immutep
LAG-3 IMMUNOTHERAPY

Global Webcast Slides for TACTI-003 Positive Data in Patients with Negative PD-L1 Expression (Cohort B)

Presented at ESMO Virtual Plenary session at 18:30-19:30 Central European Time (CEST), July 11, 2024

Global Webcast Presentation – July 12th, at 9am AEST (July 11th, at 7pm ET)

Registration: Webcast Link

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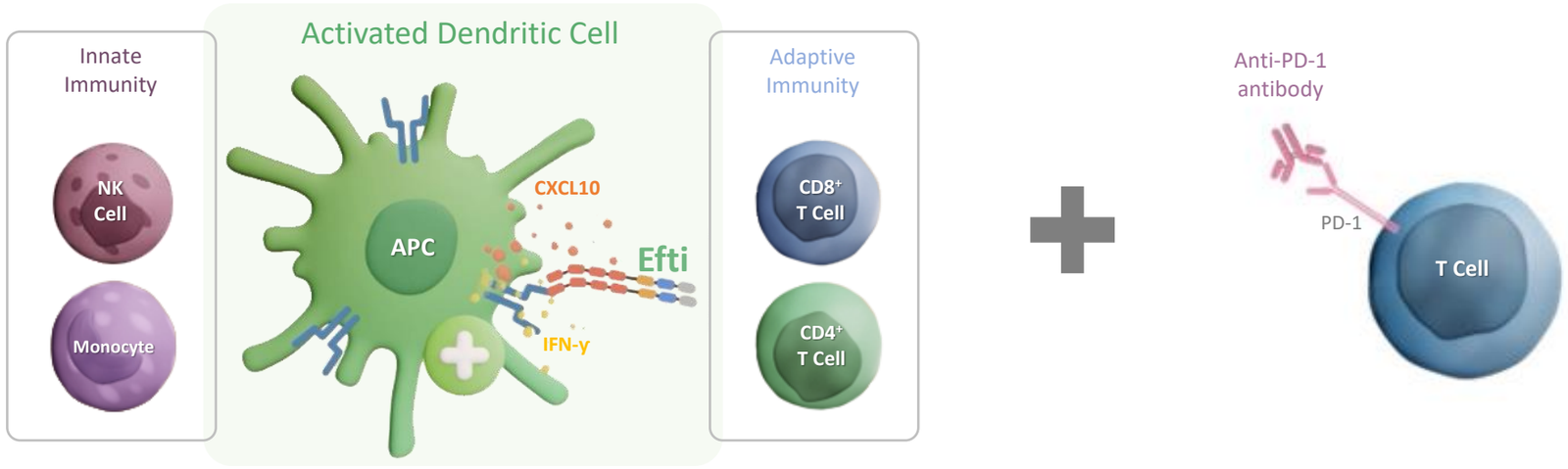
Complementary Effect of Efti with KEYTRUDA

- **Eftilagimod alfa:** a **soluble LAG-3 protein** and **MHC Class II agonist** that leads to an enhanced immune response by activating antigen presenting cells (APCs), leading to the activation/proliferation of $CD8^+$ T cells and other anti-cancer immune cells/chemokines.
- KEYTRUDA® (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. Complementary effect with KEYTRUDA leading to efficacy across "hot", "tepid", "cold" tumours and in patients with high, low, and negative PD-L1 expression.

MHC: major histocompatibility complex. KEYTRUDA® is a registered trademark of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Treatment Landscape for CPS <1 Patients

