MSD Oncology

KEYNOTE-868 (NRG-GY018): KEYTRUDA® (pembrolizumab), in combination with carboplatin and paclitaxel, is indicated for the first-line treatment of primary advanced or recurrent endometrial carcinoma in adults

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Please refer to the full Summary of Product Characteristics for KEYTRUDA and patient-targeted Risk Minimisation Materials for further information to minimise the risks associated with the use of the medicine before making any prescribing decisions. Patients should also receive the Risk Minimisation Materials.

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). By clicking the above link, you will be taken to the MHRA website.

Please click here for the UK KEYTRUDA Prescribing Information.

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MSD

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Slide deck navigation

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MoA, mechanism of action.

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MoA and licence

MoA, mechanism of action.

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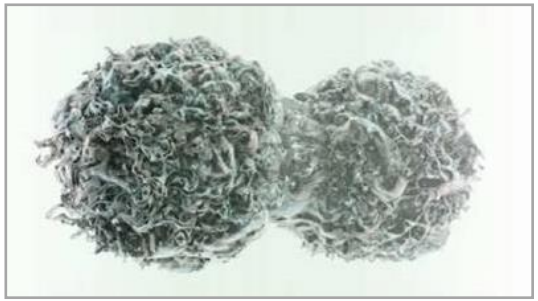
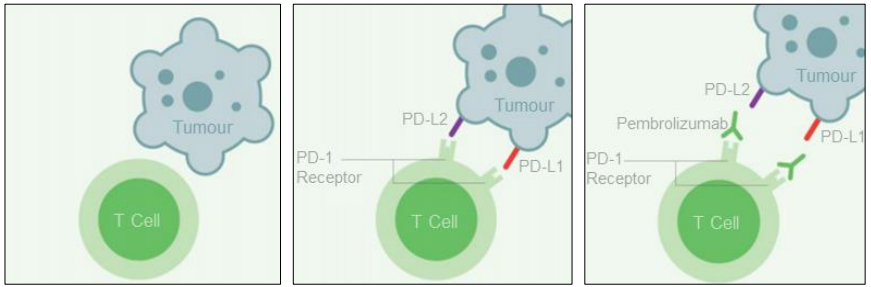
KEYTRUDA and chemotherapy: Two different MoAs

Chemotherapy induces immunogenic cell death



- Chemotherapy administration can result in the immunogenic death of tumour cells, leading to the release of tumour antigens that can be recognised by the immune system[1]

KEYTRUDA potentiates the anti-tumour immune response



- PD-L1 (and PD-L2), expressed on tumour cells and within the tumour microenvironment, binds to PD-1 on T cells to prevent their activation, leading to immune evasion[1–4]
- KEYTRUDA is a humanised monoclonal antibody that binds to PD-1, blocking its interaction with PD-L1/-L2 and potentiating T-cell responses, including anti-tumour response[4]

When combined with immunotherapies such as KEYTRUDA, chemotherapy may increase tumour immunogenicity and activate an immune response by increasing antigen shedding and presentation, and by stimulating T-cell infiltration[5]

MoA, mechanism of action; PD-1, programmed death receptor-1; PD-L1, programmed death ligand-1; PD-L2, programmed death ligand-2.

1. Emens LA, Middleton G. *Cancer Immunol Res* 2015;3:436–443; 2. Yi M et al. *J Hematol Oncol* 2021;14:10; 3. Pardoll DM. *Nat Rev Cancer* 2012;12:252–264; 4. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed May 2025; 5. Bailly C et al. *NAR Cancer* 2020;2:zcaa002.

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UK licence for KEYTRUDA in combination with carboplatin and paclitaxel in first-line primary advanced/recurrent endometrial carcinoma

- KEYTRUDA, in combination with carboplatin and paclitaxel, is indicated for the first-line treatment of primary advanced or recurrent endometrial carcinoma in adults

KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed May 2025.

