KEYTRUDA® (pembrolizumab) is the **FIRST and ONLY anti-PD-1 to present a sustained 5-year survival benefit** in monotherapy and combination with chemotherapy in first-line M/uR HNSCC (CPS ≥1)[1,a]

[a]In a Phase III registrational clinical trial

KEYTRUDA, as monotherapy or in combination with platinum and 5-fluorouracil (5-FU) chemotherapy, is indicated for the first-line treatment of metastatic or unresectable recurrent head and neck squamous cell carcinoma in adults whose tumours express PD-L1 with a CPS ≥1.[2]

Explore 5-Year Update >

SIGN UP TO LEARN MORE

Access and receive a range of educational resources on HNSCC, including real-world case studies, PD-L1 testing information, and long-term data updates.

Sign up >

This link will take you to an MSD promotional website to give your consent to receive marketing and promotional emails from MSD about our products, services and events.

Refer to the Summary of Product Characteristics before prescribing **KEYTRUDA** to help minimise the risks associated with treatment.[2]

Please click the following links for the prescribing information: GB PI | NI PI. REFERENCES

This content is intended to be viewed online, it is not intended to be printed.

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Merck Sharp & Dohme (UK) Limited (Tel: 0208 154 8000).

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KEYTRUDA® (pembrolizumab)

KEYNOTE-048 STUDY DESIGN: KEYTRUDA ± CHEMOTHERAPY VS. EXTREME[1-3,a,d]

A multicentre, randomised, open-label, active-controlled Phase III study[1-3]

Main Inclusion Criteria:

- Patients with M/uR HNSCC (N=882)
- No prior systemic treatment for metastatic illness or recurrent disease with local therapies
- Disease not classified as curable
- ECOG PS 0 or 1
- Tissue sample for PD-L1 evaluation
- Known p16 status for HNSCC in the oropharynx

R 1:1:1

KEYTRUDA monotherapy → **KEYTRUDA** 200 mg Q3W for up to 24 months

KEYTRUDA + chemotherapy → **KEYTRUDA** 200 mg + carboplatin AUC 5 mg/mL/min or cisplatin 100 mg/m² Q3W + 5-FU 1000 mg/m²/d for 4 days Q3W (maximum 6 cycles) → **KEYTRUDA** 200 mg Q3W for up to 24 months

EXTREME → Cetuximab 400 mg/m² initially and then 250 mg/m² Q1W + carboplatin AUC 5 mg/mL/min or cisplatin 100 mg/m² Q3W + 5-FU 1000 mg/m²/d over 4 days Q3W (maximum 6 cycles) → Cetuximab 250 mg/m² Q1W

Figure created by MSD after Tahara M et al. 5-year results from KEYNOTE-048; ESMO 2022.[1]

KEYNOTE-048 FINAL ANALYSIS PRIMARY EFFICACY OUTCOME DATA THAT LED TO APPROVAL OF KEYTRUDA FOR HNSCC[2-4]

KEYTRUDA monotherapy (CPS ≥1)

Median OS:

12.3 months with **KEYTRUDA**
(95% CI, 10.8–14.3; n=257)

10.3 months with **EXTREME**
(95% CI, 9.0–11.5; n=255)

- **Median follow up at 11.5 months**
- **OS significantly longer with KEYTRUDA vs. EXTREME[d]:** HR=0.74 (95% CI, 0.61–0.90); P=0.00133
- **PFS was not statistically different vs. EXTREME[d]:** HR=1.13[c] (95% CI, 0.94–1.36); P=0.89580

KEYTRUDA + chemotherapy (CPS ≥1)

Median OS:

13.6 months with **KEYTRUDA + plat/5-FU**
(95% CI, 10.7–15.5; n=242)

10.4 months with **EXTREME**
(95% CI, 9.1–11.7; n=235)