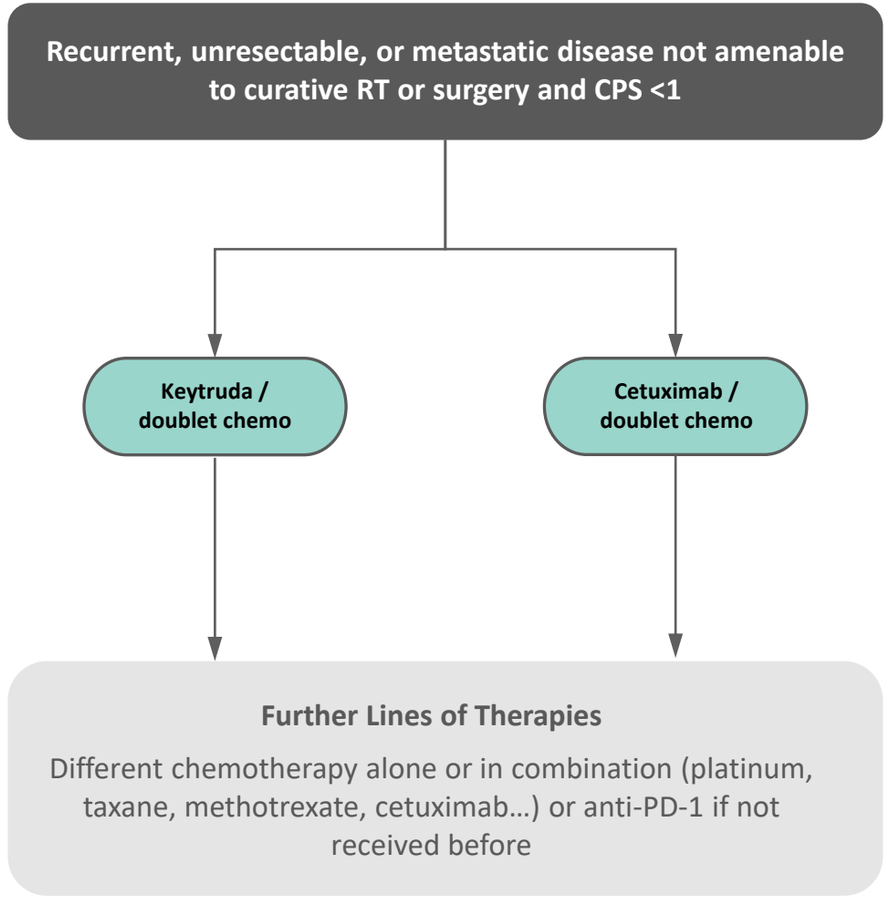
PD-L1 expression:

- PD-L1 expression as measured by Combined Proportion Score (CPS) is an FDA-approved predictive biomarker in 1L HNSCC for anti-PD-1 therapy

Limited treatment options for CPS <1 patients:

- All approved treatment combinations contain chemotherapy
- KEYTRUDA monotherapy has ~5% ORR, 2.1 months median PFS, and ~8 months median OS in negative PD-L1 patients* and is not approved in CPS <1
- KEYTRUDA with chemotherapy has ~31% ORR, 4.7 months median PFS, and ~11 months median OS in CPS <1. Cetuximab (anti-EGFR antibody) plus chemotherapy leads to slightly higher ORR/PFS, but similar OS.*
  - ***Important Note:*** *Quality and Duration of Responses (DOR) and stable diseases are decisive in translating into survival. Typically, DOR is much better with IO-only therapies (e.g., DOR for KEYTRUDA monotherapy is 22.6 months vs. 6.7 months when combined with chemotherapy**).*

High unmet medical need for well tolerated and efficacious treatment options for patients with CPS <1