Study design and baseline characteristics

KEYNOTE-868 (NRG-GY018): Study design[1–3]

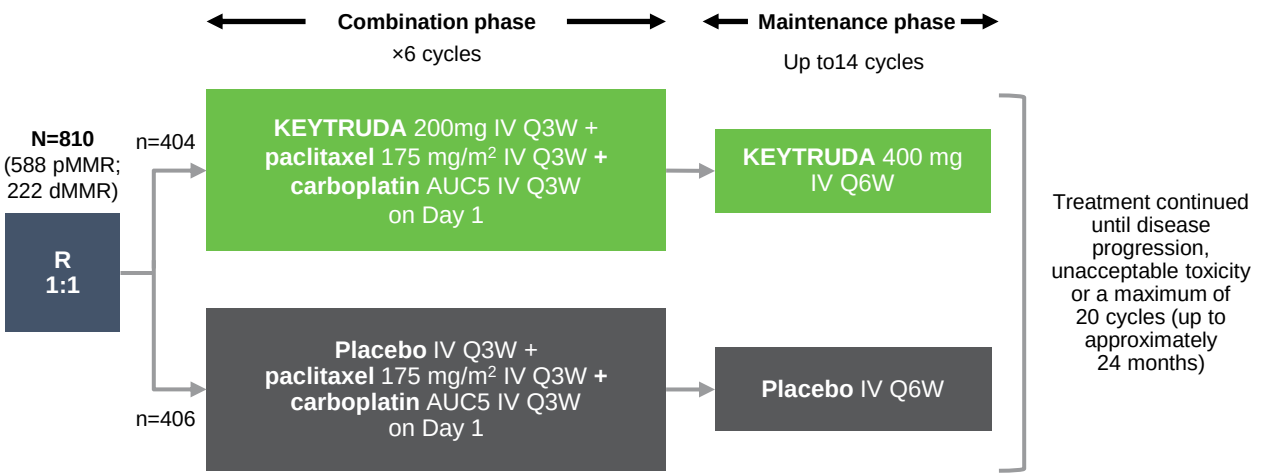
Phase 3, randomised, multicentre, double-blind, placebo-controlled trial designed to study pMMR and dMMR populations as two separate cohorts[1–3]

Key eligibility criteria

- Measurable Stage III/IVA or measurable/ non-measurable (per RECIST v1.1a) Stage IVB or recurrent endometrial carcinoma
- Results of institutional MMR IHC testing
- ECOG PS 0, 1 or 2
- No prior systemic therapy except prior adjuvant chemotherapy, if completed ≥12 months before the trial
- No endometrial sarcoma, including carcinosarcoma

Stratification factors

- MMR status (dMMR or pMMR)
- Prior adjuvant chemotherapy (yes or no)
- ECOG PS (0 or 1 vs 2)



- **Primary endpoints:** Investigator-assessed PFS per RECIST v1.1 by pMMR and dMMR
- **Selected secondary endpoints:** OS, ORR, BOR and DOR per RECIST v1.1 as assessed by investigator, concordance between local and central MMR IHC testing, HR-QoL and safety
- **Selected exploratory endpoints:** PFS per RECIST v1.1 as assessed by BICR and PFS by subgroups including demographic and baseline characteristics, PD-L1 expression and methylation status

Analysis cutoff date: 6 December 2022 for pMMR and 16 December 2022 for dMMR.[2] Subsequent mentions of chemotherapy refer to carboplatin + paclitaxel.

AUC, area under the curve; BICR, blinded independent central review; BOR, best overall response; CT, computed tomography; dMMR, mismatch repair deficient; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HR-QoL, health-related quality of life; IHC, immunohistochemistry; IV, intravenous; MMR, mismatch repair; MRI, magnetic resonance imaging; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; pMMR, mismatch repair proficient; Q3W, every 3 weeks; Q6W, every 6 weeks; R, randomisation; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1.

1. Eskander RN et al. *N Engl J Med* 2023;388:2159–2170 (and protocol); 2. Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1;
3. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed May 2025.

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KEYNOTE-868 (NRG-GY018): Baseline patient demographics and disease characteristics | Interim analysis (1/2)

MMR status

Baseline patient demographics and disease characteristics at the *ad hoc* analysis are shown in the appendix. Click the link to view.

