliminary data, cut-off 21-Aug 2020

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

Responses and Waterfall plot

- → *52.9 % iORR acc. to iRECIST in this PD-L1 all comer trial*
- → *Responses in all PD-L1 subgroups*

Tumor response - iBOR as per iRECIST	N (%) Total (N=17)
Complete Response (iCR)	1 (5.9)
Partial Response (iPR)	8 (47.1)
Stable Disease (iSD)	4 (23.5)
Progressive Disease (iPD)	4 (23.5)
Objective Response Rate (iORR)	**9 (52.9) 95 % CI [27.8 – 77.0]**
Disease Control Rate (iDCR)	**14 (76.5)**



- Responses in all PD-L1 subgroups
- 8/9 iPR confirmed
- 12/17 (71 %) patients with target lesion decrease
- 5/7 iPR with NSQ; 4/10 with SQ

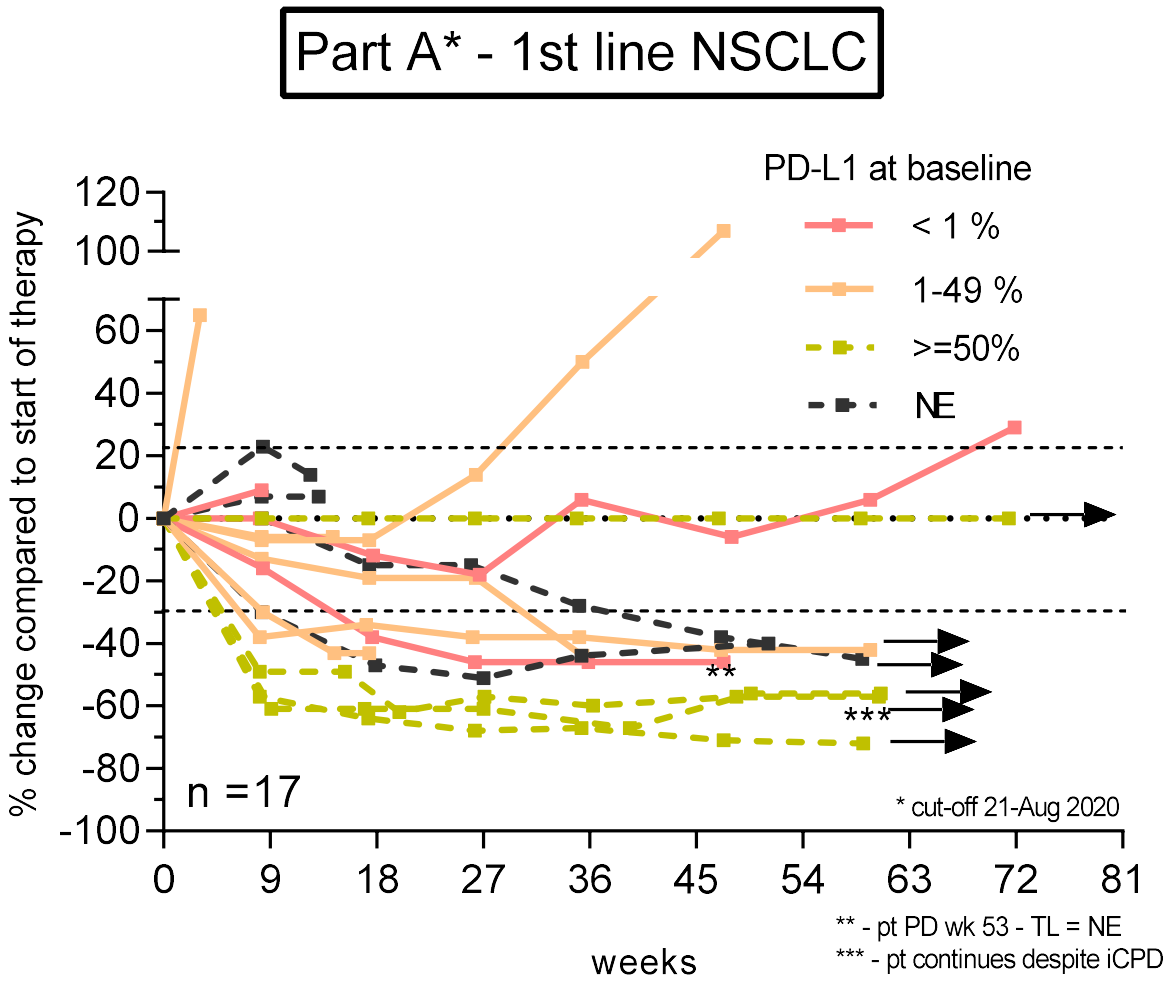
Patients by PD-L1 category	No. of Responses	No of pts
Low (< 1 %)	1	3
Medium (1-49 %)	3	6
High (≥ 50 %)	3	4
Not evaluable	2	4
Overall	**9**	17