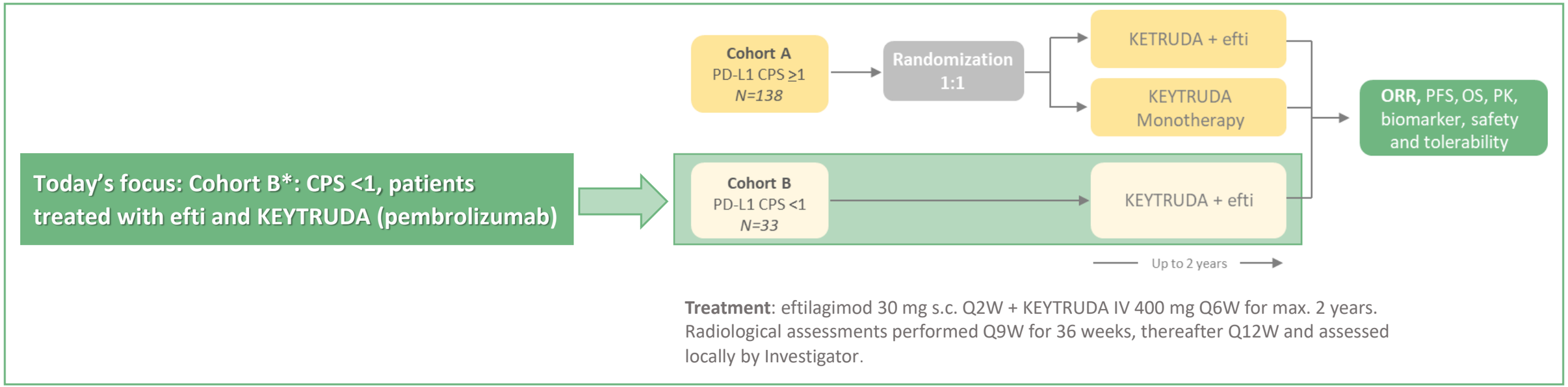


Simplified based on NCCN Guidelines Head and Neck Cancers and EHNS-ESMO-ESTRO Clinical Practice Guidelines

The Food and Drug Administration (FDA) approved KEYTRUDA in combination with ChT as first-line treatment regardless of PD-L1 expression and KEYTRUDA alone for patients with PD-L1-expressing tumours (CPS ≥1). In contrast, the European Medicines Agency (EMA) has approved KEYTRUDA with or without ChT only for patients with a CPS ≥1. Source: DOI:https://doi.org/10.1016/j.annonc.2020.07.011 *Burtness et al., *J Clin Oncol* 2022, DOI https://doi.org/10.1200/JCO.21.02198; **DOR data from KN-048 trial, Burtness et al., *The Lancet* 2019, https://doi.org/10.1016/S0140-6736(19)32591-7

TACTI-003 / KEYNOTE-PNC-34 Study Design

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



Treatment: eftilagimod 30 mg s.c. Q2W + KEYTRUDA 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 in evaluable patients by RECIST 1.1

Secondary endpoints include ORR by iRECIST, PFS, OS, PK, biomarker, safety and tolerability

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.*No randomisation.

Patient Demographics & Baseline Characteristics

Baseline parameters	N=31[1]
Median age, years (range)	64 (23-83)
Female / Male, %	25.8 / 74.2
ECOG PS 0 / 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, of which 31 patients were evaluable
- CPS used for randomisation/enrolment was assessed using FDA-approved kit (IHC 22C3 pharmDx)
- Of patients (oropharynx) with mandatory HPV status (N=11), ~64% are HPV negative[2]
- Baseline characteristics overall comparable to KN-048
- Median exposure for efti of 23.7 weeks (range: 0.1-63.3) and for KEYTRUDA 22.1 weeks (0.1-63.1)

Data cut-off date: March 11, 2024. [1]Evaluable population: ≥1 evaluable post-baseline scan. [2] in patients with primary oropharyngeal tumours only N=11 (4 pts HPV+ / 7 pts HPV-)

Continued Strong Safety Profile

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 seen in 39.4% (no grade 4-5; Grade 3 (9.1%)) → in line with expectations for KEYTRUDA monotherapy
- Local injection site reactions were observed in 18.2% of patients (all Grade 1) → in line with expectations for efti treatment

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)

Data cut-off date: March 11, 2024. TEAE: treatment-emergent adverse event; TEAR: treatment-emergent adverse reaction.
[1] Study treatment: eftilagimod and/or KEYTRUDA. [2] Immune thrombocytopenia (G4), Immune-mediated hepatitis (G3), Laryngeal obstruction (G4).

Tumour Response Rate Among Highest Recorded in CPS <1

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]

