Initial results from a Phase II study (TACTI-002) in metastatic non-small cell lung or head and neck carcinoma patients receiving eftilagimod alpha (soluble LAG-3 protein) and pembrolizumab

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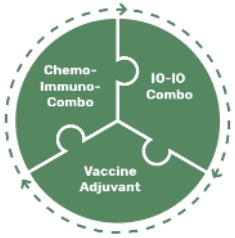
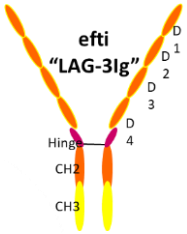


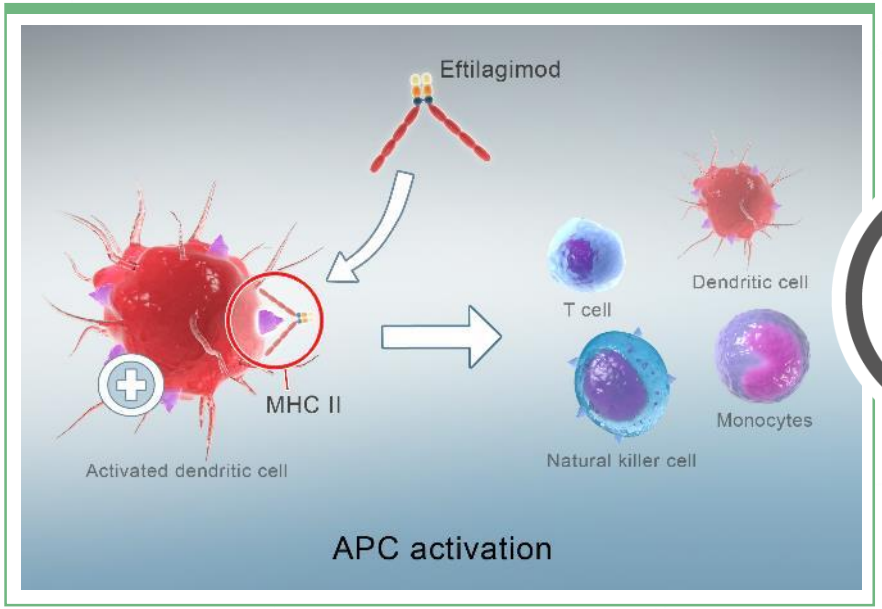
Eftilagimod alpha (efti)

Innovative LAG-3 I-O Product Candidate



- Efti is a soluble LAG-3 protein targeting a subset of MHC class II on APC
- Potentially synergistic with other therapeutic agents, e.g. I-O agents or chemotherapies

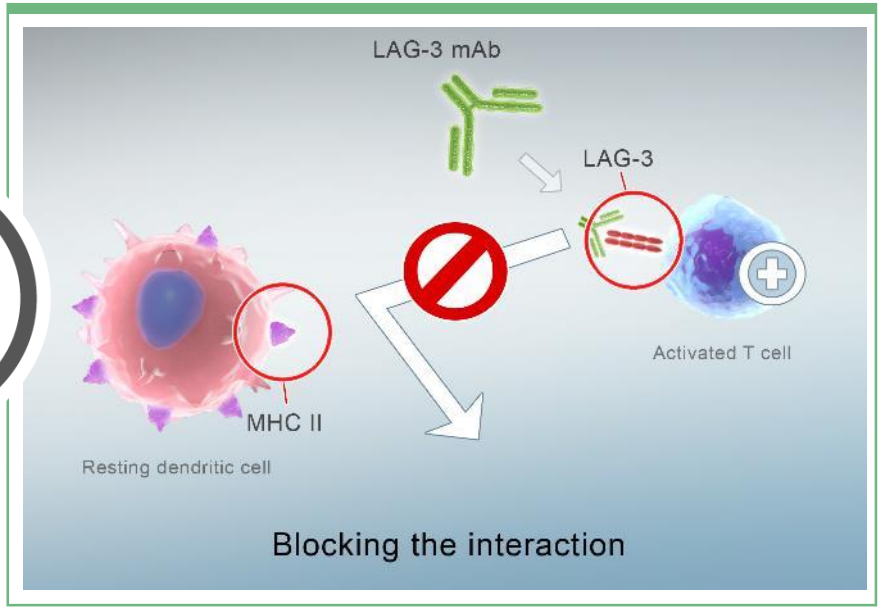
"PUSHING THE ACCELERATOR ON IMMUNE RESPONSES"