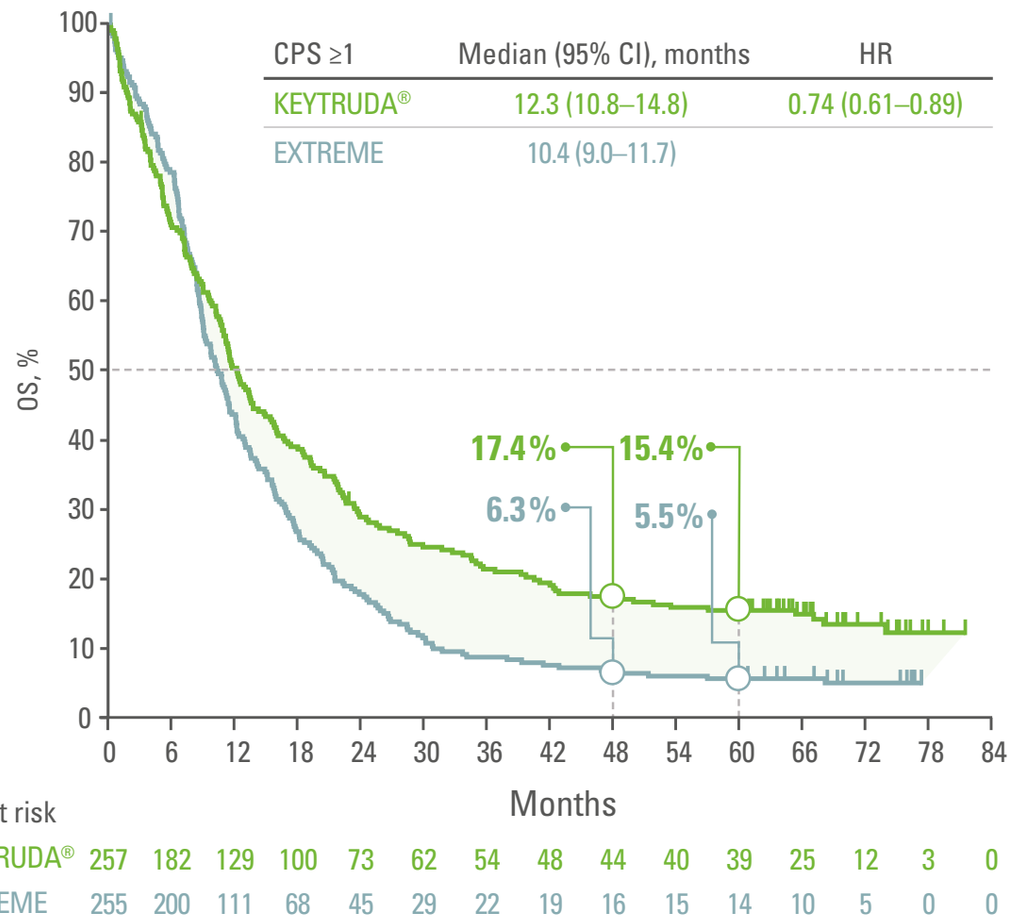
- **Median follow up at 13.0 months**
- **OS significantly longer with KEYTRUDA + chemotherapy vs. EXTREME[d]:** HR=0.65 (95% CI, 0.53–0.80); P=0.00002
- **PFS was not statistically different vs. EXTREME[d]:** HR=0.84[c] (95% CI, 0.69–1.02); P=0.03697

Primary efficacy endpoints: OS and PFS (assessed by a blinded independent central review committee according to RECIST v1.1 criteria)

KEYNOTE-048: Median OS with KEYTRUDA monotherapy vs. EXTREME[d] at 5 years[1]

KEYTRUDA monotherapy vs. EXTREME[d]: Long-term survival in a median follow-up of 69.2 months (CPS ≥1)[1]

HR=0.74 (95% CI, 0.61–0.89) (P not tested)



CPS ≥1	Median (95% CI), months	HR
KEYTRUDA®	12.3 (10.8–14.8)	0.74 (0.61–0.89)
EXTREME	10.4 (9.0–11.7)	

No. at risk															
KEYTRUDA®	257	182	129	100	73	62	54	48	44	40	39	25	12	3	0
EXTREME	255	200	111	68	45	29	22	19	16	15	14	10	5	0	0

