



**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  $\geq 1$ )<sup>1,a</sup>**

<sup>a</sup>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  $\geq 1$ .<sup>2</sup>

#### **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.

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.<sup>2</sup>

Please click the following links for the prescribing information: [GB PI](#) | [NI PI](#). [REFERENCES](#)

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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).



**KEYTRUDA®**  
(pembrolizumab)



## KEYNOTE-048 STUDY DESIGN: KEYTRUDA ± CHEMOTHERAPY VS. EXTREME<sup>1-3,a,d</sup>

A multicentre, randomised, open-label, active-controlled Phase III study<sup>1-3</sup>

### 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

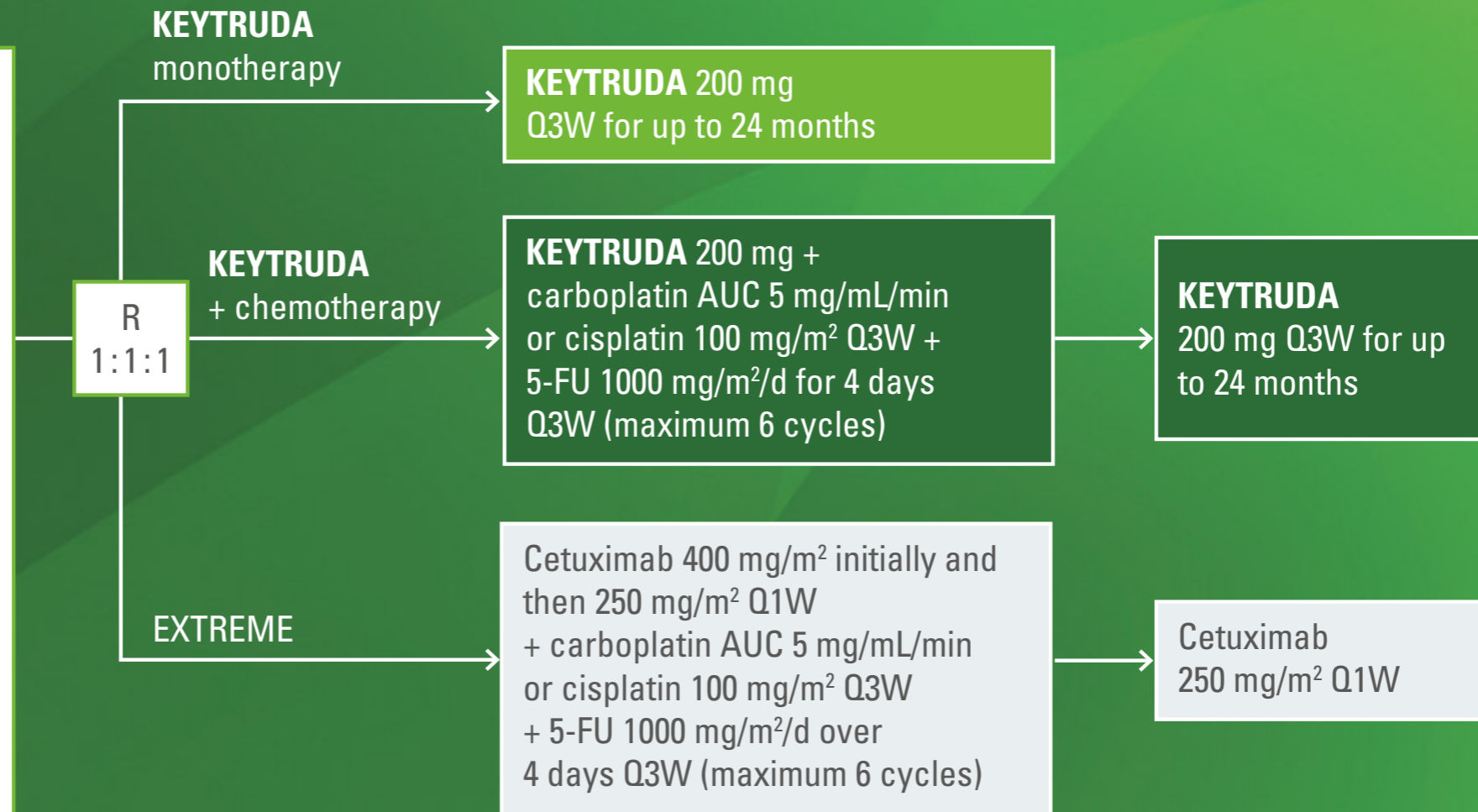


Figure created by MSD after Tahara M et al. 5-year results from KEYNOTE-048; ESMO 2022.<sup>1</sup>