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

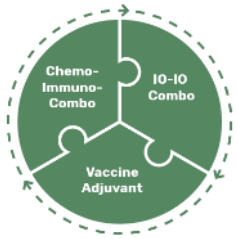
- boost and sustain the CD8⁺ T cell responses
- activate multiple immune cell subsets

"RELEASING THE BRAKE ON THE T CELL"



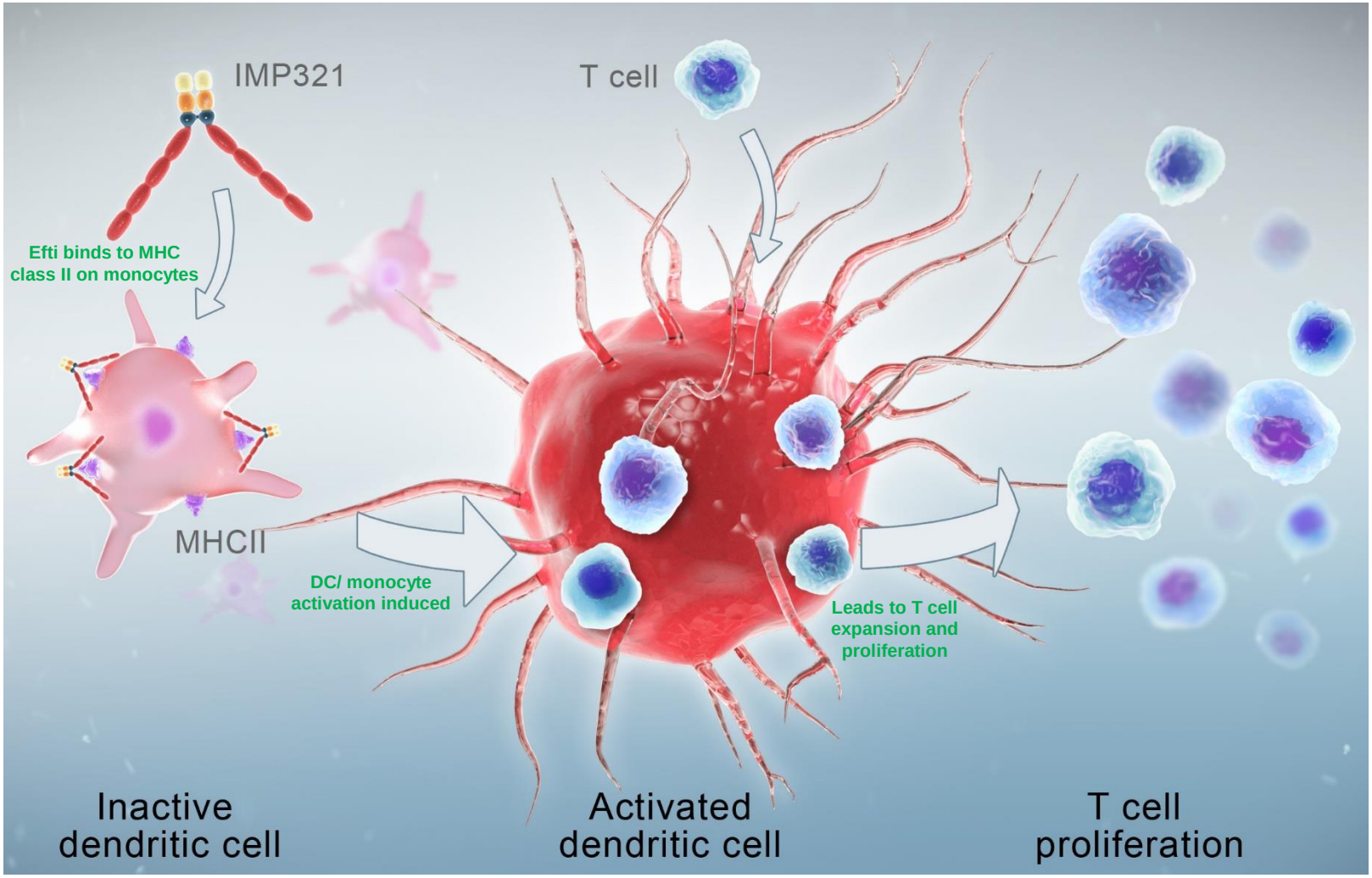
LAG-3 antagonist, or blocking, antibodies:
Immune checkpoint inhibitor

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



Eftilagimod alpha (efti): a soluble LAG-3 protein Mechanism of Action (MoA)

