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# Eftilagimod Alpha (Soluble LAG-3) & Pembrolizumab in First-Line Recurrent or Metastatic Head & Neck Squamous Cell Carcinoma: Primary Results from Cohort B (CPS <1) of the TACTI-003 Study

## Phase IIb study of soluble LAG-3 combined with an anti-PD-1 antibody as a first-line therapy in R/M HNSCC

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# DECLARATION OF INTERESTS

## Robert Metcalf

**Advisory Board**: Ayala, Bayer, Aptus Clinical, PCI Biotech, Oxsonics, Roche, Achilles Therapeutics.

**Other**: BMS, MSD, Sanofi, Merck.

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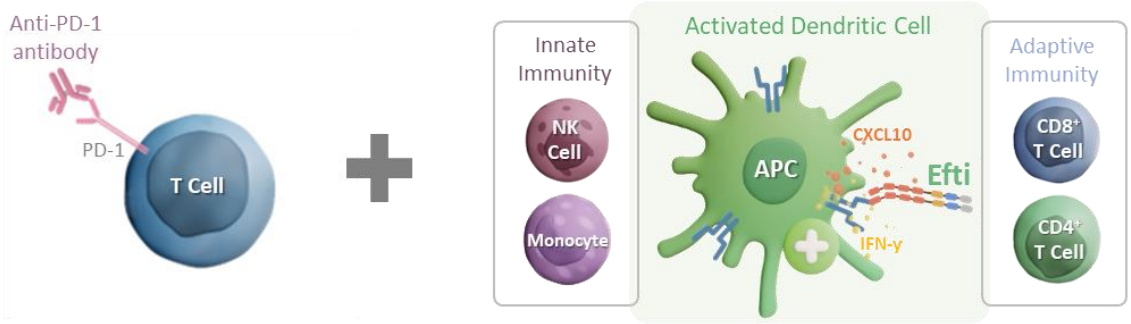
# BACKGROUND

- **Eftilagimod alpha: a soluble LAG-3 protein** and **MHC Class II agonist** that leads to an enhanced immune response through activating antigen presenting cells (APCs), leading to the activation/proliferation of $CD8^+$ T cells.
- Pembrolizumab: current standard-of-care that antagonizes PD-1 receptor on T cells, enhancing the immune response against cancer cells.




*Efti directly targets MHC Class II on APCs, having an agonistic effect, unlike LAG-3 antagonists that target T cells.*

MHC: major histocompatibility complex

# RATIONALE

- Eftilagimod activates APCs, leading to an increase in activated T cells (CD4/CD8), augmenting responses when combined with PD-(L)1 antagonists such as pembrolizumab.
- Encouraging efficacy has been seen in 2nd line HNSCC[1] pts (table, left) after failure of 1st line chemotherapy and in 1st line NSCLC regardless of PD-L1 TPS[2] (table, right) when eftilagimod was combined with pembrolizumab. Responses were observed irrespective of patients' CPS/TPS level.

**2nd line HNSCC, presented at ASCO 2023[1]**

| PD-L1 CPS | ITT, N=37 | ≥20, N=15 | <20, N=17 |
|---|---|---|---|
| Objective response rate (iRECIST), % | 29.7 | 60.0 | 11.8 |

[1] Doger B. et al, Final results from TACTI-002 Part C: A phase II study of eftilagimod alpha (soluble LAG-3 protein) and pembrolizumab in patients with metastatic 2nd line head and neck squamous cell carcinoma unselected for PD-L1, JCO; 41, 6029-6029(2023). https://doi.org/10.1200/JCO.2023.41.16_suppl.6029