## KEYNOTE-048 FINAL ANALYSIS PRIMARY EFFICACY OUTCOME DATA THAT LED TO APPROVAL OF KEYTRUDA FOR HNSCC<sup>2-4</sup>

### KEYTRUDA monotherapy (CPS $\geq 1$ )

#### 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**<sup>d</sup>:  
HR=0.74 (95% CI, 0.61–0.90); P=0.00133
- PFS was not statistically different vs. **EXTREME**<sup>d</sup>:  
HR=1.13<sup>c</sup> (95% CI, 0.94–1.36); P=0.89580

### KEYTRUDA + chemotherapy (CPS $\geq 1$ )

#### 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**<sup>d</sup>:  
HR=0.65 (95% CI, 0.53–0.80); P=0.00002
- PFS was not statistically different vs. **EXTREME**<sup>d</sup>:  
HR=0.84<sup>c</sup> (95% CI, 0.69–1.02); P=0.03697

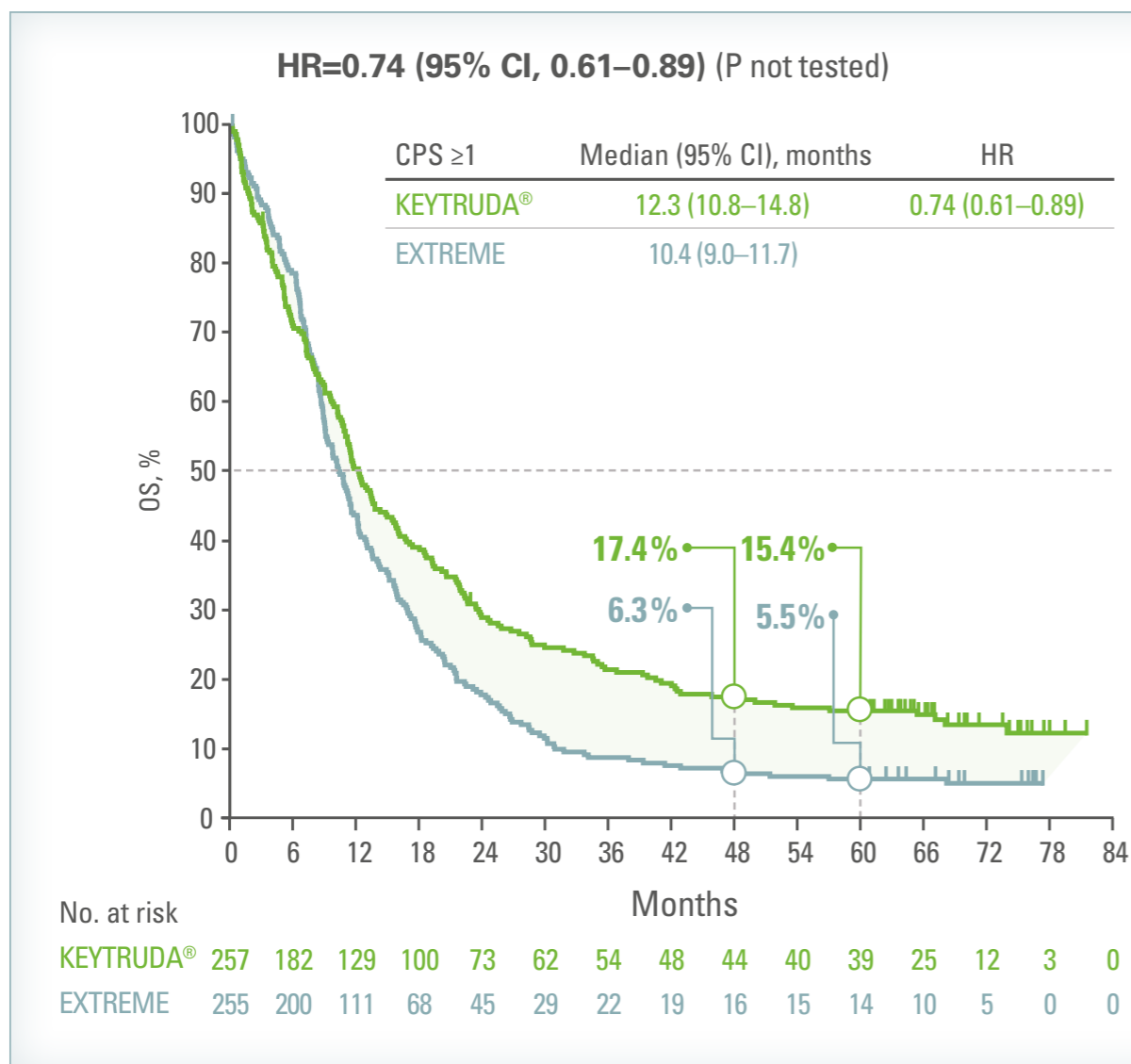
Primary efficacy endpoints: OS and PFS (assessed by a blinded independent central review committee according to RECIST v1.1 criteria)



