MSD Oncology

KEYNOTE-859: First-line treatment (KEYTRUDA® [pembrolizumab] plus chemotherapy) of locally advanced unresectable or metastatic HER2-negative gastric or gastro-oesophageal junction adenocarcinoma

Please refer to the full KEYTRUDA® (pembrolizumab) Summary of Product Characteristics (SmPC) and Risk Minimisation Materials for patients before prescribing KEYTRUDA

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ (please note that the MHRA Yellow Card link will redirect you to an external website, for which MSD does not review or control the content) 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: 020 8154 8000).

Intended for UK Healthcare Professionals only.
For the KEYTRUDA Prescribing Information, please click the following link or the PI button located on each slide.

MSD

Merck Sharp & Dohme (UK) Limited
Registered Office: 120 Moorgate, London EC2M 6UR, United Kingdom
Registered in England No. 233687

Slide deck navigation

Click the links below to navigate to the section of interest

Gastric cancer overview

KEYNOTE-859: Overview

KEYNOTE-859: Results

KEYNOTE-859: Summary

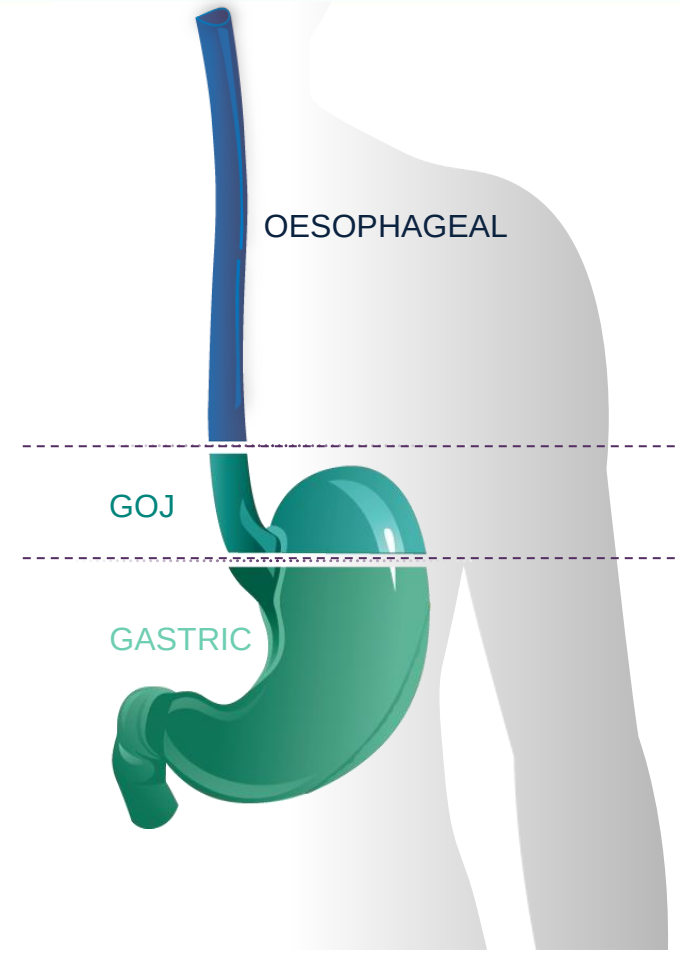
Appendix

- To access the navigation page, click the ‘Home’ icon
- The links in this slide deck will redirect you to third-party websites where indicated. Please note that MSD does not:
  - Review or control the content of any third-party website
  - Endorse and have responsibility for the accuracy, content, practices or standards of any third-party sources

PI

PI, prescribing information.

KEYTRUDA licensed and reimbursed oesophago-gastric indications in the UK



KEYNOTE-590: KEYTRUDA + chemotherapy in patients with CPS ≥10[1]

KEYTRUDA, in combination with platinum and fluoropyrimidine-based chemotherapy, is indicated for the first-line treatment of locally advanced unresectable or metastatic carcinoma of the oesophagus in adults whose tumours express PD-L1 with CPS ≥10[1]

£ NICE and SMC reimbursed[2,3]

KEYNOTE-859: KEYTRUDA + chemotherapy in patients with CPS ≥1[1]

KEYTRUDA, in combination with fluoropyrimidine and platinum-containing chemotherapy, is indicated for the first-line treatment of locally advanced unresectable or metastatic HER2-negative gastric or gastro-oesophageal junction adenocarcinoma in adults whose tumours express PD-L1 with CPS ≥1[1]

£ NICE and SMC reimbursed[4,5]

CPS, combined positive score; GOJ, gastro-oesophageal junction; HER2, human epidermal growth factor receptor 2; NICE, National Institute for Health and Care Excellence; PD-L1, programmed death ligand-1; PI, prescribing information; SMC, Scottish Medicines Consortium.

1. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc#about-medicine Accessed September 2024;
2. SMC Medicines Advice (SMC2420) April 2022. Available at: pembrolizumab-keytruda-final-april-2022-amended-4522-for-website.pdf (scottishmedicines.org.uk). Accessed September 2024; 3. NICE. Technology appraisal guidance [TA737] October 2021. Available at: https://www.nice.org.uk/guidance/ta737. Accessed September 2024; 4 SMC Medicines Advice. July 2024 news release. Available at: https://scottishmedicines.org.uk/about-us/latest-update/july-2024-decisions-news-release/. Accessed September 2024; 5. NICE. Technology appraisal guidance [GID-TA11039]. In development. Available at: https://www.nice.org.uk/guidance/indevelopment/gid-ta11039. Accessed September 2024.

