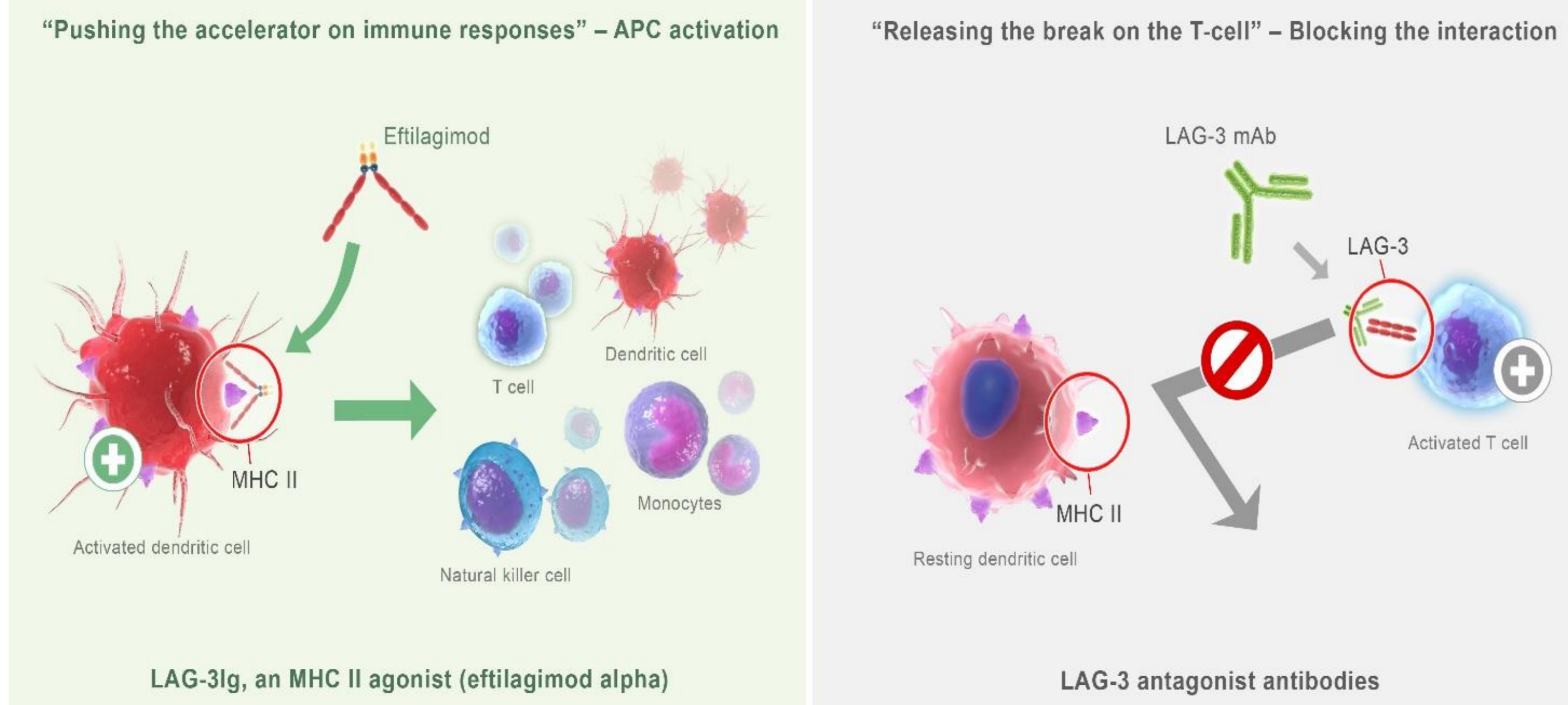


# Initial results from a Phase II study (TACTI-002) of eftilagimod alpha (a soluble LAG-3 protein) and pembrolizumab in patients with PD-L1 unselected metastatic 1<sup>st</sup> line non-small cell lung carcinoma (NSCLC)

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## Background



Eftilagimod alpha (efti; previously IMP321) is a soluble LAG-3 protein that binds to a subset of MHC class II molecules to mediate antigen presenting cell (APC) and then activate CD8 T-cells.