5-year update:

- **Median OS of 12.3 months with KEYTRUDA** and 10.4 months with EXTREME
- **26% reduction of mortality risk with KEYTRUDA** vs. EXTREME

KEYTRUDA + chemotherapy vs. EXTREME[d]: Long-term survival in a median follow-up of 68.6 months (CPS ≥1)[4]

- mPFS in CPS ≥1 population was 3.2 months (95% CI, 2.2–3.4) for **KEYTRUDA** and 5.0 months (95% CI, 4.8–6.1) for EXTREME (HR=1.14; 95% CI, 0.95–1.37)
- ORR was 19.1% (95% CI, 14.5–24.4) for **KEYTRUDA** and 34.9% (95% CI, 29.1–41.1) for EXTREME
- mDOR was 23.4 months (range, 1.5+ to 75.5+) for **KEYTRUDA** and 4.5 months (range, 1.2+ to 73.9+) for EXTREME
- This data was from an exploratory post-hoc analysis where significance was not tested therefore no statistical conclusions can be drawn from this analysis[1]

Figure created by MSD after Tahara M et al. 5-year results from KEYNOTE-048; ESMO 2022.[1]

Prescribing information GB | NI

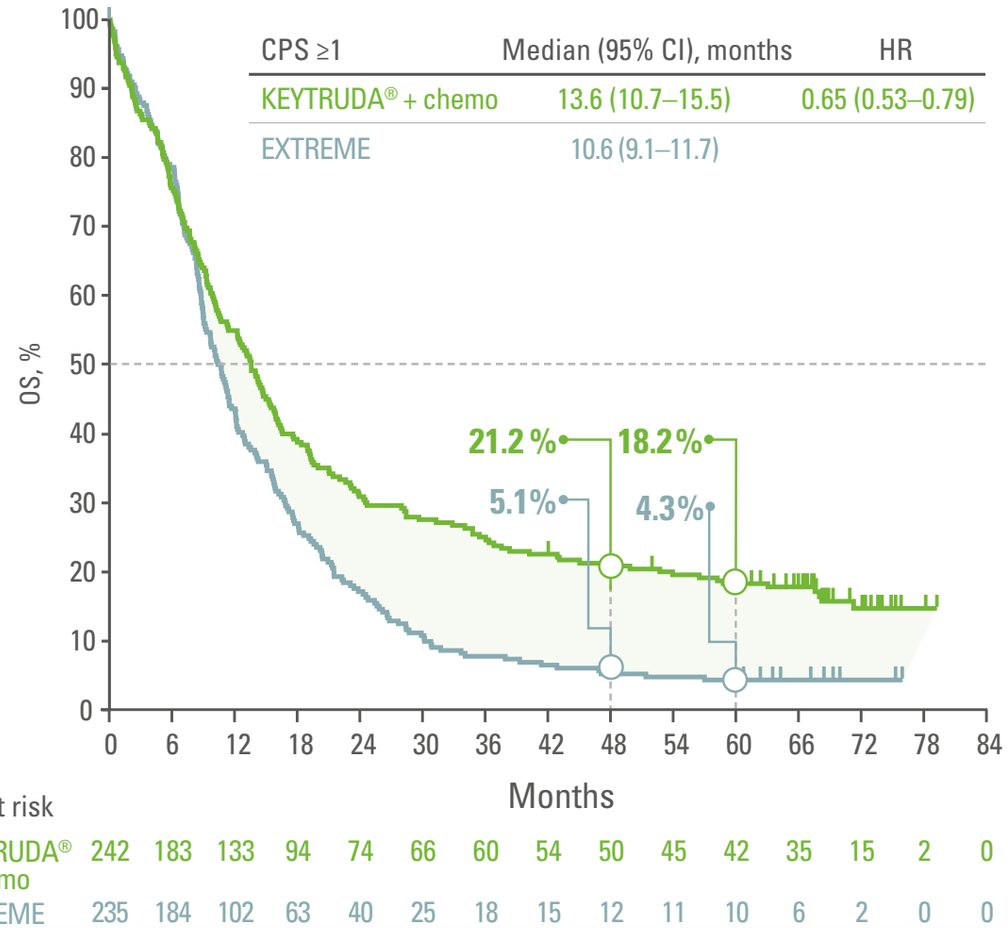
KEYTRUDA® (pembrolizumab)