PI

In the UK, there are ~4200 deaths due to gastric cancer per year[a]

Gastric cancer is the **17th most commonly diagnosed cancer** in the UK[b]

In the UK, **approximately 6500** new cases of gastric cancer are diagnosed each year[b]

Approximately 17% of patients with gastric cancer **in England will survive their cancer for ≥10 years**[c]

Gastric cancer has the highest incidence rate in those aged **85–89 years**[b]

2 in 3 cases of gastric cancer are in men[b]

[a]Data collected from 2017–2019; [b]Data collected from 2016–2018; [c]Data collected from 2013–2017.

PI, prescribing information.

Cancer Research UK. Stomach cancer statistics. Available at: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/stomach-cancer. Accessed September 2024.

PI

Chemotherapy treatment for advanced HER2-negative gastric or GOJ cancer is associated with poor survival outcomes[1]

Patients with HER2-negative tumours

~80% of patients with advanced GOJ cancer have **HER2-negative** tumours[2]

IO therapy

Recent studies have showed that the addition of **IO therapy** to chemotherapy **improves clinical outcomes,** including OS, in patients with advanced HER2-negative **gastric or GOJ cancer**[3]

KEYNOTE-859

KEYTRUDA in combination with chemotherapy has been shown to **improve clinical outcomes** in patients with advanced cancer, and was recently investigated in patients with advanced HER2-negative **gastric or GOJ cancer**[4]

IO + chemotherapy has become an important treatment option in patients with gastric or GOJ cancer. **KEYNOTE-859** provides additional data on treatment options available for patients with advanced HER2-negative gastric or GOJ cancer[4]

GOJ, gastro-oesophageal junction; HER2, human epidermal growth factor receptor 2; IO, immuno-oncology; OS, overall survival; PD-L1, programmed death ligand-1; PI, prescribing information.

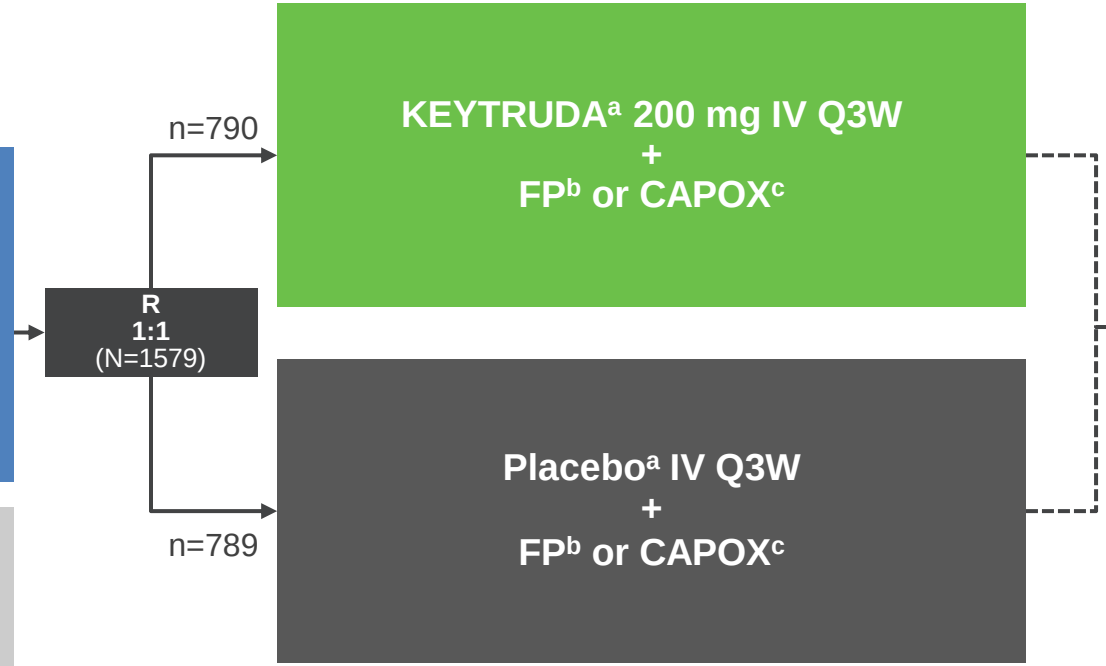
1. Sexton RE et al. *Cancer Metastasis Rev* 2020;39:1179–1203; 2. Ross JS et al. *Gastrointest Cancer Res* 2011;4:62–66; 3. Janjigian YY et al. *Lancet Oncol* 2021;398:27–40;
4. Rha SY et al. *Lancet Oncol* 2023;24:1181–1195.

PI

KEYNOTE-859: Study design[1,2]

Multicentre, randomised, double-blind, placebo-controlled Phase 3 trial

Patients enrolled until 3 October 2022 (N=1579)



Key eligibility criteria

- Advanced gastric or GOJ adenocarcinoma
- HER2-negative
- Known PD-L1 status
- ECOG PS 0 or 1
- No prior systemic treatment for metastatic disease

Stratification factors at randomisation

- Geographic region
- PD-L1 CPS (<1 vs ≥1)
- Investigator's choice of chemotherapy (FP vs CAPOX)

Until unacceptable toxicity, disease progression or for a maximum of 35 cycles

- **Primary endpoint**: OS
- **Secondary endpoints**: PFS, ORR and DOR, as assessed by BICR using RECIST v1.1, and safety

Figure adapted from Tabernero J et al. 2021.

[a]Administered on Day 1 of each cycle; [b]Cisplatin 80 mg/m^2 IV Q3W + 5-FU 800 mg/m^2/day IV on Days 1–5; [c]Oxaliplatin 130 mg/m^2 IV Q3W + capecitabine 1000 mg/m^2 BID on Days 1–14.