**1st line NSCLC, presented at ESMO 2023[2]**

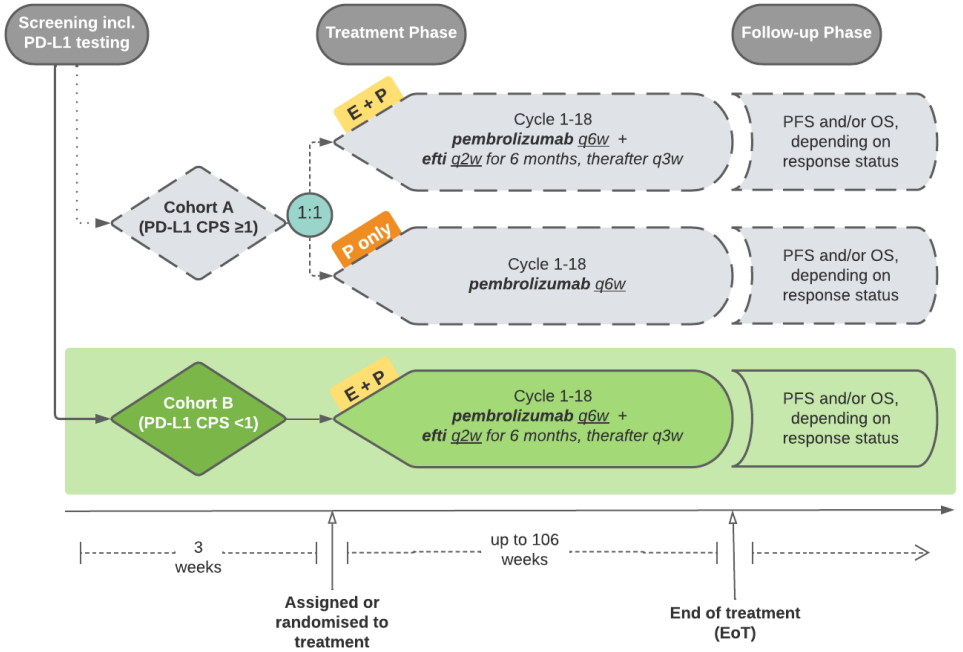
| PD-L1 TPS | <1%, N=32 | 1-49%, N=38 | ≥50%, N=20 |
|---|---|---|---|
| Objective response rate (iRECIST), % | 31.3 | 44.7 | 55.0 |

[2] Carcereny E et al, Combining the antigen-presenting cell activator eftilagimod alpha (soluble LAG-3) and pembrolizumab: Overall survival data from the first line non-small cell lung carcinoma (NSCLC) cohort of TACTI-002 (phase II), Annals of Oncology; 34, S755-S851(2023). https://doi.org/10.1016/j.annonc.2023.09.2346

# STUDY DESIGN

TACTI-003: a multicentre, randomized, open-label Phase IIb trial with 2 cohorts:

- Cohort A*: CPS ≥1 patients randomized 1:1 to receive eftilagimod plus pembrolizumab or pembrolizumab alone.
- **Cohort B**: CPS <1 patients treated with eftilagimod and pembrolizumab.**




CPS: combined positive score; OS: overall survival; PD-L1: programmed cell death ligand 1; PFS: progression free survival; Q(2,3..)W: every (2,3..) weeks; Note 1 cycle= 6 weeks.

*Detailed results from Cohort A will be presented in H2 2024.
**no randomization.

# TREATMENT, ASSESSMENTS & ENDPOINTS

**Treatment**: eftilagimod 30 mg s.c. + pembrolizumab IV 400 mg Q6W for max. 2 years.

Radiological assessments performed Q9W for 36 weeks, thereafter Q12W and assessed locally by Investigator.

Primary endpoint: ORR by RECIST 1.1.

Secondary endpoints: ORR by iRECIST, DoR, TTR, safety, PFS, OS, immunogenicity & QoL.

CPS: combined positive score; DoR: duration of response; IV: intravenous; ORR: objective response rate; OS: overall survival; PD-L1: programmed cell death ligand 1; PFS: progression free survival; Q(2,3..)W: every (2,3..) weeks; QoL: quality of life; s.c.: subcutaneous; TTR: time to response.

# DEMOGRAPHICS & BASELINE CHARACTERISTICS

| Baseline parameters | N=31[1] |
|---|---|
| Median age, years (range) | 64 (23-83) |
| Female / Male, % | 25.8 / 74.2 |
| ECOG 0 / ECOG 1, % | 32.3 / 67.7 |
| Current / Ex-smoker / Never smoker, % | 25.8 / 61.3 / 12.9 |
| Primary tumour, % | |
| Oral cavity | 29.0 |
| Oropharynx (HPV + / - ) | 35.5 (12.9 / 22.6) |
| Hypopharynx | 3.2 |
| Larynx | 32.3 |
| Baseline disease status, % | |
| Local only | 16.1 |
| Local and metastatic | 22.6 |
| Metastatic only | 61.3 |

- 33 patients were recruited at 14 sites across 6 countries between Apr 2022-Oct 2023.
- 31 patients were evaluable for efficacy per protocol (≥1 evaluable post-baseline scan).
- CPS used for randomization/enrollment was assessed using FDA-approved kit (IHC 22C3 pharmDx).
- Median exposure for eftilagimod of 23.7 weeks (range: 0.1-63.3) and for pembrolizumab 22.1 weeks (0.1-63.1).