# KEYNOTE-048: Median OS with KEYTRUDA monotherapy vs. EXTREME<sup>d</sup> at 5 years<sup>1</sup>

## KEYTRUDA monotherapy vs. EXTREME<sup>d</sup>: Long-term survival in a median follow-up of 69.2 months (CPS ≥1)<sup>1</sup>

## KEYTRUDA + chemotherapy vs. EXTREME<sup>d</sup>: Long-term survival in a median follow-up of 68.6 months (CPS ≥1)<sup>4</sup>



### 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

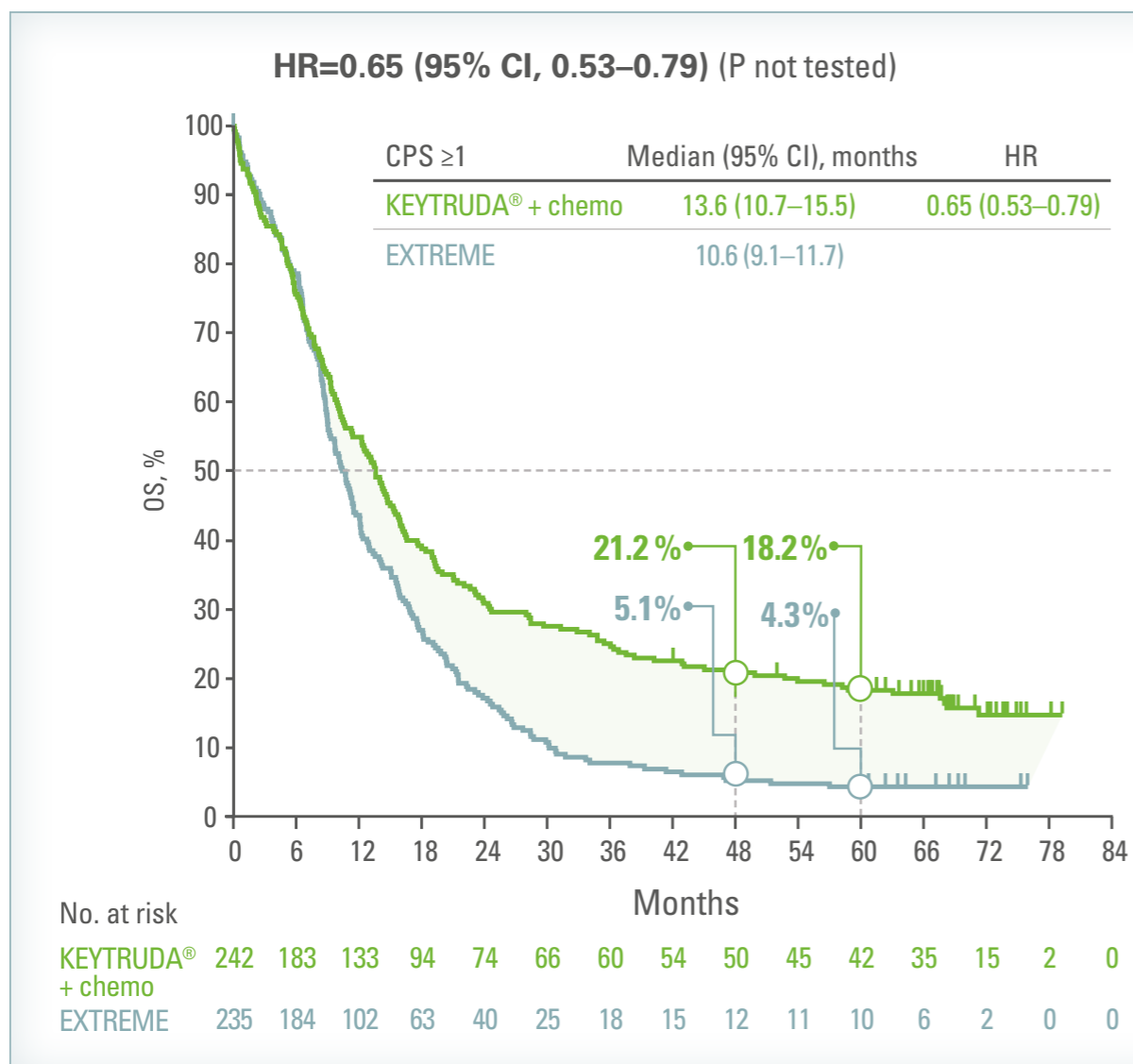
- mPFS in CPS ≥1 population was 3.2 months (95% CI, 2.2–3.4) for KEYTRUDA and 5.0 months (95% CI, 4.8–6.1) for EXTREME (HR=1.14; 95% CI, 0.95–1.37)
- ORR was 19.1% (95% CI, 14.5–24.4) for KEYTRUDA and 34.9% (95% CI, 29.1–41.1) for EXTREME
- mDOR was 23.4 months (range, 1.5+ to 75.5+) for KEYTRUDA and 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<sup>1</sup>