5-FU, 5-fluorouracil; BICR, blinded independent central review; BID, twice a day; CAPOX, capecitabine and oxaliplatin; CPS, combined positive score; DOR, duration of response; ECOG PS: Eastern Cooperative Oncology Group performance status; FP, 5-fluorouracil and cisplatin; GOJ, gastro-oesophageal junction; HER2, human epidermal growth factor receptor 2; IV, intravenous; ORR, objective response rate; OS, overall survival; PD-L1, programmed death ligand-1; PFS, progression-free survival; PI, prescribing information; Q3W, every 3 weeks; R, randomisation; RECIST v1.1, Response Evaluation Criteria In Solid Tumors Version 1.1.

1. Tabernero J et al. *Future Oncol* 2021;17:2847–2855; 2. Rha SY et al. *Lancet Oncol* 2023;24:1181–1195.

PI

KEYNOTE-859: Baseline characteristics

Characteristic	KEYTRUDA + FP or CAPOX (n=790)	Placebo + FP or CAPOX (n=789)
Age, median (IQR), years	61 (52–67)	62 (52–69)
Age ≥65 years, n (%)	304 (38)	310 (39)
Male sex, n (%)	527 (67)	544 (69)
Geographic region, n (%)		
Asia	263 (33)	262 (33)
Western Europe, Israel, North America and Australia	201 (25)	202 (26)
Rest of world	326 (41)	325 (41)
ECOG PS, n (%)		
0	281 (36)	301 (38)
1	509 (64)	488 (62)
Disease status,[a] n (%)		
Locally advanced	28 (4)	30 (4)
Metastatic	761 (96)	759 (96)
Primary tumour location,[b] n (%)		
Adenocarcinoma of the GOJ	149 (19)	185 (23)
Adenocarcinoma of the stomach	640 (81)	603 (76)

Characteristic	KEYTRUDA + FP or CAPOX (n=790)	Placebo + FP or CAPOX (n=789)
MSI-H status[c] high, n (%)	39 (5)	35 (4)
PD-L1 status,[d] n (%)		
CPS ≥1 at baseline	618 (78)	617 (78)
CPS ≥10 at baseline	279 (35)	272 (34)
Combination chemotherapy at randomisation		
CAPOX	682 (86)	681 (86)
FP	108 (14)	108 (14)
Histological subtype,[e] n (%)		
Diffuse	318 (40)	301 (38)
Indeterminate	186 (24)	215 (27)
Intestinal	284 (36)	273 (35)
Liver metastases present[f]	314 (40)	311 (39)
Prior gastrectomy/oesophagectomy[g]	172 (22)	162 (21)

Table adapted from Rha SY et al. 2023.

Analysis cut-off date: 3 October 2022.

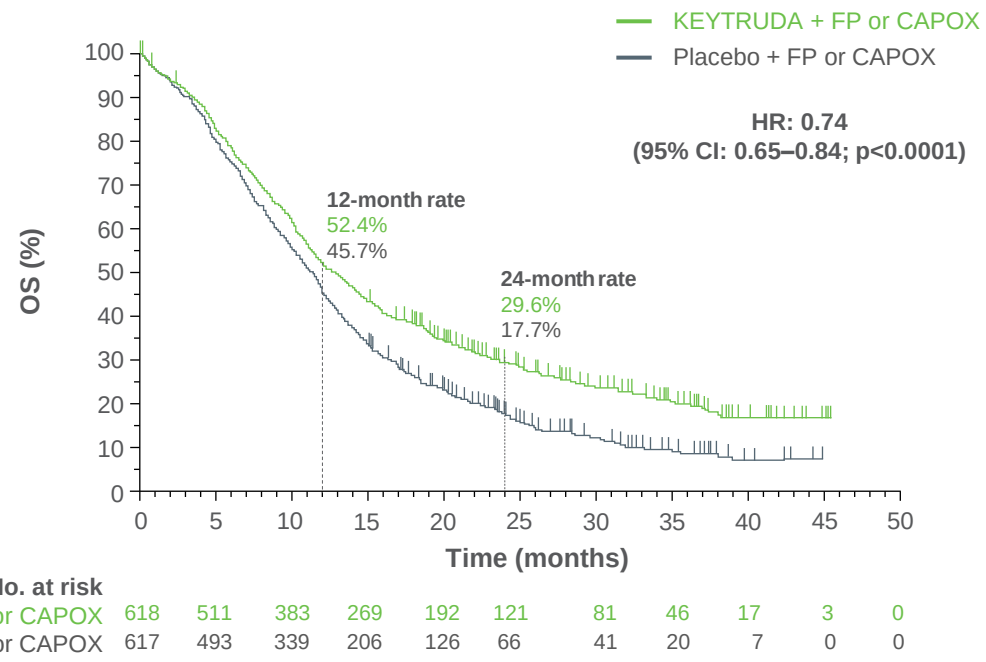
[a]Missing in 1 patient (<1%) in the KEYTRUDA + FP or CAPOX group; [b]Other in 1 patient (<1%) in the placebo + FP or CAPOX group and missing in 1 patient (<1%) in the KEYTRUDA + FP or CAPOX group; [c]Missing in 110 patients (14%) in the KEYTRUDA + FP or CAPOX group and in 114 patients (14%) in the placebo + FP or CAPOX; [d]Missing in 2 patients (<1%) in the KEYTRUDA + FP or CAPOX group; [e]Unknown in 1 patient (<1%) and missing in 1 patient (<1%) in the KEYTRUDA + FP or CAPOX group; [f]Missing in 1 patient (<1%) in the KEYTRUDA + FP or CAPOX group; [g]Missing in 5 patients (1%) in each group.