### Efti is a first-in-class APC activator.

The rationale to combine efti and pembrolizumab comes from their complementary mechanisms of action. Efti activates APCs, leading to an increase in activated T cells, which in effect potentially reduces the number of non-responders to pembrolizumab.

Combining an APC activator such as efti to pembrolizumab is therefore fundamentally different from many other trials combining two checkpoint inhibitors such as an anti-LAG-3 mAb with an anti-PD-1 mAb.

Previous clinical trial experience with the same combination used in metastatic melanoma patients (TACTI-mel, NCT02676869) suggests that the combination is safe and shows encouraging signs of efficacy.

We hereby report results from stage 1 part A of a phase II umbrella trial (TACTI-002, NCT03625323).



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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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APC...antigen-presenting cell  
AE...adverse event  
BOR...best overall response  
DCR...disease control rate  
DMC...Data Monitoring Committee  
ECOG...Eastern Cooperative Oncology Group  
HNSCC...head and neck squamous cell cancer  
ICI...immune checkpoint inhibitor  
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-L1, PD-L2...Programmed Death ligand-1, -2  
PD-X...PD-1 or PD-L1 targeted therapy  
PFS...progression-free survival  
ORR...objective response rate  
SAE...serious adverse event  
TEAE...treatment emergent adverse event

## Trial Design

**Part A: 1st line, PD-X naïve NSCLC;** stage IIIB not amenable to curative treatment or stage IV not amenable to EGFR/ALK based therapy, treatment-naïve for advanced/metastatic disease

**Part B: 2nd line, PD-X refractory NSCLC;** pts after failure of 1st line therapy for metastatic disease which incl. at least 2 cycles of PD-X

**Part C: 2nd line PD-X naïve HNSCC;** recurrent disease not amenable to curative treatment, or metastatic disease incurable by local therapies after failure of prior platinum-based therapy

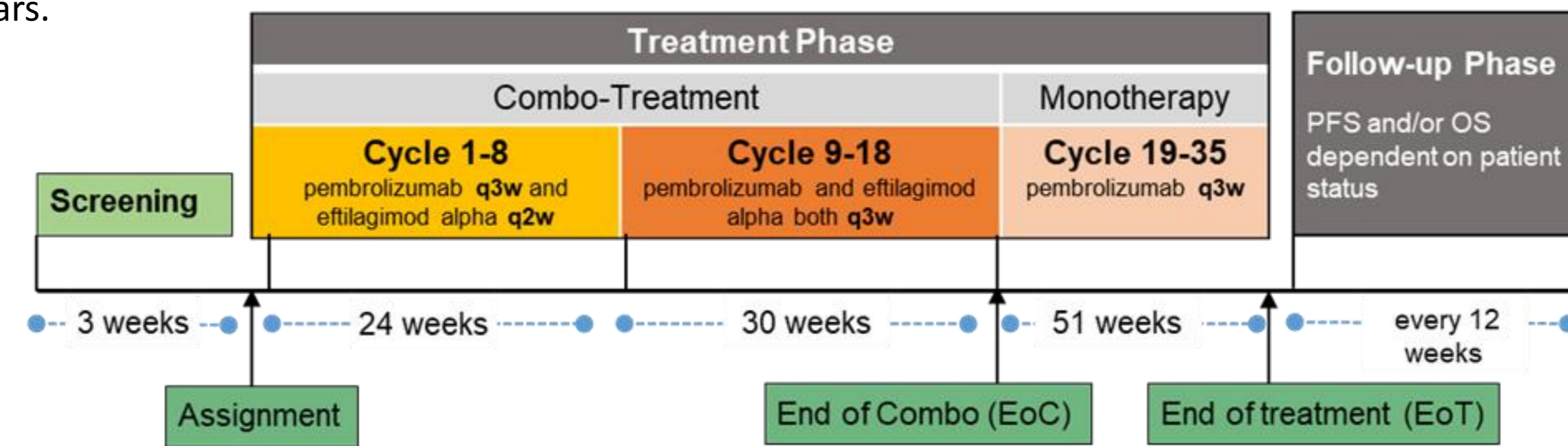
General Features/Objectives:

- Primary endpoint: objective response rate (iORR) as per iRECIST
- Secondary endpoints: progression free survival (PFS) and overall survival (OS)
- Central assessment of tumor cell PD-L1 expression after enrollment
- Blood samples for PK/PD assessments and anti-drug antibody evaluation are collected

The study has a Simon's two-stage design: during the first stage, the 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 are planned to be enrolled.