Figure created by MSD after Tahara M et al. 5-year results from KEYNOTE-048; ESMO 2022.<sup>1</sup>

# KEYNOTE-048: Median OS with KEYTRUDA plus chemotherapy vs. EXTREME<sup>d</sup> at 5 years<sup>1</sup>

**KEYTRUDA monotherapy vs. EXTREME<sup>d</sup>:**  
Long-term survival in a median follow-up of 69.2 months (CPS ≥1)<sup>1</sup>

**KEYTRUDA + chemotherapy vs. EXTREME<sup>d</sup>:**  
Long-term survival in a median follow-up of 68.6 months (CPS ≥1)<sup>1</sup>



### 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<sup>1</sup>

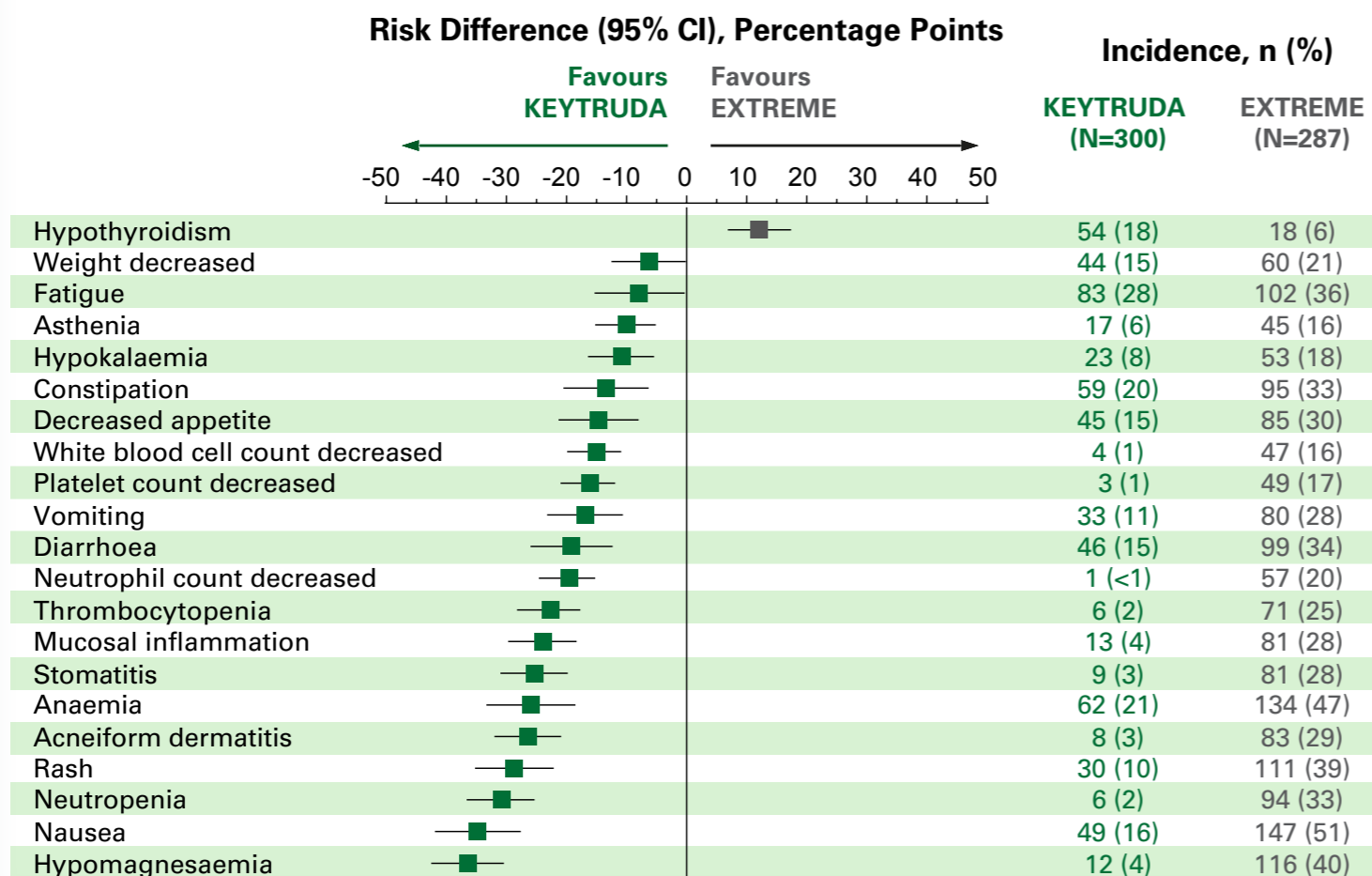
Figure created by MSD after Tahara M et al. 5-year results from KEYNOTE-048; ESMO 2022.<sup>1</sup>

# KEYNOTE-048: KEYTRUDA monotherapy demonstrated a favourable safety profile vs. EXTREME<sup>d</sup> and KEYTRUDA combination with chemotherapy demonstrated a comparable safety profile to EXTREME<sup>4,d</sup>

## Final analysis: Adverse events with KEYTRUDA monotherapy at 2 years in the as-treated population<sup>e</sup> vs. EXTREME<sup>4,d,f</sup>

## Final analysis: Adverse events with KEYTRUDA + chemotherapy at 2 years in the as-treated population<sup>e</sup> vs. EXTREME<sup>4,d,f</sup>