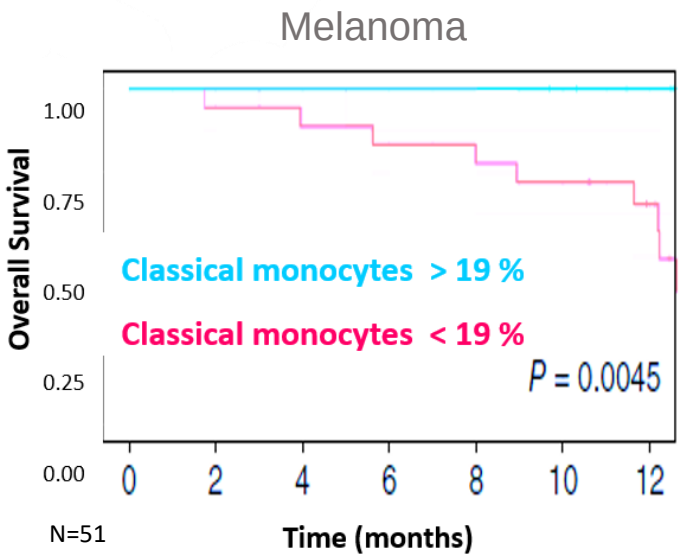
Efti's unique agonistic MoA leads to T cell expansion and proliferation
→ pushing the gas on the immune response



eftilagimod alpha
TACTI-002

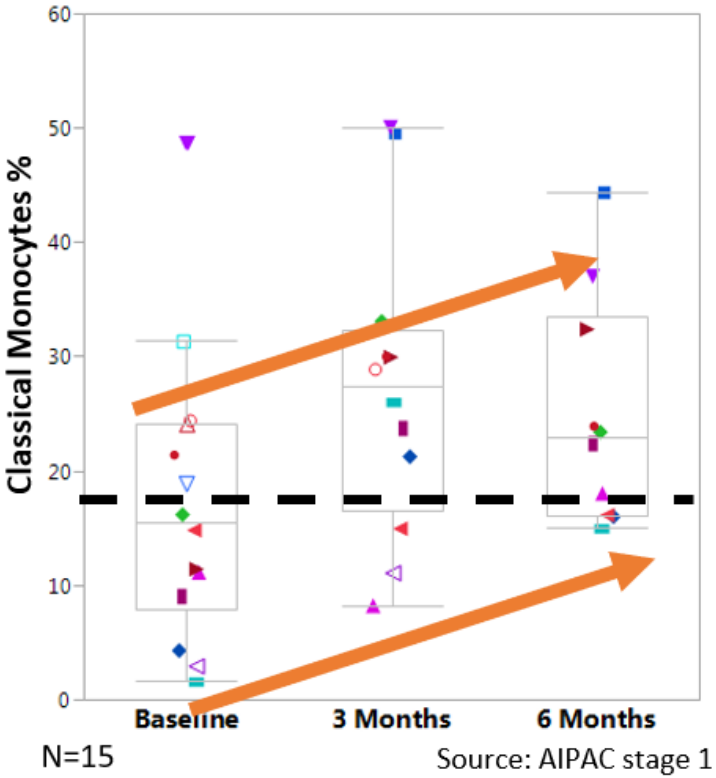
Rationale combination eftilagimod alpha plus PD-1 antagonist (e.g. pembrolizumab)

→ *Efti increases peripheral monocyte counts in cancer patients*



Source: Krieg et al., Nat. Med. 24, 2018.

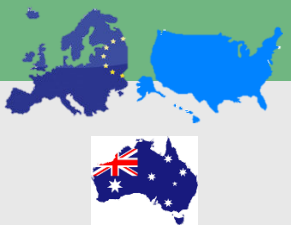
- → Baseline innate immunity status seems to be important for the response (OS) to pembrolizumab
- → Data suggests that low monocyte numbers at baseline are associated with poor efficacy of anti-PD-1 therapy in melanoma patients
- → Data shows that the APC activator eftilagimod alpha boosts innate immunity



Source: AIPAC stage 1

eftilagimod alpha
TACTI-002

Trial Design + Introduction



- → *Phase II, multi-national, open label, Simon`s 2 stage design; PD-L1 all comer*
- → *In collaboration with Merck Sharp & Dohme (MSD)*