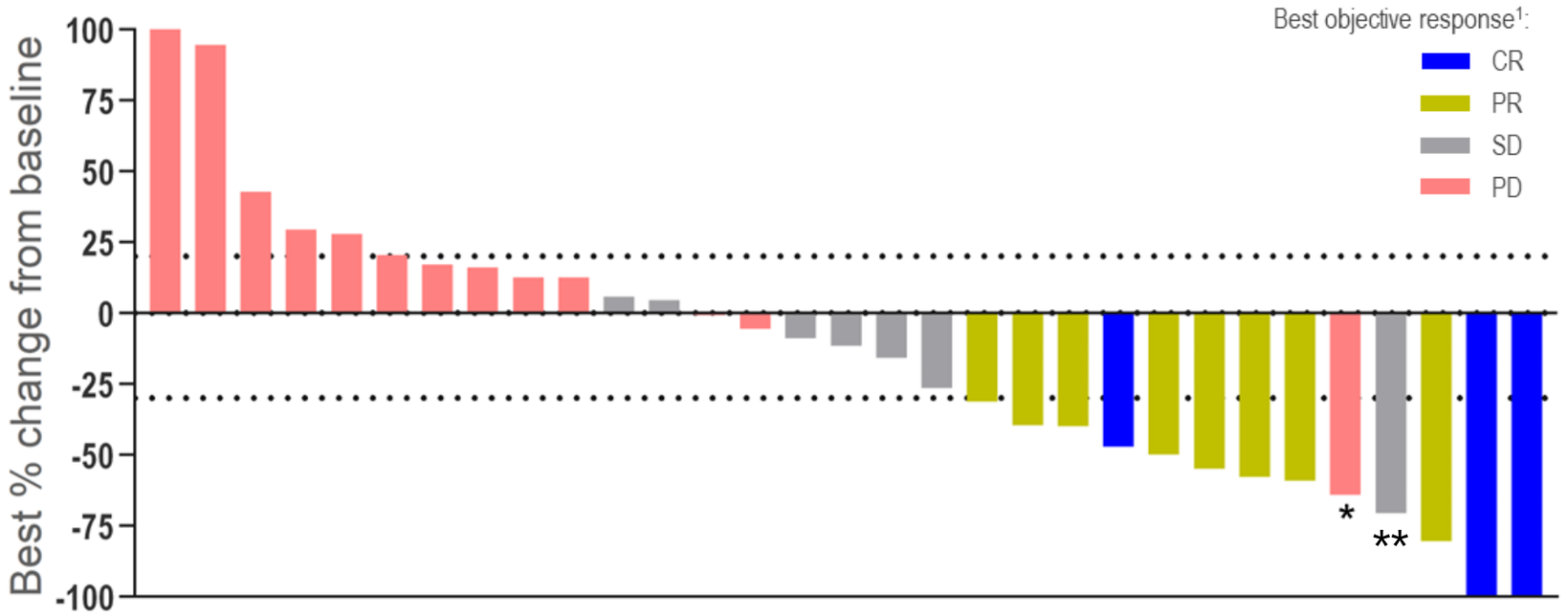
Key Takeaways:

- ORR of 35.5% and DCR of 58.1%, according to RECIST 1.1
- The 35.5% ORR is among the highest recorded for a chemo-free approach in 1L HNSCC patients with negative PD-L1 (CPS <1)
- ~10% complete responses
- Responses are observed regardless of HPV status*

Data cut-off date: March 11, 2024; [1]Per Investigator read. [2] Calculated using Clopper-Pearson method.
* In patients with primary oropharyngeal tumours only (1/4 HPV-positive and 2/7 HPV-negative patients were responders)