### Risk difference for adverse events of any cause with incidence $\geq 15\%$ <sup>4</sup>



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

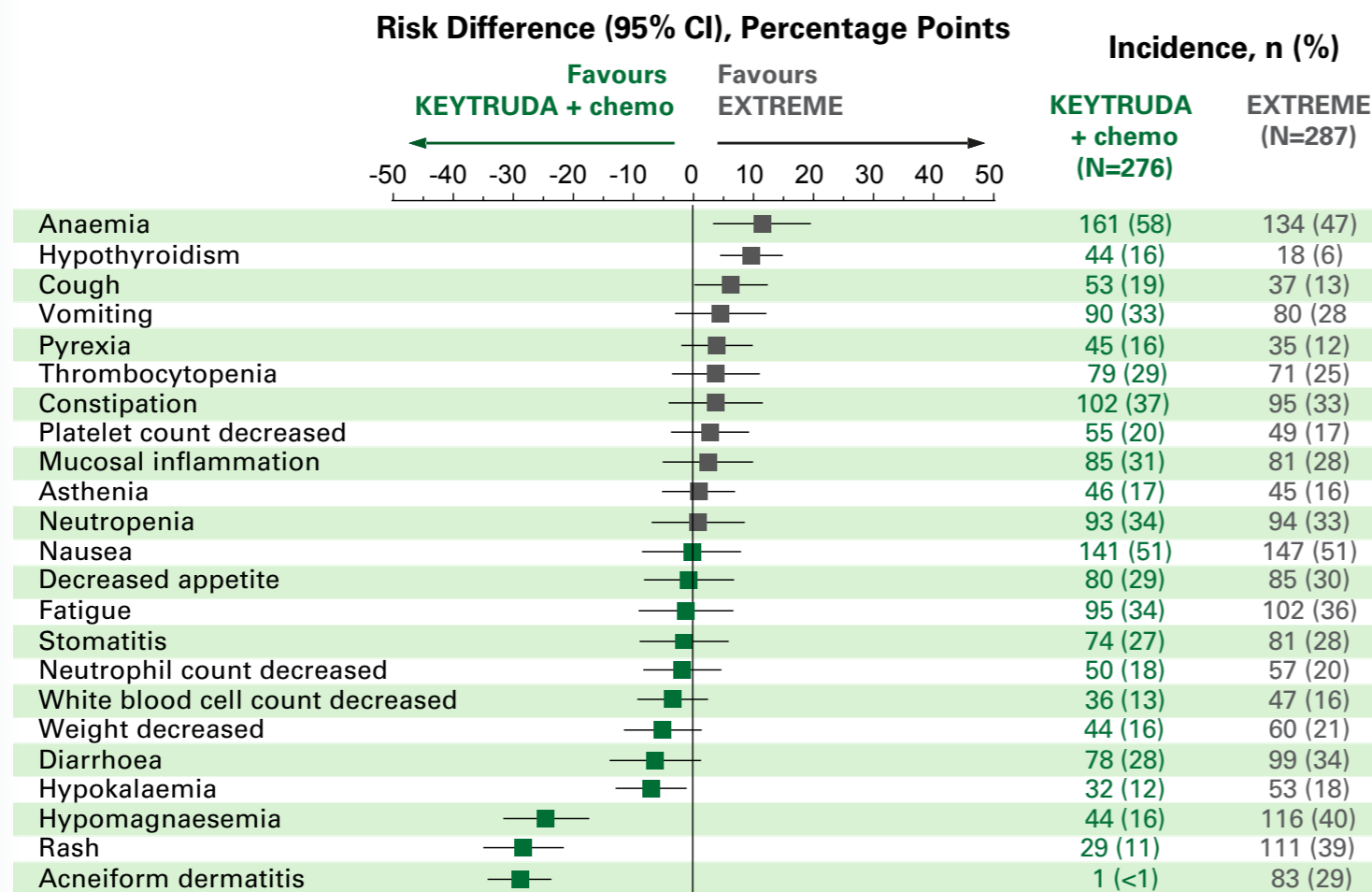
**A favourable safety profile of KEYTRUDA monotherapy vs. EXTREME regimen was demonstrated, with the exception of hypothyroidism and pneumonitis<sup>2,3</sup>**

# KEYNOTE-048: KEYTRUDA monotherapy demonstrated a favourable safety profile vs. EXTREME<sup>d</sup> and KEYTRUDA combination with chemotherapy demonstrated a comparable safety profile to EXTREME<sup>4,d</sup>

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

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

## Risk difference for adverse events of any cause with incidence $\geq 15\%$ <sup>4</sup>



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

The overall safety profile for KEYTRUDA + chemotherapy was similar to EXTREME<sup>3</sup>

<sup>a</sup>PD-(L)1 antibody therapy.

<sup>b</sup>5-year update, median follow-up was 69.2 months for **KEYTRUDA** monotherapy and 68.6 months for **KEYTRUDA** + chemotherapy.

<sup>c</sup>HR based on the “stratified Cox proportional hazard model”; P value based on the stratified log rank test.

<sup>d</sup>EXTREME = cetuximab + carboplatin or cisplatin + 5-fluorouracil.

<sup>e</sup>Any cause that occurred in ≥5% of patients.

<sup>f</sup>As-treated population included all patients who received at least one dose of allocated treatment.<sup>3</sup>

#### 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.