Eligiblity

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

Part A:
1st line met. NSCLC

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

Part C:
2nd line met. HNSCC after platinum

→

30 mg efti SC
+
200 mg pembrolizumab IV

Up to 12 months then pembrolizumab alone for another 12 months

→

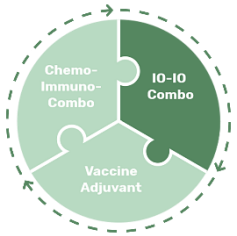
Primary: ORR (iRECIST)

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

Study – Part	Stage 1 (N) Actual/target	Stage 2 (N) target
Part A	17/17	19 (opened)
Part B	13/23	13
Part C	18/18	19 (opened)

Results from stage 1 are reported today

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

- 48 pts were enrolled between Mar 2019 and Jan 2020(1). Pts received median 7 (range 1-20) efti injections and median of 5 (range 1-16) pembrolizumab (Keytruda®) infusions.
- 16 pts (33.3%) had ≥ 1 treatment emergent SAE
- 2 fatal TEAE (hemoptysis; respiratory failure) unrelated to therapy
- 2 TEARs leading to permanent discontinuation:
  - Hepatitis grade 4 – both study drugs discontinued
  - Diarrhea grade 3 – pembro discontinued

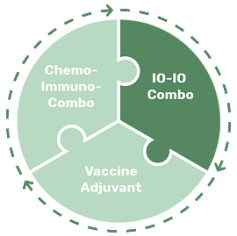
TEAEs occurred in > 10 % of pts (N=48 in total)

Adverse event (PT)	Any Grade N (%)	Grade 2 N (%)	Grade 3 N (%)
Cough	15 (31.3)	*5 (10.4)*	-
Asthenia	11 (22.9)	*4 (8.3)*	-
Decreased appetite	9 (18.8)	*5 (10.4)*	-
Fatigue	9 (18.8)	*2 (4.2)*	*1 (2.1)*
Dyspnoea	8 (16.7)	*2 (4.2)*	*3 (6.3)*
Diarrhea	7 (14.6)	*2 (4.2)*	*1 (2.1)*
Constipation	6 (12.5)	*1 (2.1)*	*1 (2.1)*

- No grade 4 or 5 for the TEAEs described in the table
- Injection site reactions (n=18 events in 10 subjects) all grade 1 severity were reported for efti
- No new safety signals observed thus far

Notes:

(1) Preliminary data, cut-off 31-Jan 2020



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

Baseline Characteristics

→ *PD-L1 distribution as expected → PD-L1 all comer trial*

→ *Patients are typical NSCLC 1st line pts*

Baseline Parameters (n=17)	N (%)
Median age, yrs (range)	65 (53 – 76)
Sex Female Male	 6 (35.3) 11 (64.7)
ECOG 0 1	 12 (70.6) 5 (29.4)
Smoking status Never Current / former	 1 (5.9) 16 (94.1)
Histology Squamous Non-squamous	 10 (58.8) 7 (41.2)
Location of disease at study entry Lung Bone	 8 (47.1) 5 (29.4)

Central assessment of tumor cell PD-L1 expression done post enrollment		
PD-L1 (n=13)[2]	N (%)	Historical[3] Distribution
< 1 %	3 (23%)	35%
1-49 %	6 (46%)	35%
≥ 50 %	4 (31%)	30%

Notes:

(1) Preliminary data, cut-off January 31 2020

(2) % in reference to evaluable samples; 4 specimens not evaluable by central lab using standard IHC kit

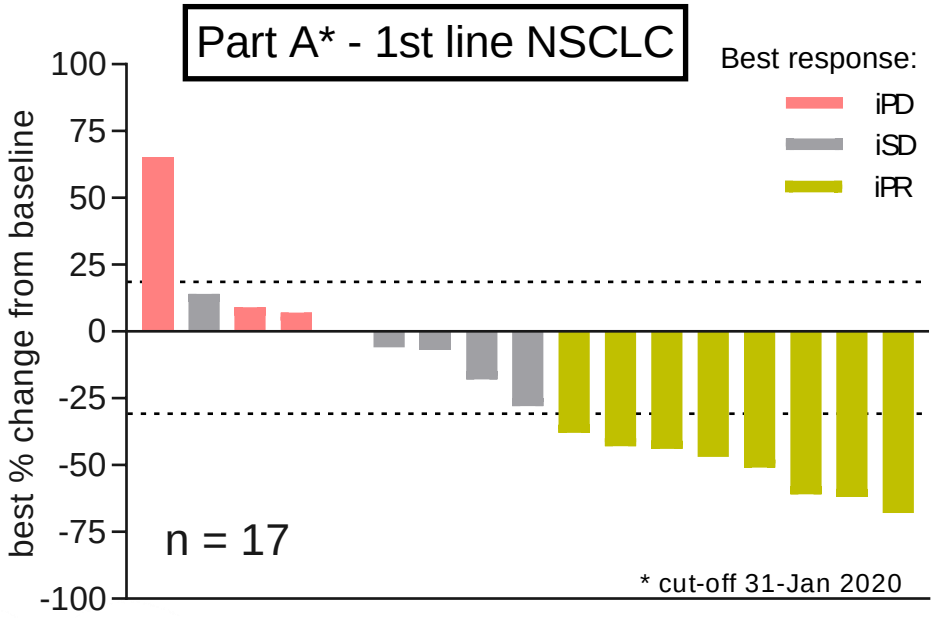
(3) Garon et al N Engl J Med 2015;372:2018-28