KEYNOTE-048: Median OS with KEYTRUDA plus chemotherapy vs. EXTREME[d] at 5 years[1]

KEYTRUDA monotherapy vs. EXTREME[d]: Long-term survival in a median follow-up of 69.2 months (CPS ≥1)[1]

KEYTRUDA + chemotherapy vs. EXTREME[d]: Long-term survival in a median follow-up of 68.6 months (CPS ≥1)[1]

HR=0.65 (95% CI, 0.53–0.79) (P not tested)



CPS ≥1	Median (95% CI), months	HR
KEYTRUDA® + chemo	13.6 (10.7–15.5)	0.65 (0.53–0.79)
EXTREME	10.6 (9.1–11.7)	

No. at risk

KEYTRUDA® + chemo	242	183	133	94	74	66	60	54	50	45	42	35	15	2	0
EXTREME	235	184	102	63	40	25	18	15	12	11	10	6	2	0	0

5-year update:

- **Median OS of 13.6 months with KEYTRUDA + chemotherapy** and 10.6 months with EXTREME
- **35% reduction of mortality risk with KEYTRUDA + chemotherapy** vs. EXTREME

- mPFS in CPS ≥1 population was 5.1 months (95% CI, 4.7–6.2) for **KEYTRUDA + chemotherapy** and 5.0 months (95% CI, 4.8–6.1) for EXTREME (HR=0.87; 95% CI, 0.72–1.05)
- ORR was 38.0% (95% CI, 31.9–44.5) for **KEYTRUDA + chemotherapy** and 35.7% (95% CI, 29.6–42.2) for EXTREME
- mDOR was 6.7 months (range, 1.6+ to 73.8+) for **KEYTRUDA + chemotherapy** and 4.3 months (range, 1.2+ to 66.5+) for EXTREME
- This data was from an exploratory post-hoc analysis where significance was not tested therefore no statistical conclusions can be drawn from this analysis[1]