CAPOX, capecitabine + oxaliplatin; CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; FP, 5-fluorouracil + cisplatin; GOJ, gastro-oesophageal junction; IQR, interquartile range; ITT, intention-to-treat; MSI-H, microsatellite instability-high; PD-L1, programmed death ligand-1.

Rha SY et al. *Lancet Oncol* 2023;24:1181–1195.

KEYNOTE-859: Primary endpoint – OS in patients with PD-L1 CPS ≥1[a,1,2]

Median (IQR) follow-up time: 31.0 (23.0–38.3) months



OS[b]	KEYTRUDA + FP or CAPOX (n=618)	Placebo + FP or CAPOX (n=617)
Patients with event, %	75.1	85.3
Median OS[c] (95% CI), months	13.0 (11.6–14.2)	11.4 (10.5–12.0)

Figure and table adapted from Rha SY et al. 2023.[1,2]

Analysis cut-off date: 3 October 2022.
[a]OS in the PD-L1 CPS ≥1 population was an alpha-controlled analysis; [b]OS was compared between treatment arms using the log-rank test stratified by the randomisation stratification factors; the magnitude of the treatment effect was assessed using a Cox regression model stratified by the randomisation stratification factors; [c]Based on Kaplan–Meier estimates.

CAPOX, capecitabine and oxaliplatin; CI, confidence interval; CPS, combined positive score; FP, 5-fluorouracil and cisplatin; HR, hazard ratio; IQR, interquartile range; OS, overall survival; PD-L1, programmed death ligand-1; PFS, progression-free survival; PI, prescribing information.

1. Rha SY et al. *Lancet Oncol* 2023;24:1181–1195; 2. Rha SY et al. Poster presented at American Society of Clinical Oncology (ASCO) Congress 2023, 2–6 June 2023, Chicago, USA.

PI

KEYNOTE-859: Secondary endpoint – PFS in patients with PD-L1 CPS ≥1[a,1,2]

Median (IQR) follow-up time: 31.0 (23.0–38.3) months

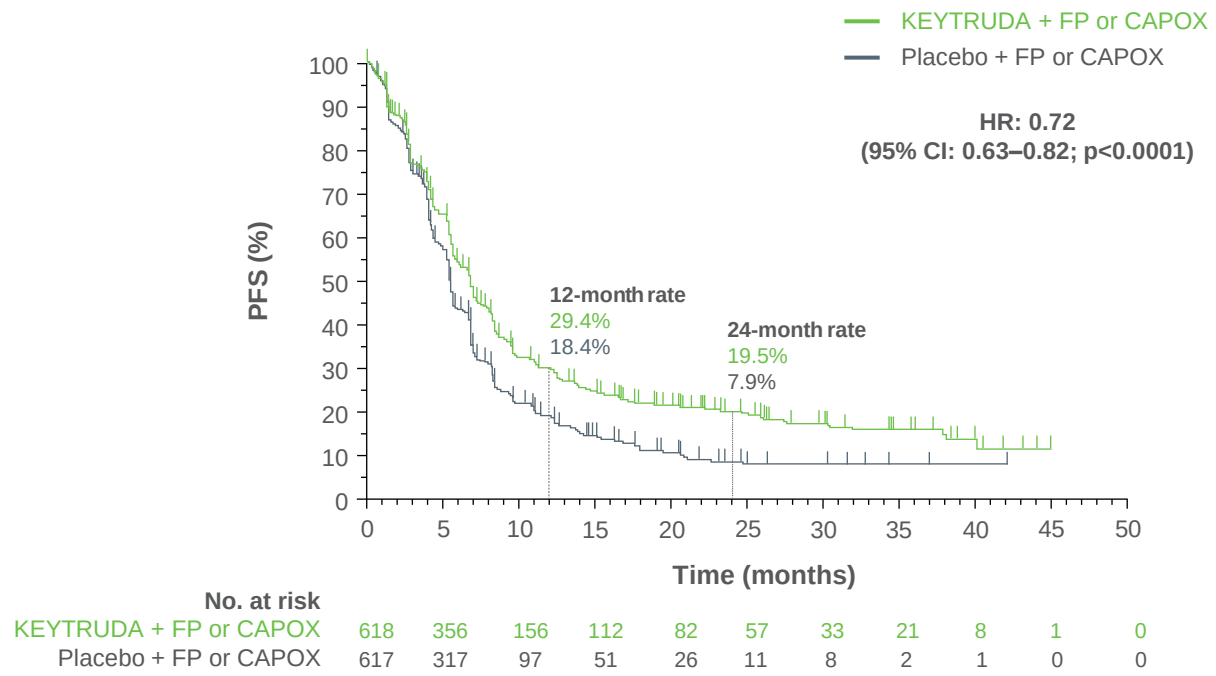


Figure and table adapted from Rha SY et al. 2023.[1,2]

PFS[b,c]	KEYTRUDA + FP or CAPOX (n=618)	Placebo + FP or CAPOX (n=617)
Patients with event, %	71.7	78.3
Median PFS[d] (95% CI), months	6.9 (6.0–7.2)	5.6 (5.4–5.7)

Analysis cut-off date: 3 October 2022.

[a]PFS in the PD-L1 CPS ≥1 population was an alpha-controlled analysis; [b]PFS was compared between treatment arms using the log-rank test stratified by the randomisation stratification factors; the magnitude of the treatment effect was assessed using a Cox regression model stratified by the randomisation stratification factors; [c]Assessed by BICR using RECIST v1.1; [d]Based on Kaplan–Meier estimates.