[1]Evaluable population.

Data cut-off date: March 11, 2024

# SAFETY

## Summary of TEARs (Safety population)

| Safety parameters, n (%) | N=33 |
|---|---|
| Any TEARs | 24 (72.7) |
| Any TEARs with Grade ≥3 | 5 (15.2) |
| Any TEARs Leading to Discontinuation of Study Treatment[1] | 3 (9.1)[2] |

- No new safety signals were observed.
- Immune-mediated adverse reactions were seen in 39.4% of patients, Grade 1-2 (30.4%) and Grade 3 (9.1%).
- Local injection site reactions were observed in 18.2% of patients (all Grade 1).

## Most frequent TEAEs (Safety population)

| Preferred term (incidence ≥15%), n (%) | N=33 |
|---|---|
| Fatigue | 7 (21.2) |
| Weight decreased | 6 (18.2) |
| Hypothyroidism | 6 (18.2) |
| Pyrexia | 5 (15.2) |
| Arthralgia | 5 (15.2) |
| Gamma-glutamyltransferase increased | 5 (15.2) |
| Anaemia | 5 (15.2) |

[1] Study treatment: eftilagimod and/or pembrolizumab.
[2] Immune thrombocytopenia (G4), Immune-mediated hepatitis (G3), Laryngeal obstruction (G4).
TEAE: treatment-emergent adverse event; TEAR: treatment-emergent adverse reaction.

Data cut-off date: March 11, 2024

# TUMOUR RESPONSE SUMMARY

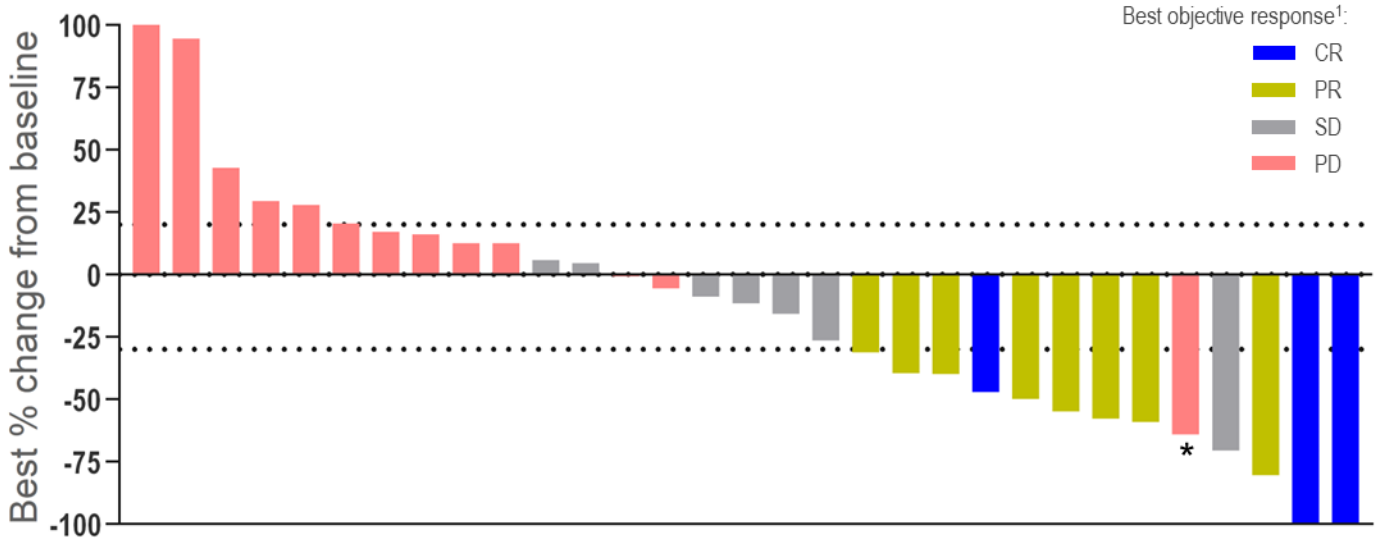
| Best objective response[1], n (%) | RECIST 1.1 N=31 | iRECIST N=31 |
|---|---|---|
| Complete response | 3 (9.7) | 3 (9.7) |
| Partial response | 8 (25.8) | 9 (29.0) |
| Stable disease | 7 (22.6) | 8 (25.8) |
| Progressive disease | 13 (41.9) | 11 (35.5) |
| **ORR**, [95% CI][2] | **11 (35.5)** [19.2-54.6] | **12 (38.7)** [21.8-57.8] |
| **DCR**, [95% CI][2] | **18 (58.1)** [39.1-75.5] | **20 (64.5)** [45.4-80.8] |