Notes:
(1) Preliminary data, cut-off 21-Aug 2020

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

Spiderplot

→ *At data cut-off 6 pts (35 %) still under treatment (12+ months)*



- 2 late responders at 8 / 11 months
- 6 pts (35%) still under therapy at 12+ months

Notes:
(1) Preliminary data, cut-off 21 Aug 2020

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

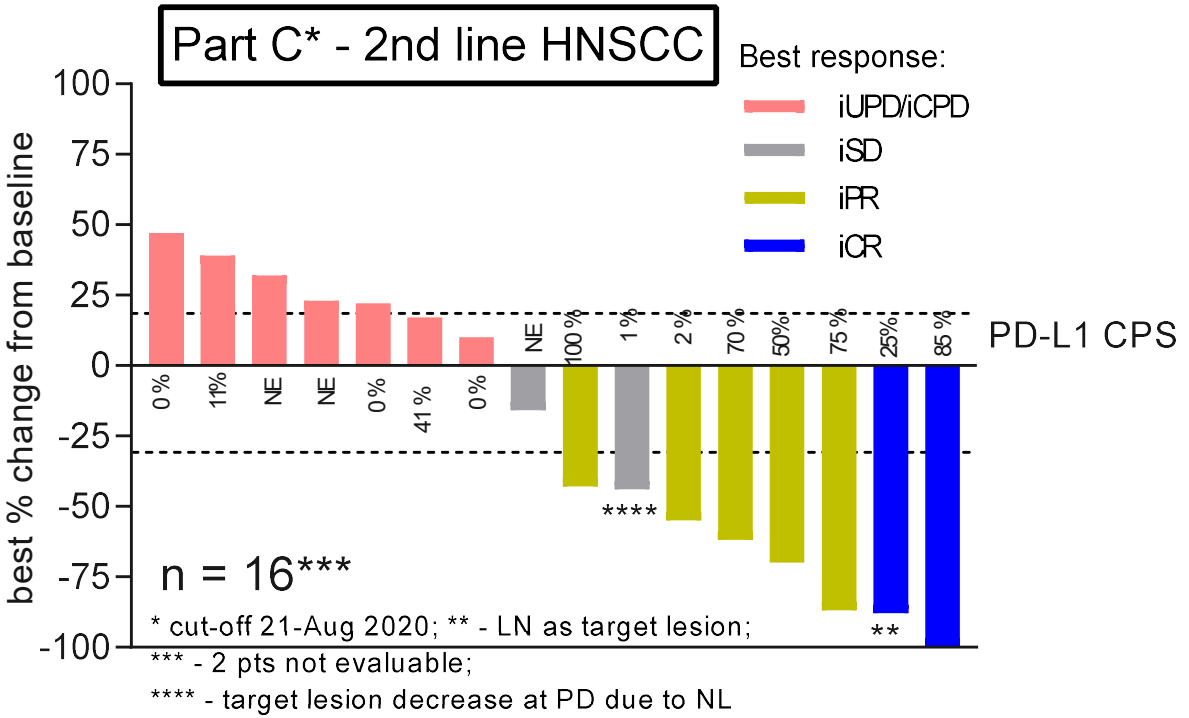
Responses and Waterfall plot

→ *Initial iORR of 39 % in this PD-L1 all comer HNSCC 2nd line patients*

- 18 patients enrolled, treated and evaluated (16 with ≥ 1 post baseline scan)

Tumor response - as per iRECIST	N (%) Total (N=18)
Complete Response (iCR)	**2 (11.1)**
Partial Response (iPR)	5 (27.8)
Stable Disease (iSD)	2 (11.1)
Progressive Disease (iUPD/ICPD)	7 (38.9)
Not Evaluable*	2 (11.1)
Objective Response Rate (iORR) [95 % CI interval]	**7 (38.9) [17.3 – 64.3]**
Disease Control Rate (iDCR)	9 (50.0 %)
iORR – evaluable pts only	*43.8 %*