Baseline characteristics	pMMR			dMMR		
	KEYTRUDA + chemotherapy (n=294)	Placebo + chemotherapy (n=294)	All (n=588)	KEYTRUDA + chemotherapy (n=110)	Placebo + chemotherapy (n=112)	All (n=222)
Median age (range), years	66.0 (31.0–94.0)	66.1 (29.0–91.0)	66.1 (29.0–94.0)	67.2 (39.0–82.0)	66.0 (37.0–86.0)	66.1 (37.0–86.0)
Age ≥65 years, n (%)	–	–	318 (54.1)	–	–	123 (55.4)
Race/ethnicity, n (%)						
White	212 (72.1)	212 (72.1)	424 (72.1)	91 (82.7)	85 (75.9)	176 (79.3)
Black	46 (15.6)	50 (17.0)	96 (16.3)	10 (9.1)	9 (8.0)	19 (8.6)
Asian	17 (5.8)	14 (4.8)	31 (5.3)	3 (2.7)	4 (3.6)	7 (3.2)
Hispanic	21 (7.1)	14 (4.8)	35 (6.0)	4 (3.6)	7 (6.3)	11 (5.0)
ECOG PS, n (%)						
0	198 (67.3)	197 (67.0)	395 (67.2)	70 (63.6)	72 (64.3)	142 (64.0)
1	87 (29.6)	88 (29.9)	175 (29.8)	39 (35.5)	35 (31.3)	74 (33.3)
2	9 (3.1)	9 (3.1)	18 (3.1)	1 (0.9)	5 (4.5)	6 (2.7)
Disease status, n (%)						
Recurrent/persistent	–	–	334 (56.8)	–	–	139 (62.6)
Primary advanced	–	–	254 (43.2)	–	–	83 (37.4)

Adapted from Eskander RN et al. *Nat Med* 2025.

Analysis cutoff date: 6 December 2022 for pMMR and 16 December 2022 for dMMR.
dMMR, mismatch repair deficient; ECOG PS, Eastern Cooperative Oncology Group performance status; MMR, mismatch repair; pMMR, mismatch repair proficient.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

KEYNOTE-868 (NRG-GY018): Baseline patient demographics and disease characteristics | Interim analysis (2/2)

MMR status

Baseline patient demographics and disease characteristics at the *ad hoc* analysis are shown in the appendix. Click the link to view.

Baseline characteristics	pMMR			dMMR		
	KEYTRUDA + chemotherapy (n=294)	Placebo + chemotherapy (n=294)	All (n=588)	KEYTRUDA + chemotherapy (n=110)	Placebo + chemotherapy (n=112)	All (n=222)
Previous therapy, n (%)						
Adjuvant chemotherapy	74 (25.2)	76 (25.9)	150 (25.5)	4 (3.6)	8 (7.1)	12 (5.4)
Radiotherapy	118 (40.1)	124 (42.2)	242 (41.2)	42 (38.2)	54 (48.2)	96 (43.2)
Surgery	265 (90.1)	248 (84.4)	513 (87.2)	97 (88.2)	104 (92.9)	201 (90.5)
Histologic subtype, n (%)						
Endometrioid carcinoma						
Grade 1	55 (18.7)	45 (15.3)	100 (17.0)	20 (18.2)	34 (30.4)	54 (24.3)
Grade 2	51 (17.3)	59 (20.1)	110 (18.7)	52 (47.3)	43 (38.4)	95 (42.8)
Grade 3	53 (18.0)	42 (14.3)	95 (16.2)	15 (13.6)	16 (14.3)	31 (14.0)
Serous	79 (26.9)	76 (25.9)	155 (26.4)	4 (3.6)	1 (0.9)	5 (2.3)
Adenocarcinoma NOS	24 (8.2)	35 (11.9)	59 (10.0)	12 (10.9)	12 (10.7)	24 (10.8)
Clear cell carcinoma	19 (6.5)	20 (6.8)	39 (6.6)	0 (0)	0 (0)	0 (0)
Other	13 (4.4)[a]	17 (5.8)[a]	30 (5.1)[a]	7 (6.4)[a]	6 (5.4)[a]	13 (5.9)[a]

Adapted from Eskander RN et al. *Nat Med* 2025.