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

Responses and Waterfall plot

- → *47.1 % iORR acc. to iRECIST in this PD-L1 all comer trial*
- → *Responses in all PD-L1 subgroups*

Tumor response - BOR as per iRECIST	N (%) Total (N=17)
Complete Response (iCR)	0 (0.0)
Partial Response (iPR)	8 (47.1)
Stable Disease (iSD)	6 (35.3)
Progressive Disease (iPD)	3 (17.7)
Objective Response Rate (iORR)	**8 (47.1)**
Disease Control Rate (iDCR)	**14 (82.4)**



- Responses in all PD-L1 subgroups
- 6/8 iPR confirmed already → 7/8 pts with iPR still under therapy (none discontinued due to PD)
- 12/17 (71 %) patients with target lesion decrease

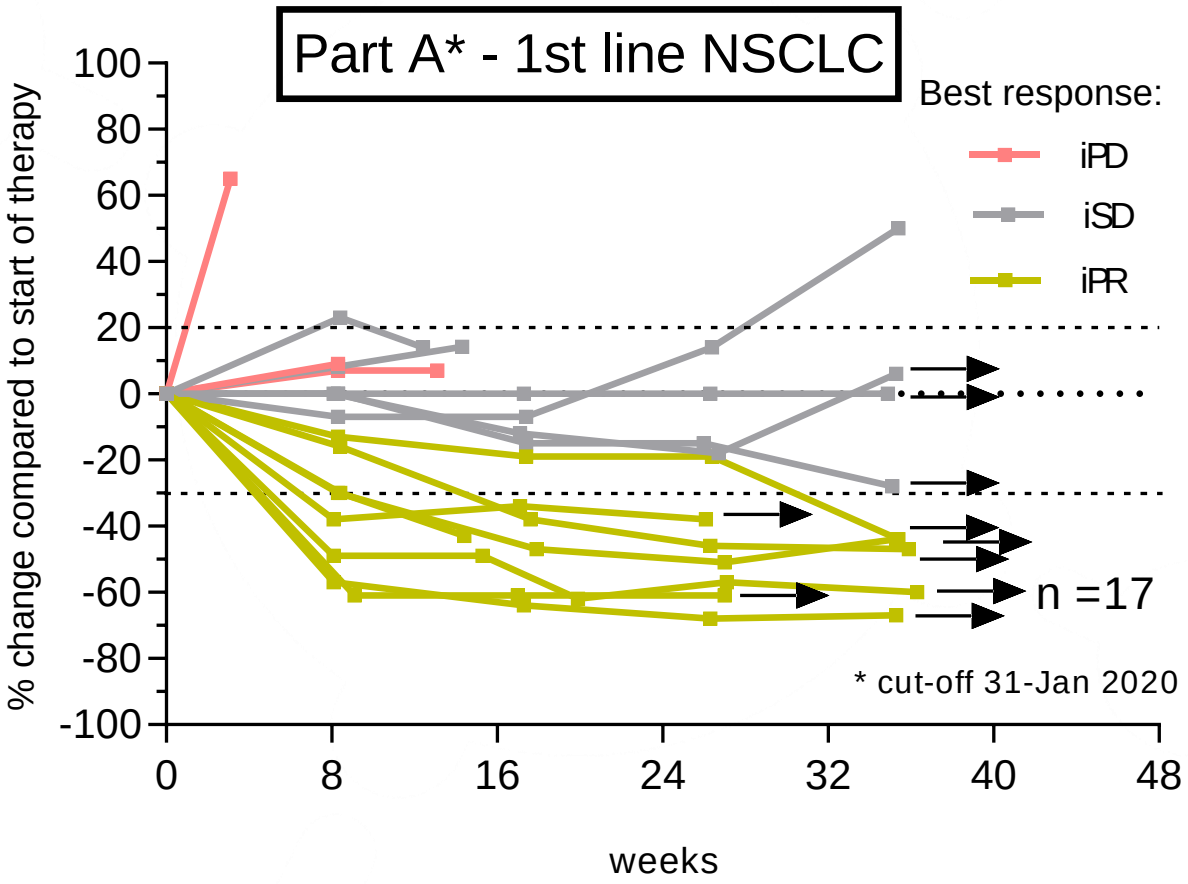
Patients by PD-L1 category	No. of Responses
Low (< 1 %)	1
Medium (1-49 %)	3
High (≥ 50 %)	3
Not evaluable	1
Overall	**8**