Tumour Shrinkage in 60% of Patients

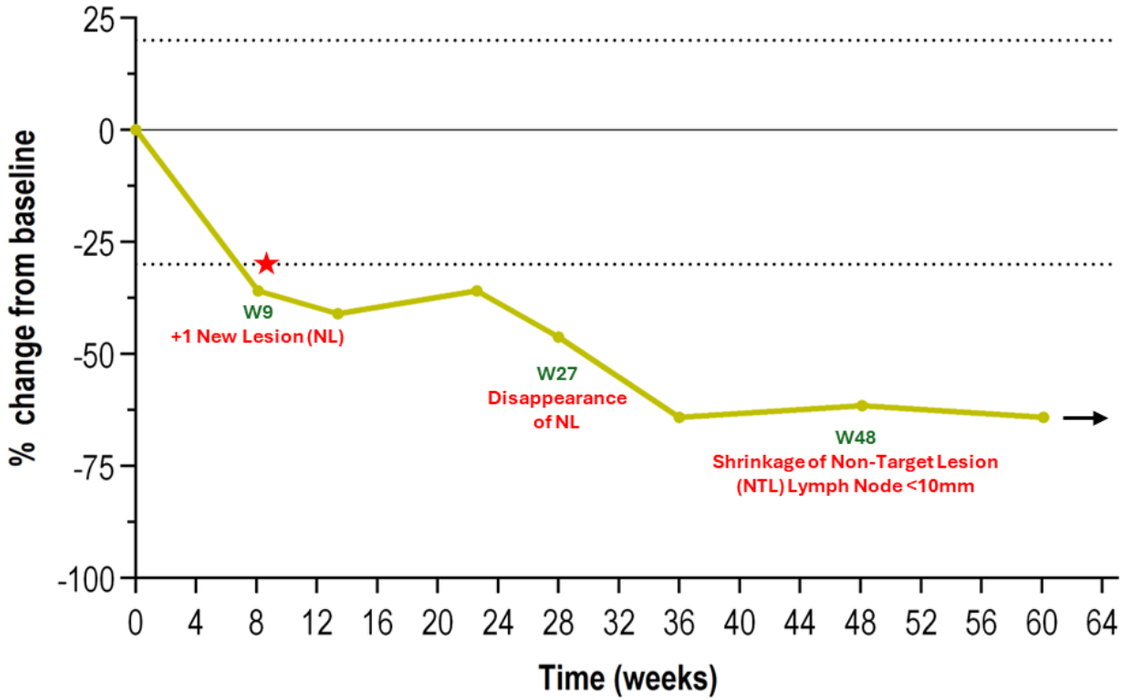
Change in Tumour Burden



- ~60% of patients experienced tumour shrinkage
- Despite deep responses in target lesions, two patients not counted as responders:
  - One patient (*) with pseudoprogression later had a confirmed partial response (PR) according to iRECIST yet not RECIST 1.1 (more details on next slide)
  - Another patient (**) with -71% shrinkage in target lesion diameters at week 27 had progression in a non-target lesion

Data cut-off date: March 11, 2024; [1] 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.

Confirmed Partial Response per *iRECIST* after Pseudoprogression



→ Patient remains on treatment after 14+ months
Assessment by iRECIST

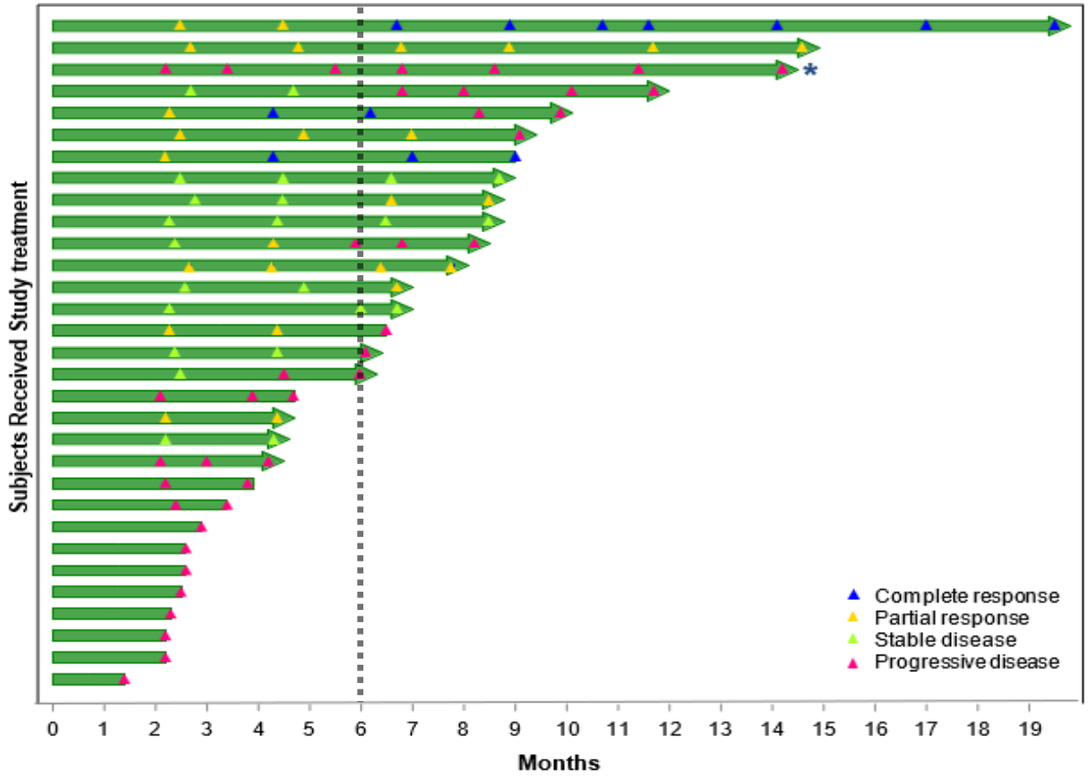
55-year-old male; HNSCC of oropharyngeal origin (HPV negative)