BICR, blinded independent central review; CAPOX, capecitabine and oxaliplatin; CI, confidence interval; CPS, combined positive score; FP, 5-fluorouracil and cisplatin; HR, hazard ratio; IQR, interquartile range; PD-L1, programmed death ligand-1; PFS, progression-free survival; PI, prescribing information; RECIST v1.1, Response Evaluation Criteria In Solid Tumors Version 1.1.

1. Rha SY et al. *Lancet Oncol* 2023;24:1181–1195; 2. Rha SY et al. Poster presented at American Society of Clinical Oncology (ASCO) Congress 2023, 2–6 June 2023, Chicago, USA.

PI

KEYNOTE-859: ORR and DOR in the PD-L1 CPS ≥1 population[1,2]

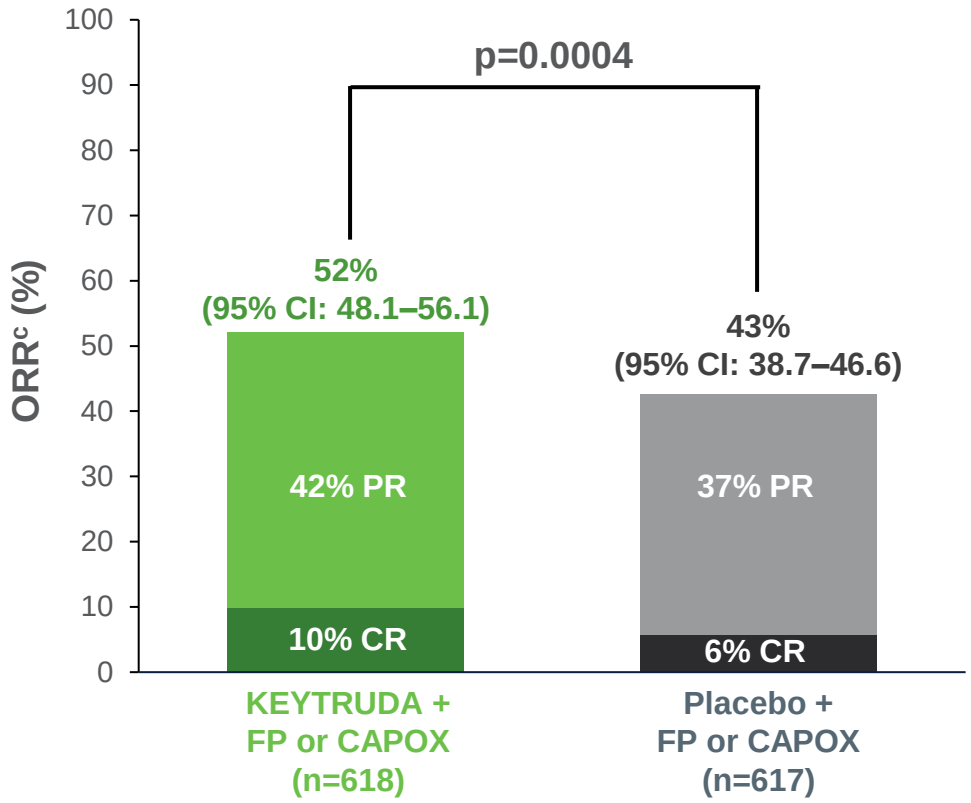


Figure adapted from Rha SY et al. 2023.[1,2]

DOR	KEYTRUDA + FP or CAPOX (n=322)	Placebo + FP or CAPOX (n=263)
Median DOR[c] (95% CI), months	8.3 (7.0–10.9)	5.6 (5.4–6.9)
% with duration ≥12 months	41.2	25.6
% with duration ≥24 months	30.0	11.1

[a]Along with OS, PFS and ORR in the overall population, OS, PFS and ORR in the PD-L1 CPS ≥1 and CPS ≥10 populations were alpha-controlled analyses;
[b]ORR was compared between treatment arms using the Miettinen and Nurminen method stratified by the randomisation stratification factors;
[c]Assessed by BICR using RECIST v1.1.

BICR, blinded independent central review; CAPOX, capecitabine and oxaliplatin; CI, confidence interval; CPS, combined positive score; CR, complete response; DOR, duration of response; FP, 5-fluorouracil and cisplatin; ORR, objective response rate; OS, overall survival; PD-L1, programmed death ligand-1; PI, prescribing information; PR, partial response; RECIST v1.1, Response Evaluation Criteria In Solid Tumors Version 1.1.

1. Rha SY et al. *Lancet Oncol* 2023;24:1181–1195; 2. Rha SY et al. Poster presented at American Society of Clinical Oncology (ASCO) Congress 2023, 2–6 June 2023, Chicago, USA.

PI

KEYNOTE-859: Safety results – AEs in the as-treated population

Median (IQR) follow-up time: 31.0 (23.0–38.3) months

AEs	KEYTRUDA + FP or CAPOX (n=785)	Placebo + FP or CAPOX (n=787)
AEs of any cause (any grade), n (%)	776 (99)	771 (98)
TRAEs, n (%)	751 (96)	736 (94)
Grade 3–5	466 (59)	402 (51)
Serious	184 (23)	146 (19)
Led to death	8 (1)[a]	16 (2)[b]
Led to discontinuation of any drug	207 (26)	158 (20)

Table adapted from Rha SY et al. 2023.

Analysis cut-off date: 3 October 2022. The as-treated population included all patients who were randomised and received ≥1 dose of study treatment.