Analysis cutoff date: 6 December 2022 for pMMR and 16 December 2022 for dMMR.
[a]Including missing, mixed epithelial and dedifferentiated/undifferentiated.
dMMR, mismatch repair deficient; MMR, mismatch repair; NOS, not otherwise specified; pMMR, mismatch repair proficient.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

KEYNOTE-868 (NRG-GY018): Statistical considerations

Analysis considerations[1]

- pMMR and dMMR populations evaluated separately and independently
- Interim OS futility analysis planned at time of final or significant interim PFS analysis

Power calculations for PFS (primary endpoint)[1]

- pMMR population: If true HR is 0.70, the study has at least 90% power when 394 events occurred
- dMMR population: If true HR is 0.60, the study has at least 85% power when 168 events occurred
- Null hypothesis of equal hazard rates tested at alpha of 0.0125 using a stratified log-rank test
  - If the null hypothesis for one population is rejected, all alpha is forwarded to other population

Treatment benefit[2]

- Statistical parameters for PFS were met for both pMMR and dMMR cohorts at pre-specified interim analysis (analysis cut-off date 6 December 2022 for pMMR and 16 December 2022 for dMMR)
- All alpha for the PFS primary endpoint was spent at the primary analysis and PFS was not re-evaluated during the *ad hoc* analysis. Therefore, PFS analysis at *ad hoc* analysis is descriptive with a nominal p-value only
- Statistical analyses for secondary and exploratory endpoints are descriptive in nature and p-values are nominal

Please refer to the Eskander RN et al. 2025 data supplement for additional information on the statistical methods for the confounding effect of subsequent anticancer therapy on OS[2]

dMMR, mismatch repair deficient; HR, hazard ratio; OS, overall survival; PFS, progression-free survival; pMMR, mismatch repair proficient.

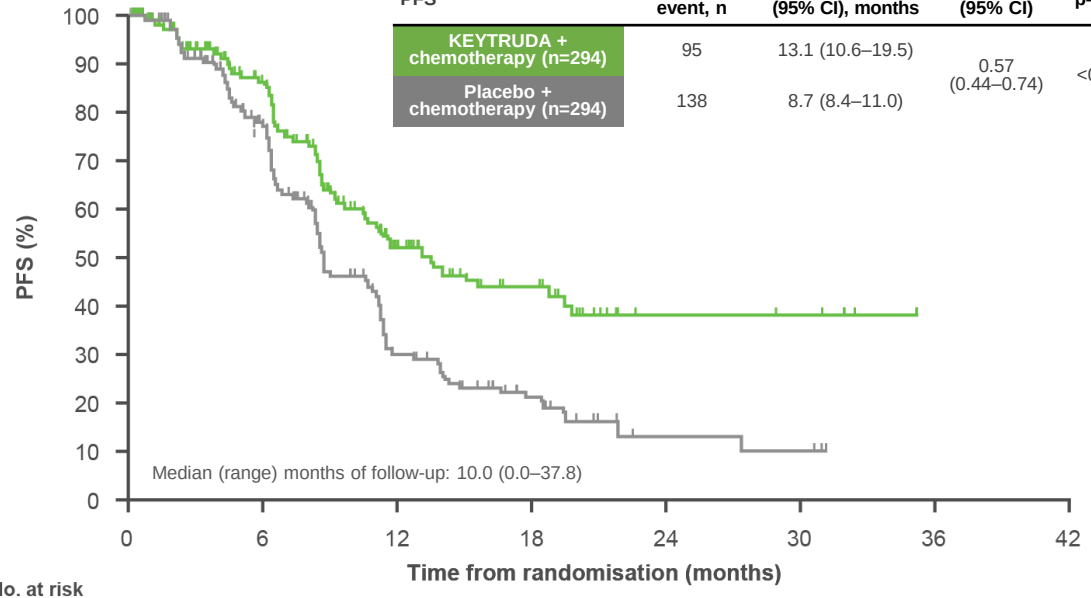
1. Eskander RN et al. *N Engl J Med* 2023;388:2159–2170 (protocol); 2. Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