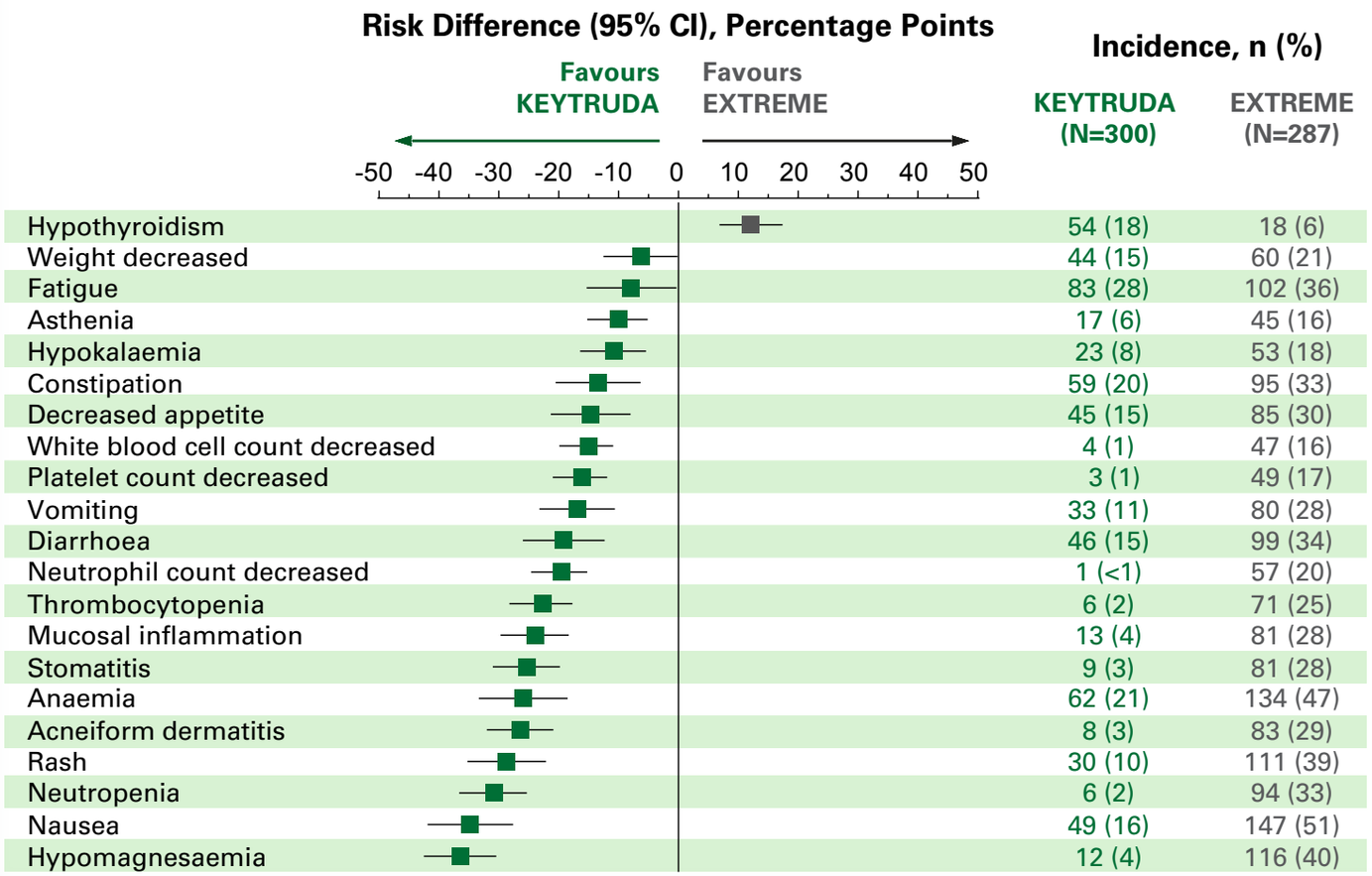
Figure created by MSD after Tahara M et al. 5-year results from KEYNOTE-048; ESMO 2022.[1]

KEYNOTE-048: KEYTRUDA monotherapy demonstrated a favourable safety profile vs. EXTREME[d] and KEYTRUDA combination with chemotherapy demonstrated a comparable safety profile to EXTREME[4,d]

Final analysis: Adverse events with KEYTRUDA monotherapy at 2 years in the as-treated population[e] vs. EXTREME[4,d,f]

Final analysis: Adverse events with KEYTRUDA + chemotherapy at 2 years in the as-treated population[e] vs. EXTREME[4,d,f]

Risk difference for adverse events of any cause with incidence ≥15%[4]



ALL AEs[3]	KEYTRUDA (N=300)	EXTREME (N=287)
Grade 3–5 AEs[4,e]	55%	83%
AEs leading to death[4,e]	8%	10%
TRAEs leading to death[4]	1%	3%
Discontinuation rate due to AEs[3,e]	12%	28%

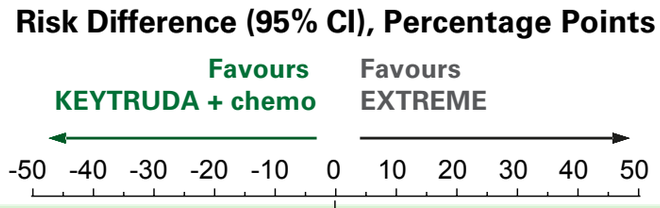
A favourable safety profile of **KEYTRUDA monotherapy** vs. EXTREME regimen was demonstrated, with the exception of hypothyroidism and pneumonitis[2,3]