- Patient had two malignant lymph nodes (LN) as target lesions and one LN non-target lesion (NTL) at baseline
- The target lesions started to shrink at week 9, yet the appearance of a new lesion (NL) led to progressive disease according to RECIST 1.1
- Patient stayed on treatment according to protocol*
- Further decrease in target lesions and disappearance of the new lesion resulted in confirmed partial response (iPR) from week 27 onwards according to iRECIST
- Later at week 48, the NTL (lymph node) also shrunk to non-pathological size (<10 mm)
- Patient remains on treatment after 14+ months

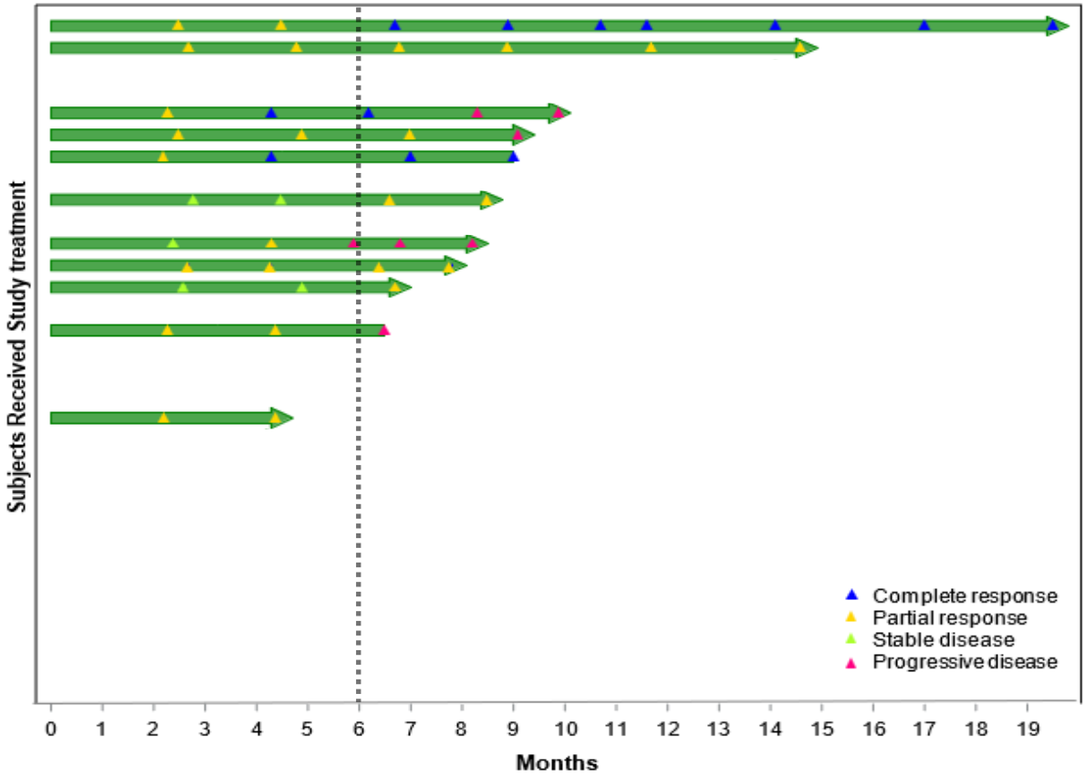
 Data cut-off date: March 11, 2024; LN ~ Lymph Node; NL ~ New Lesion; TL ~ Target Lesion; NTL ~ Non-Target Lesion. * Treatment related decisions based on iRECIST principles