Indication	Threshold r1	Initial no. of pts (N1)	Add. no. of pts (N2)	N total
Part A: NSCLC 1 <sup>st</sup> line	4	17	19	36
Part B: NSCLC 2 <sup>nd</sup> line	1	23	13	36
Part C: HNSCC	2	18	19	37

Efti is administered as 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 2 years.



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

Enrolment to Part A + C stage 1 was completed in 2019, while Part B stage 1 and Part A stage 2 was completed in 2020. Recruitment in Part C stage 2 is ongoing.

## Exposure and Safety<sup>1</sup>

### Summary - Exposure:

- In total, 88 pts were enrolled in all three parts and all stages until data cut-off<sup>1</sup>.
- Pts received median 5.5 (range 1-22) efti injections and median of 4 (range 1-25) pembrolizumab infusions

### Overview - Safety:

- No treatment-related deaths
- 3 treatment-related adverse events leading to permanent discontinuation of treatment (drug induced hepatitis G4; ALT & AST elevation G3; diarrhea G1)
- No new safety signals of this new combination identified until cut-off

Safety Parameters	No of patients (%)
Pts with any TEAE	80 (90.9)
Pts with any SAE	27 (30.7)
thereof related to efti / pembrolizumab	5 (5.7) / 6 (6.8)
Pts with any grade ≥3 TEAE	42 (47.7)
thereof related to efti / pembrolizumab	8 (9.1) / 9 (10.2)

### Treatment emergent adverse events occurred in ≥ 10 % of pts (total N=88)

Adverse event (PT)	Any Grade N (%)	Grade 3 N (%)	Grade 4 N (%)	Grade 5 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)	-	-	-

<sup>1,2</sup> - Data cut-off date: 21<sup>st</sup> Aug 2020

## Part A stage 1 - 1<sup>st</sup> line NSCLC<sup>2</sup>, PD-L1 all comer

- 17 patients with 1<sup>st</sup> line NSCLC (squamous and non-squamous) were enrolled, treated and evaluated for efficacy.

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 (iUPD/iCPD)	4 (23.5)
Objective Response Rate (iORR) [95 % CI interval]	9 (52.9) [27.8 – 77.0]

Baseline Parameters (n=17)	N (%)
Median age, yrs (range)	65 (53 – 76)
Female / Male	6 (35.3) / 11 (64.7)
ECOG 0 / 1	12 (70.6) / 5 (29.4)
Current / former smoker	16 (94.1)
Squamous / Non-squamous	10 (58.8) / 7 (41.2)

- Patients with all different PD-L1 subgroups enrolled → proportions comparable to historical controls