KEYNOTE-048: KEYTRUDA monotherapy demonstrated a favourable safety profile vs. EXTREME[d] and KEYTRUDA combination with chemotherapy demonstrated a comparable safety profile to EXTREME[4,d]

Final analysis: Adverse events with KEYTRUDA monotherapy at 2 years in the as-treated population[e] vs. EXTREME[4,d,f]

Final analysis: Adverse events with KEYTRUDA + chemotherapy at 2 years in the as-treated population[e] vs. EXTREME[4,d,f]

Risk difference for adverse events of any cause with incidence ≥15%[4]



	Incidence, n (%)	
	KEYTRUDA + chemo (N=276)	EXTREME (N=287)
Anaemia	161 (58)	134 (47)
Hypothyroidism	44 (16)	18 (6)
Cough	53 (19)	37 (13)
Vomiting	90 (33)	80 (28
Pyrexia	45 (16)	35 (12)
Thrombocytopenia	79 (29)	71 (25)
Constipation	102 (37)	95 (33)
Platelet count decreased	55 (20)	49 (17)
Mucosal inflammation	85 (31)	81 (28)
Asthenia	46 (17)	45 (16)
Neutropenia	93 (34)	94 (33)
Nausea	141 (51)	147 (51)
Decreased appetite	80 (29)	85 (30)
Fatigue	95 (34)	102 (36)
Stomatitis	74 (27)	81 (28)
Neutrophil count decreased	50 (18)	57 (20)
White blood cell count decreased	36 (13)	47 (16)
Weight decreased	44 (16)	60 (21)
Diarrhoea	78 (28)	99 (34)
Hypokalaemia	32 (12)	53 (18)
Hypomagnaesemia	44 (16)	116 (40)
Rash	29 (11)	111 (39)
Acneiform dermatitis	1 (<1)	83 (29)

ALL AEs[3]	KEYTRUDA + CHEMO (N=276)	EXTREME (N=287)
Grade 3–5 AEs[4,e]	85%	83%
AEs leading to death[4,e]	12%	10%
TRAEs leading to death[4]	4%	3%
Discontinuation rate due to AEs[3,e]	33%	28%

The overall safety profile for **KEYTRUDA + chemotherapy** was **similar** to EXTREME[3]

[a]PD-(L)1 antibody therapy.
[b]5-year update, median follow-up was 69.2 months for **KEYTRUDA** monotherapy and 68.6 months for **KEYTRUDA** + chemotherapy.
[c]HR based on the "stratified Cox proportional hazard model"; P value based on the stratified log rank test.
[d]EXTREME = cetuximab + carboplatin or cisplatin + 5-fluorouracil.
[e]Any cause that occurred in ≥5% of patients.
[f]As-treated population included all patients who received at least one dose of allocated treatment.[3]

REFERENCES

1. Tahara M et al. Presented at ESMO 2022. September 9–13, 2022. Abstract 659MO.
2. **KEYTRUDA** Summary of Product Characteristics.
3. Burtness B et al. *Lancet*. 2019;394(10212): 1915–1928.
4. Burtness B et al. *Lancet*. 2019:394;1915–28 (suppl. appx.).

ABBREVIATIONS

5-FU = 5-fluorouracil; **AE** = adverse event; **AUC** = area under the curve; **chemo** = chemotherapy; **CI** = confidence interval; **CPS** = combined positive score; **ECOG PS** = Eastern Cooperative Oncology Group performance status; **ESMO** = European Society for Medical Oncology; **HNSCC** = head and neck squamous cell carcinoma; **HR** = hazard ratio; **M/uR** = metastatic or unresectable recurrent; **mDOR** = median duration of response; **mPFS** = median progression-free survival; **ORR** = objective response rate; **OS** = overall survival; **PD-L1** = programmed death ligand 1; **PFS** = progression-free survival; **Q1W** = every week; **Q3W** = every 3 weeks; **R** = randomization; **RECIST v1.1** = Response Evaluation Criteria in Solid Tumors version 1.1; **TRAE** = treatment-related adverse event.