Excellent Duration of Treatment

Tumour response dynamics over time*



Tumour response dynamics (RESPONDERS only)



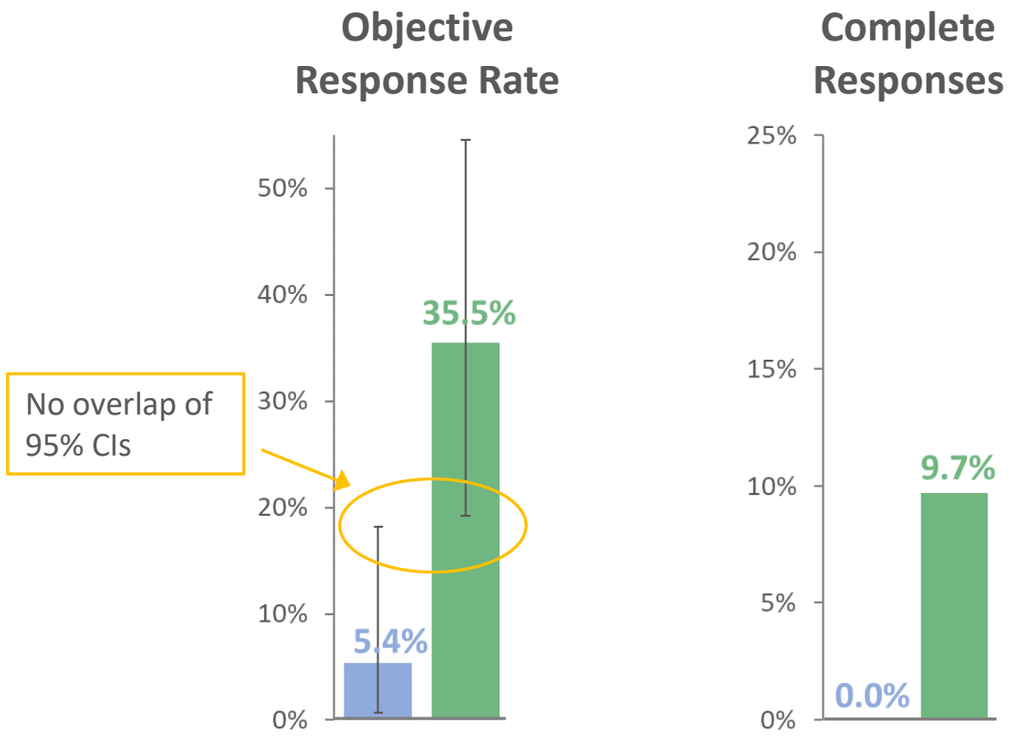
- Durability of treatment / responses tracks very well
- >50% patients remain on treatment 6+ months
- >90% of responders remain on treatment 6+ months

Data cut-off date: March 11, 2024. Patient treatment is decided based on iRECIST allowing for treatment beyond RECIST 1.1 progression. Each bar represents one patient in the study. The right arrow cap indicates patients who are ongoing on the study. Responses are per RECIST 1.1. One patient with clear early pseudoprogression (acc. to RECIST 1.1) and durable response later (acc. iRECIST; still on treatment at 14+ months → see previous slide).

Benchmarking: Exceptional Results for a Chemo-Free Regimen

Key takeaways, Cohort B (CPS <1)

- ✓ ORR of 35.5% and DCR of 58.1% are exceptional for a chemo-free regimen in this patient population
- ✓ Compares favorably to historical results from KEYTRUDA monotherapy[#] (see figures on the right)
- ✓ ORR similar to KEYTRUDA + chemo (~31%) and in the range of EXTREME regimen (~40%), without the associated toxicity of chemotherapy
- ✓ Early trends in durability look favourable (90% of responders ongoing treatment at 6 months)
  → Typically, duration of responses (DOR) is much better with IO-only therapies (e.g., DOR for KEYTRUDA monotherapy is 22.6 months vs. 6.7 months when combined with chemo[**])