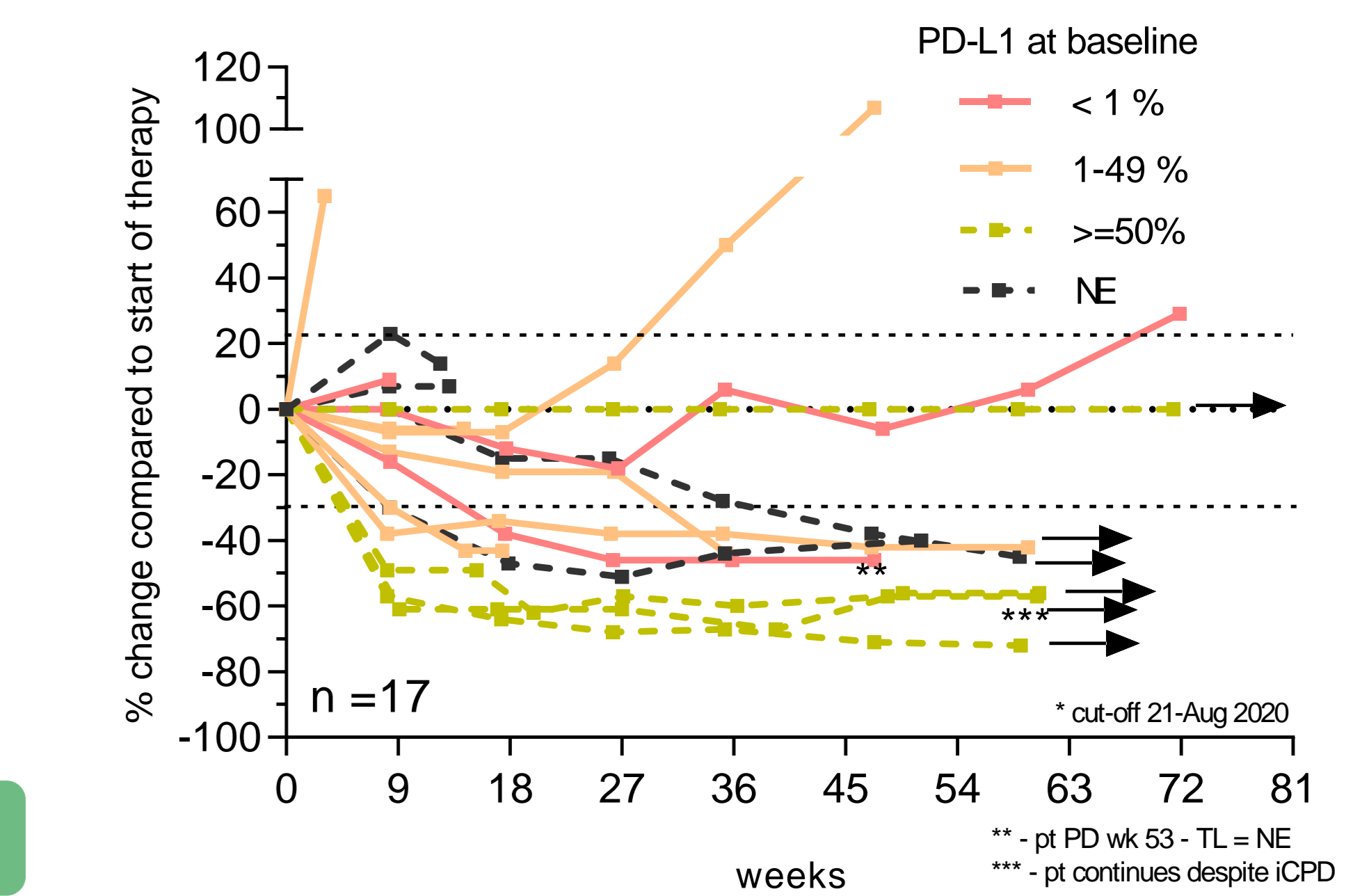
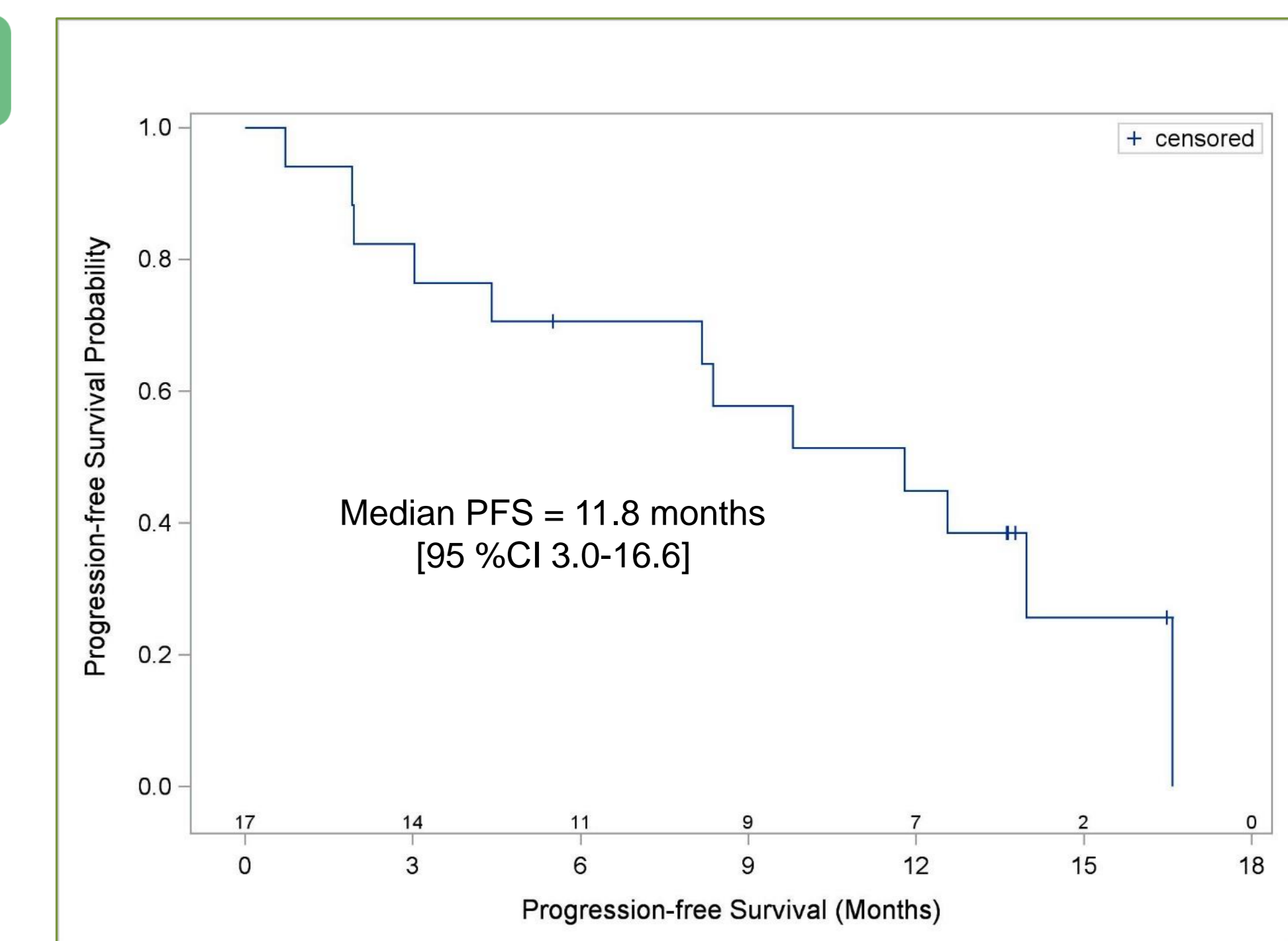
PD-L1 distribution*	N (%)	Historically expected**	Pts with iPR/iCR
Low TPS < 1 %	3 (17.6 %)	35 %	1
Moderate TPS 1-49 %	6 (35.3 %)	35 %	3
High TPS ≥ 50 %	4 (23.5 %)	30 %	3
NE	3 (17.6 %)	-	2