Notes:
(1) Preliminary data, cut-off 31-Jan 2020

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

Spiderplot

→ *At data cut-off 10 pts (59 %) still under treatment at 7+ months → median PFS not yet reached*



Main reason for discontinuation

- *Progressive disease (n=4)*
- *Clinical deterioration (n=1)*
- *Adverse events (n=2):*
  - *G4 hepatitis (treatment related)*
  - *G5 hemoptysis (disease related)*

Notes:

(1) Preliminary data, cut-off 31 Jan 2020

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

Responses and Waterfall plot

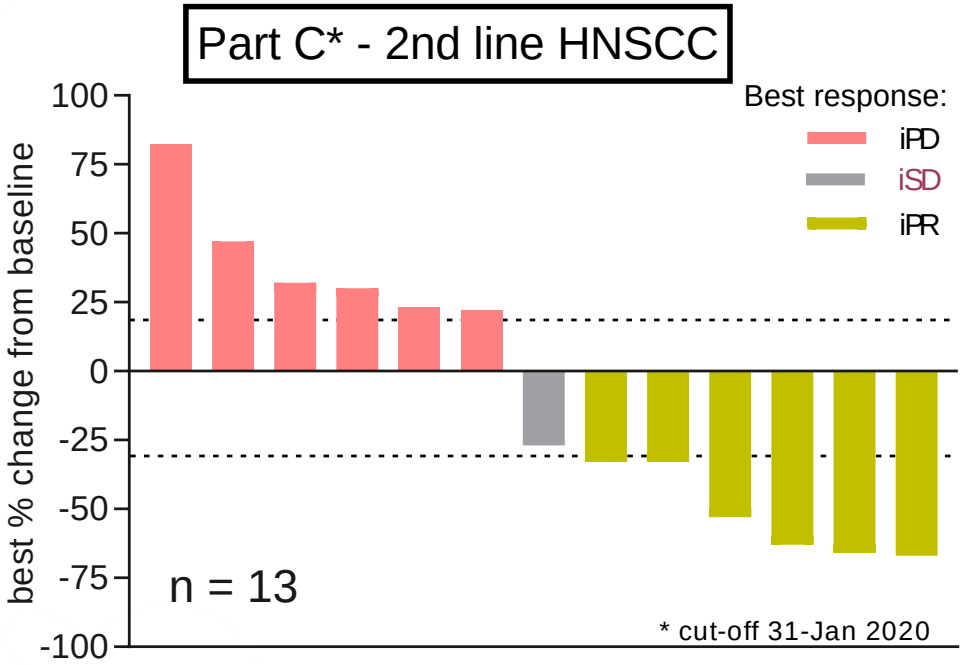
→ *Initial iORR of 33.3 % in this PD-L1 all comer HNSCC 2nd line patients*

- Median Age of 66, mostly male (94 %)
- ECOG 1 in 47 %
- Different subtypes

Tumor response - BOR as per iRECIST	N (%) Total (N=18)
Complete Response (iCR)	0 (0.0)
Partial Response (iPR)	6 (33.3)
Stable Disease (iSD)	1 (5.6)
Progressive Disease (iPD)	6 (33.3)
Not evaluable*	2 (11.1)
Not yet evaluated**	3 (16.7)
Objective Response Rate (iORR)	**6 (33.3)**
Disease Control Rate (iDCR)	**7 (38.9)**

* - dropped out prior to first restaging

** - not yet staged (on therapy < 9 weeks)



- LPI - Dec 2019 → 3 pts with outstanding imaging
- 7 pts (39 %) had a target lesions decrease
- All pts with iSD or iPR are still under treatment (median 6.4 months)

Note:

(1) Preliminary data, cut-off 31 Jan 2020

Thank you!