[a]n=1 each due to diarrhoea, peripheral embolism, pneumonitis, pulmonary haemorrhage, sepsis, septic shock, thrombotic thrombocytopenia purpura and death (cause unknown); [b]n=3 due to septic shock, n=2 due to acute myocardial infarction and n=1 each due to cerebral haemorrhage, cerebrovascular accident, diarrhoea, gastric perforation, hepatic function abnormal, neurotoxicity, pneumonitis, pulmonary embolism, sepsis, sudden death and urosepsis.

AE, adverse event; CAPOX, capecitabine + oxaliplatin; FP, 5-fluorouracil + cisplatin; IQR, interquartile range; PI, prescribing information; TRAE, treatment-related adverse event.

Rha SY et al. *Lancet Oncol* 2023;24:1181–1195.

PI

KEYNOTE-859: Safety results – TRAEs in ≥15% of patients in the as-treated population[1,2]

Median (IQR) follow-up time: 31.0 (23.0–38.3) months

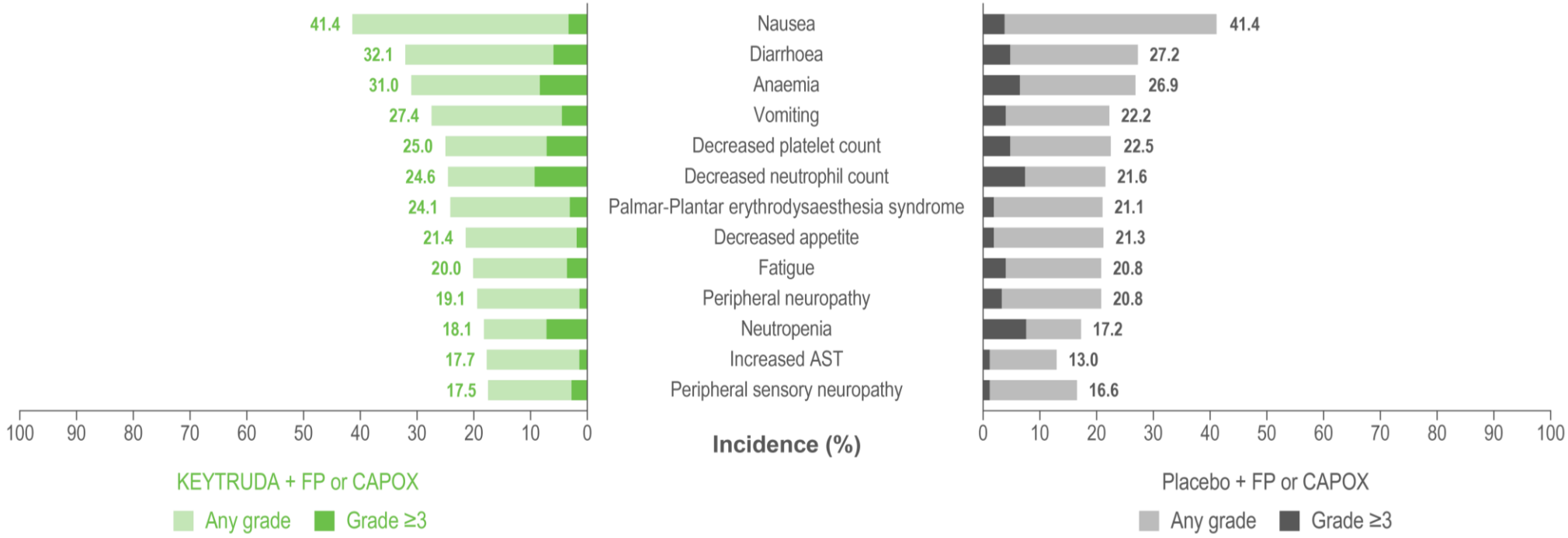


Figure adapted from Rha SY et al. 2023.

The safety profile was as expected for the KEYTRUDA + chemotherapy regimen

Analysis cut-off date: 3 October 2022. The as-treated population included all patients who were randomised and received ≥1 dose of study treatment.

AST, aspartate aminotransferase; CAPOX, capecitabine + oxaliplatin; FP, 5-fluorouracil + cisplatin; IQR, interquartile range; PI, prescribing information; TRAE, treatment-related adverse event.

1. Rha SY et al. *Lancet Oncol* 2023;24:1181–1195; 2. Rha SY et al. Presented at the European Society for Medical Oncology (ESMO) Virtual Plenary 2023, 16 February 2023. Abstract VP1-2023.

PI

KEYNOTE-859: Safety results – immune-mediated AEs[1,2]

All immune-mediated AEs, n (%)	KEYTRUDA + FP or CAPOX (n=785)	Placebo + FP or CAPOX (n=787)
Any grade	213 (27.1)	73 (9.3)
Grade 3–5	62 (7.9)	13 (1.7)
Led to death	1 (0.1)[a]	1 (0.1)[a]