\*Centrally assessed by Dako PD-L1 IHC 22C3 pharmDx  
\*\* Garon et al N Engl J Med 2015;372:2018-28

## Kaplan-Meier Plot for PFS

### Summary:

- iORR of 52.9 % [95 % CI 27.8-77.0]
- Confirmed responses for 8 out of 9 patients with iPR/iCR
- 1 pt with a complete response
- 12/17 (71 %) with target lesion decrease
- Responses in all PD-L1 subgroups
- 4 responses in patients with PD-L1 expression of < 50 %; 1 response in PD-L1 negative patients
- Two late responders after 8 and 11 months
- Median PFS: 11.8 months [95 % CI 3.0;16.6]; PFS at 12 months: 45 %
- 12-months overall survival rate: 71 % → median OS not yet reached; minimum FU of 14 months
- At data cut-off 6 pts still under therapy → all 12+ months on therapy



## Spider Plot

## Conclusion

### NSCLC

- iORR of 53 %, median PFS of 11.8 months in PD-L1 all comer 1<sup>st</sup> line NSCLC population
- Tumour responses in low/moderate (< 50 %) PD-L1 expressors are an important signal
- Encouraging efficacy when referenced to pembrolizumab alone in comparable patient population with ≥1 % PD-L1 expression (KN-024; KN-042)

### Overall

- Combination of efti and pembrolizumab in NSCLC and HNSCC patients is safe and well-tolerated
- Results underlining the potential synergy of the APC activator efti with the checkpoint inhibitor pembrolizumab may result in synergistic therapeutic activity with an excellent safety profile
- Data from the HNSCC part C stage 1 is presented on poster 927P