* - dropped out prior to first restaging



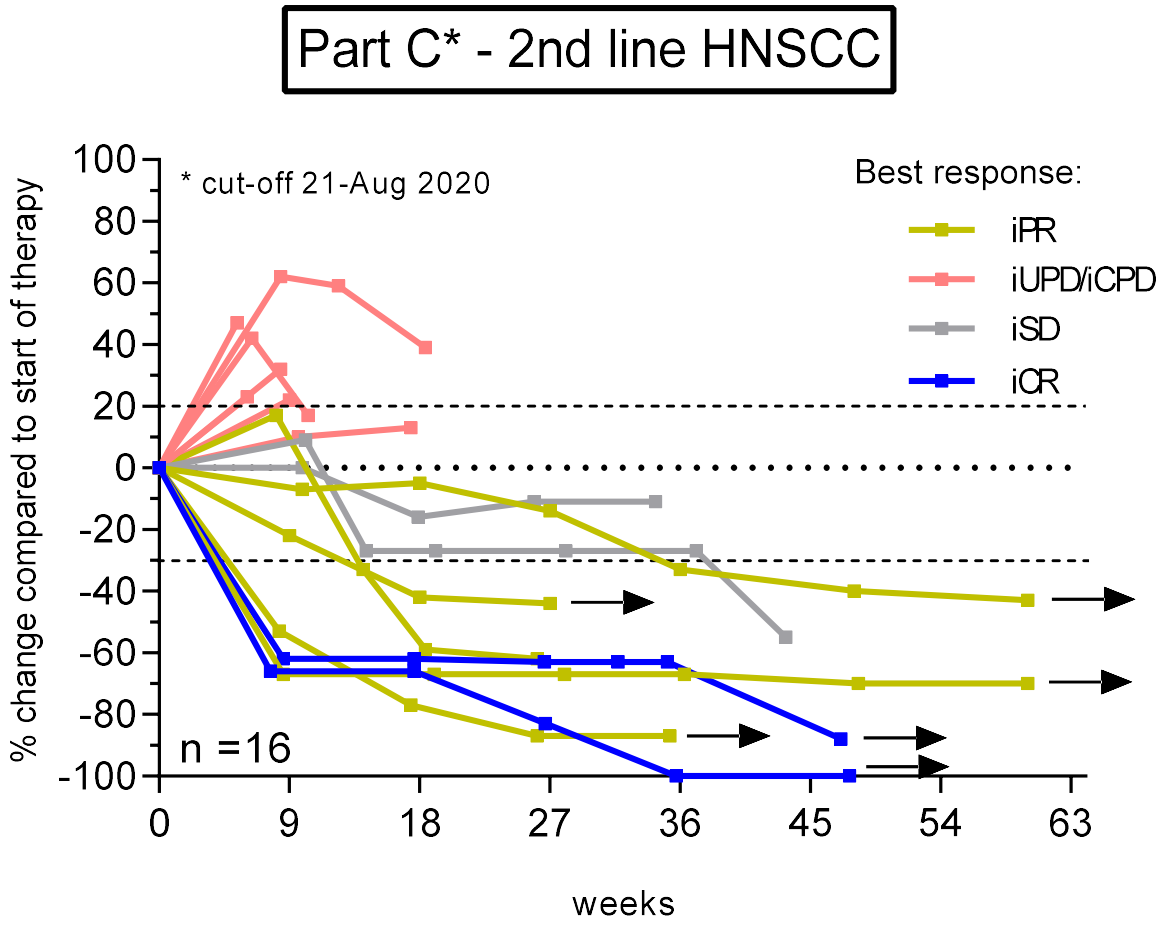
- 6 responses confirmed, 1 pt dropped out with iCPD all other on therapy
- 1 confirmed PR with < 20 % CPS

Notes:
(1) Preliminary data, cut-off 21 Aug 2020

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

Spiderplot

→ *At cut-off 8 pts (44 %) still under therapy - HNSCC 2nd line patients*



- 1 iPR after pseudoprogression
- 1 iPR very late at 8 months
- Responses getting deeper over time

Notes:
(1) Preliminary data, cut-off 21 Aug 2020

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Thank you

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