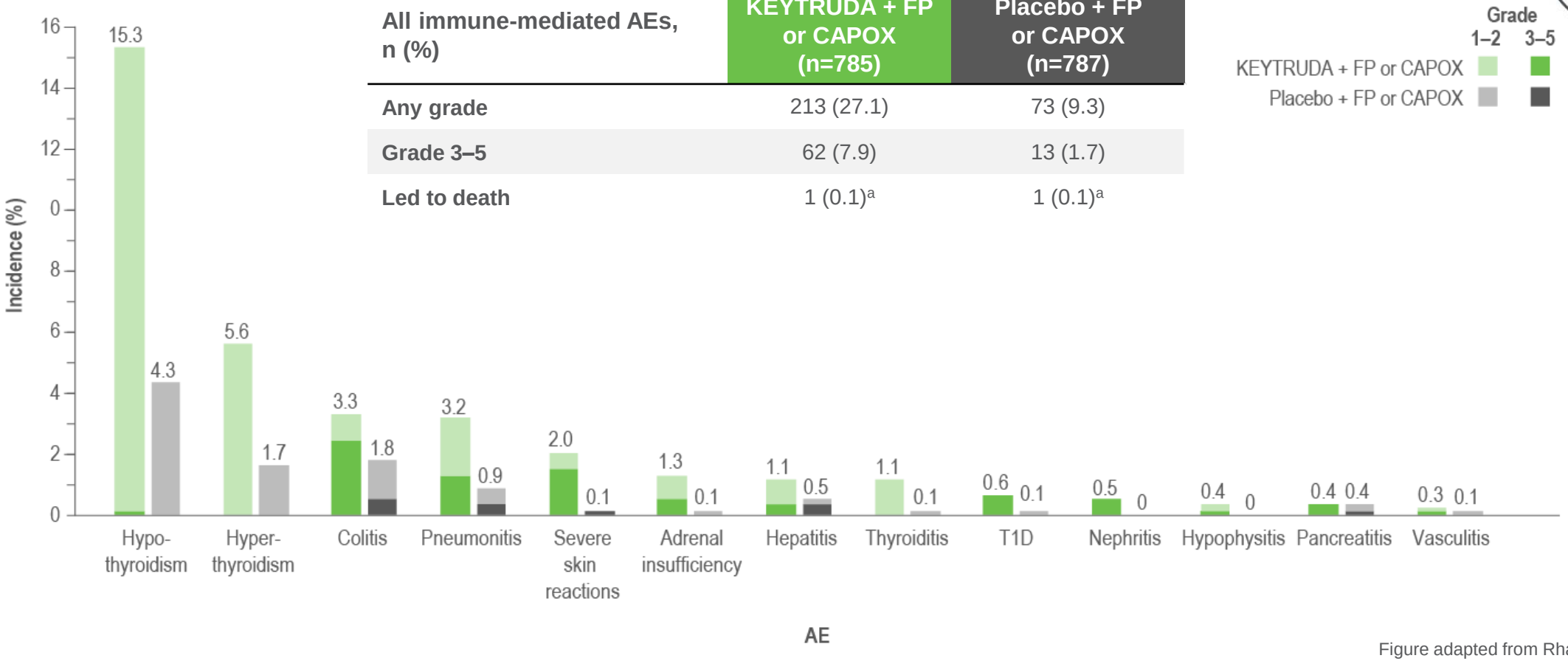


Figure adapted from Rha SY et al. 2023.

Analysis cut-off date: 3 October 2022. The as-treated population included all patients who were randomised and received ≥1 dose of the study treatment. Figure presenting immune-mediated AEs with incidence in ≥2 participants, based on a list of terms prepared by the funder and considered regardless of attribution to trial treatment by the investigator. Related terms were included.

[a]One participant in each arm due to pneumonitis.

AE, adverse event; CAPOX, capecitabine + oxaliplatin; FP, 5-fluorouracil + cisplatin; PI, Prescribing Information; T1D, type 1 diabetes.

1. Rha SY et al. *Lancet Oncol* 2023;24:1181–1195; 2. Rha SY et al. Presented at the European Society for Medical Oncology (ESMO) 2023, 16 February 2023. Abstract VP1-2023.

PI

KEYTRUDA dosing[1,2]

Administered as an IV infusion

Over 30 minutes

Adults: 200 mg

Adults: 400 mg

- Patients should be treated with KEYTRUDA until disease progression or unacceptable toxicity[1]
- Atypical responses (i.e. an initial transient increase in tumour size or small new lesions within the first few months followed by tumour shrinkage) have been observed[1]
- It is recommended to continue treatment for clinically stable patients with initial evidence of disease progression until disease progression is confirmed[1]
- No dose reductions of KEYTRUDA are recommended. KEYTRUDA should be withheld or discontinued to manage AEs as described within the SmPC[1]
- When administering KEYTRUDA in combination with intravenous chemotherapy, KEYTRUDA should be administered first[1]

The regimen assessed in all clinical Phase 2 and 3 registration studies for KEYTRUDA was the 200 mg Q3W dosing. The study that led to the approval of the Q6W for monotherapy and combination patients assessed the 400 mg Q6W dosing schedule based on an exposure–response evaluation using modelling and simulation. It concluded that the 400 mg Q6W dosing regimen for KEYTRUDA monotherapy and combination is predicted to have a similar efficacy and safety profile as the approved 200 mg Q3W dosing regimen[2]

AE, adverse event; IV, intravenous; Q3W, every 3 weeks; Q6W, every 6 weeks; SmPC, Summary of Product Characteristics.

1. KEYTRUDA (pembrolizumab) SmPC. Available at: https://www.medicines.org.uk/emc/product/2498/smpc#about-medicine. Accessed September 2024; 2. Lala M *et al. Eur J Cancer* 2020;131:68–75.

PI

Conclusions

- KEYTRUDA as first-line treatment provided statistically significant and clinically meaningful improvement in OS compared with placebo when both were used in combination with FP or CAPOX in patients with PD-L1 CPS ≥1 status (HR: 0.74 [95% CI: 0.65–0.84]; p<0.0001)
- Patients treated with KEYTRUDA + FP + CAPOX also showed a statistically significant improvement in PFS compared with those treated with placebo + FP + CAPOX in patients with PD-L1 CPS ≥1 status (0.72 [95% CI: 0.63–0.82]; p<0.0001)
- No new safety signals for KEYTRUDA were observed in the study, and the tolerability profile was as expected for a KEYTRUDA + chemotherapy regimen

CAPOX, capecitabine + oxaliplatin; CI, confidence interval; CPS, combined positive score; FP, 5-fluorouracil + cisplatin; HR, hazard ratio; OS, overall survival; PD-L1, programmed death ligand-1; PFS, progression-free survival; PI, prescribing information.