PD-L1 CPS <1	KEYTRUDA mono (N=37) (KN-048)[#]	Efti + KEYTRUDA (N=31) (TACTI-003)
ORR, [95% CI]*	**2 (5.4%)** [0.7-18.2]	**11 (35.5%)** [19.2-54.6]
Complete Responses	0 (0.0%)	3 (9.7%)
Partial Responses	2 (5.4%)	8 (25.8%)

Comparison of data is from different clinical trials. # Data for pembrolizumab monotherapy from KN-048 (https://ascopubs.org/doi/10.1200/JCO.21.02198) in 37 evaluable patients with negative PD-L1 expression (CPS <1). The Food and Drug Administration (FDA) approved pembrolizumab in combination with ChT as first-line treatment regardless of PD-L1 expression and pembrolizumab alone for patients with PD-L1-expressing tumours (CPS ≥1). In contrast, the European Medicines Agency (EMA) has approved pembrolizumab with or without ChT only for patients with a CPS ≥1. Source: DOI:https://doi.org/10.1016/j.annonc.2020.07.011. * Calculated using Clopper-Pearson method. ** DOR data from KN-048 trial, Burtness et al., *The Lancet* 2019, https://doi.org/10.1016/S0140-6736(19)32591-7

Limited Competition in a Valuable Market

Limited competition in CPS <1

- 35.5% ORR among the highest reported for chemotherapy-free regimen in CPS <1
- Durability tracking well: >50% patients remain on treatment 6+ months and >90% of responders remain on treatment 6+ months
- Most IO combinations with anti-PD-1 therapy like KEYTRUDA exclude CPS <1 patients as anti-PD-1 alone is not very active

~$2.8 billion market

Overall head and neck cancer market valued at ~$2.8 billion[1] with HNSCC representing ~90% cases[2]

~100,000 metastatic HNSCC patients

>890,000 HNSCC diagnoses per annum worldwide[3] with ~100,000 patients who develop metastatic disease in 8 major market countries[1]

~Up to 20% of HNSCC population

CPS <1 patients represent up to ~20% of the HNSCC patient population[4]

Next Steps

- Discuss the path forward in 1L HNSCC CPS <1, where we have FDA Fast Track designation, with regulatory agencies
- Discuss results with key stakeholders (investigators, payers, etc.)

1. Extracted from GlobalData in June 2024, 8 Major Markets : US, China, Japan, France, Germany, Italy, Spain, UK. 2. Gormley, M., Creaney, G., Schache, A. et al. Reviewing the epidemiology of head and neck cancer: definitions, trends and risk factors. *Br Dent J* (2022). https://doi.org/10.1038/s41415-022-5166-x. 3. Johnson, D.E., Burtness, B., Leemans, C.R. et al. Head and neck squamous cell carcinoma. Nat Rev Dis Primers 6, 92 (2020), https://doi.org/10.1038/s41572-020-00224-3. 4. Burtness, B. et al. Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study The Lancet Volume 394, Issue 10212, P1915-1928, Nov 2019.

Outlook

Milestones & Catalysts Ahead

- **Non-Small Cell Lung Cancer –** TACTI-004 preparations for study start with FPI in late 2024 / early 2025
- **Non-Small Cell Lung Cancer –** Update from triple combo INSIGHT-003 trial
- **Head and Neck Squamous Cell Carcinoma –** Additional data will be presented in H2 CY2024
- **Soft Tissue Sarcoma –** Update from investigator-initiated EFTISARC-NEO study
- **Metastatic Breast Cancer –** Update from AIPAC-003 study evaluating 90mg vs 30mg efti dosing
- **Metastatic Urothelial Carcinoma –** Update from investigator-initiated INSIGHT-005 study
- **Autoimmune Diseases –** Continue IND-enabling studies of IMP761 and move toward to clinic in mid-2024
- **Other indications –** Updates from partnered programs and potential expansion of clinical trial pipeline
- **Cash Balance –** Pro forma cash balance of ~$195 million (US$ ~130 million)[1] providing cash runway to late CY2026

1. Based on cash balance as at 31 March 2024 and completion of a capital raising of A$100.2 million, excluding offer costs; estimate of US$130 million based on USD/AUD of $1.506

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Thank you