- ORR[1,3] of 35.5% and DCR[1,3] of 58.1%, including ~10% complete responses.
- 10 responses[4] were confirmed until data cut-off.
- Responses are observed regardless of HPV status* (1/4 HPV-positive and 2/7 HPV-negative patients were responders).

[1] unconfirmed responses per Investigator read.
[2] calculated using Clopper-Pearson method.
[3] per RECIST 1.1.
[4] per iRECIST.

*in patients with primary oropharyngeal tumours only.
Data cut-off date: March 11, 2024

# CHANGE IN TUMOUR BURDEN BY RECIST 1.1



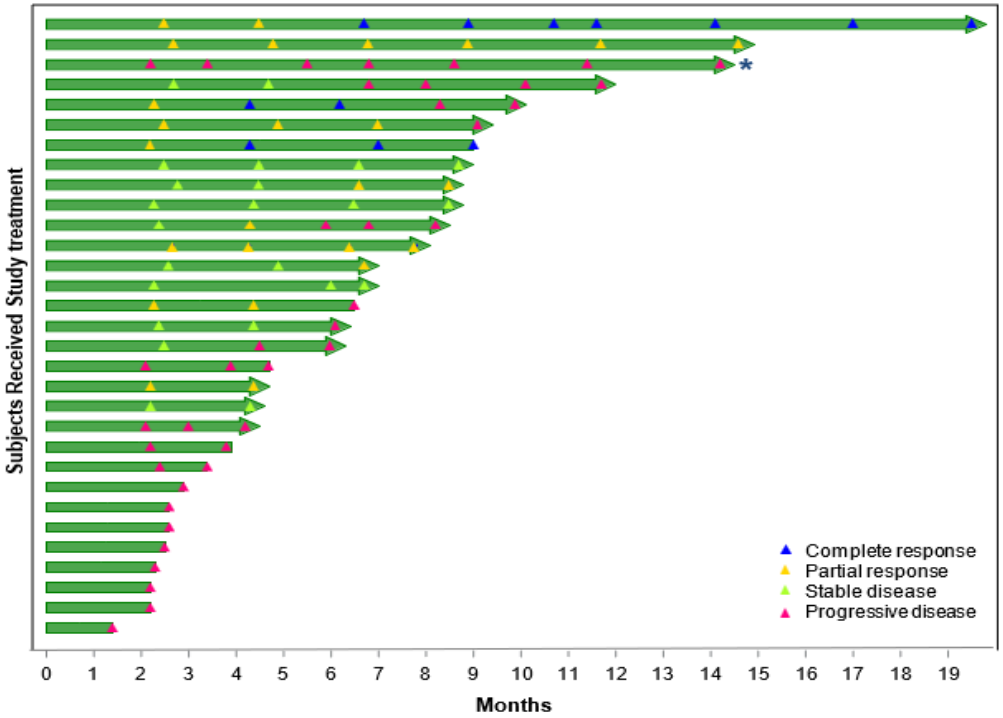

- ~60% experienced tumour shrinkage.
- 1 patient* with early pseudoprogression, resulting in later durable response (still on treatment >14 mo).

[1] unconfirmed responses per RECIST 1.1, Investigator-assessed.

Includes one complete response with a best % change of -47%. This patient had one target lesion of the lymph node, which shrunk to <10 mm.