Rha SY et al. *Lancet Oncol* 2023;24:1181–1195.

PI

Appendix

KEYNOTE-859: HRQoL analysis

LSM score change from baseline to Week 18 in EORTC QLQ-STO22 symptom scales

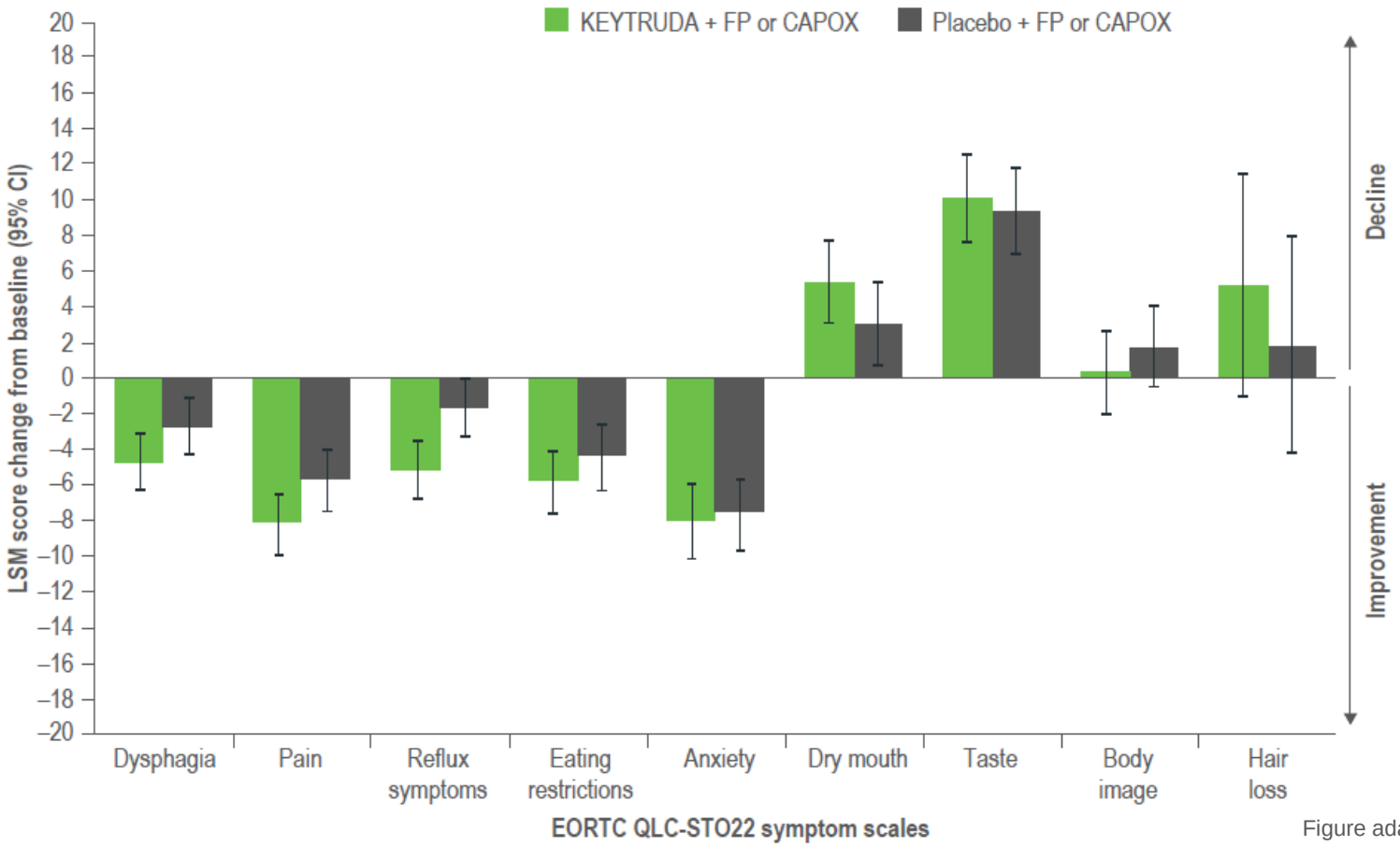


Figure adapted from Lowery M et al. 2023.

Analysis cut-off date: 3 October 2022.

CAPOX, capecitabine + oxaliplatin; CI, confidence interval; EORTC QLQ-STO22, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Stomach 22; FP, 5-fluorouracil + cisplatin; HRQoL, health-related quality of life; LSM, least squares mean; PI, Prescribing Information.

Lowery M et al. Presented at the European Society for Medical Oncology (ESMO) 2023, 20–24 October 2023. Abstract 1516P.

PI

Promotional Material Certificate

Version: 1 . 0

Document Number: GB-ESO-00054

Document Name: GOJ-Gastric KN-859 Clinical Summary MSDC version - Aug '25

Country: United Kingdom

Product: GB KEYTRUDA Esophageal

Type: Material

Sub Type: Healthcare Professional Resource

Promotional Material Statement - Signatory

I (the undersigned) certify that I have examined the final form of this material and that in my belief it is in accordance with the requirements of the relevant advertising regulations and the ABPI Code of Practice, is not inconsistent with the marketing authorisation and the summary of product characteristics and is a fair and truthful presentation of the facts about the medicine.

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Daniel McHugh - Medical Signatory Certification (daniel.mchugh1@msd.com)	Capacity: Medical Signatory Date: 14-Aug-2025 08:45:40 GMT+0000