Data cut-off date: March 11, 2024

# TUMOUR RESPONSE DYNAMICS OVER TIME




- 71% of patients remain on treatment for at least 4 months.
- ~50% remain on treatment >6 months.

Each bar represents one patient in the study. The right arrow cap indicates patients who are ongoing. Responses are per RECIST 1.1.
* 1 patient with clear pseudoprogression early and durable response later (still on treatment >14 months).

Data cut-off date: March 11, 2024

# CONCLUSIONS

- Eftilagimod plus pembrolizumab led to a clinically meaningful objective response rate (ORR) of 35.5% (95% CI: 19.2-54.6) in 1st line HNSCC patients with PD-L1 CPS <1.
- ORR compares favorably to historical results (5.4% ORR in 2/37 evaluable patients) of anti-PD-1 monotherapy in 1L HNSCC[1].
- DCR is above 50% and ~50% of patients are on treatment beyond 6 months.
- Eftilagimod plus pembrolizumab is safe and well-tolerated with no new safety signals.
- Based on the encouraging response rate and the high unmet medical need in this indication, further investigation of eftilagimod plus pembrolizumab is warranted.

[1]KN-048: J Clin Oncol. 2022 Jul 20;40(21):2321-2332. doi: 10.1200/JCO.21.02198.

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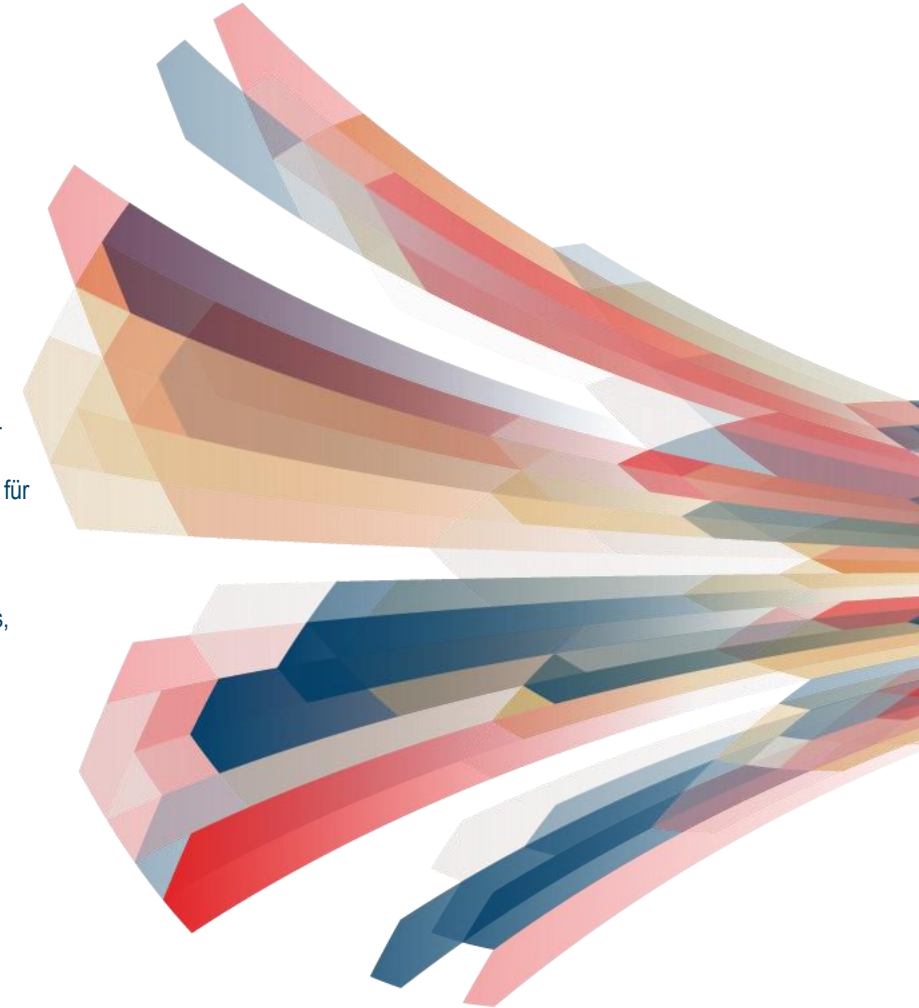

*Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, US