Efficacy results: Interim analysis

Primary endpoint: pMMR population – PFS by investigator per RECIST v1.1 | Interim analysis

pMMR

PFS	Patients with event, n	Median PFS (95% CI), months	HR[a] (95% CI)	p-value[b]
KEYTRUDA + chemotherapy (n=294)	95	13.1 (10.6–19.5)	0.57 (0.44–0.74)	<0.0001
Placebo + chemotherapy (n=294)	138	8.7 (8.4–11.0)		



No. at risk								
KEYTRUDA + chemotherapy	294	162	57	29	7	6	0	0
Placebo + chemotherapy	294	144	36	15	4	3	0	0

In the pMMR population:
KEYTRUDA + chemotherapy followed by KEYTRUDA maintenance resulted in a 43% relative risk reduction of disease progression or death compared with placebo + chemotherapy followed by placebo maintenance (HR[a]: 0.57; 95% CI: 0.44–0.74; p<0.0001[b])

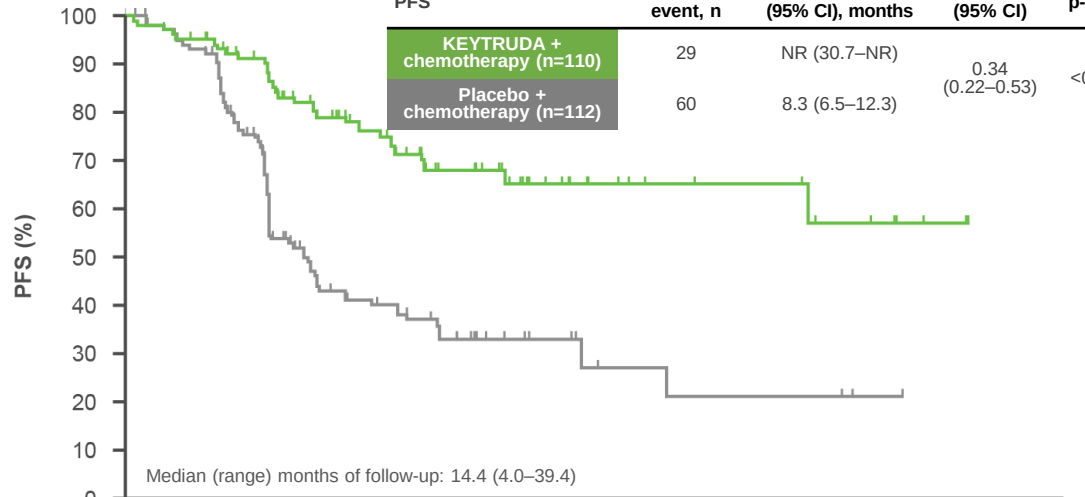
Adapted from Eskander RN et al. *Nat Med* 2025.

Analysis cutoff date: 6 December 2022. Tick-marks indicate censored data.
[a]Stratified HR for progression or death, based on a stratified Cox regression model; [b]Based on a one-sided stratified log-rank test (compared to an alpha boundary of 0.00116 for pMMR).
CI, confidence interval; HR, hazard ratio; PFS, progression-free survival; pMMR, mismatch repair proficient; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

Primary endpoint: dMMR population – PFS by investigator per RECIST v1.1 | Interim analysis

dMMR

PFS	Patients with event, n	Median PFS (95% CI), months	HR[a] (95% CI)	p-value[b]
KEYTRUDA + chemotherapy (n=110)	29	NR (30.7–NR)	0.34 (0.22–0.53)	<0.0001
Placebo + chemotherapy (n=112)	60	8.3 (6.5–12.3)		



No. at risk								
KEYTRUDA + chemotherapy	110	85	45	24	10	9	2	0
Placebo + chemotherapy	112	69	25	9	4	3	0	0

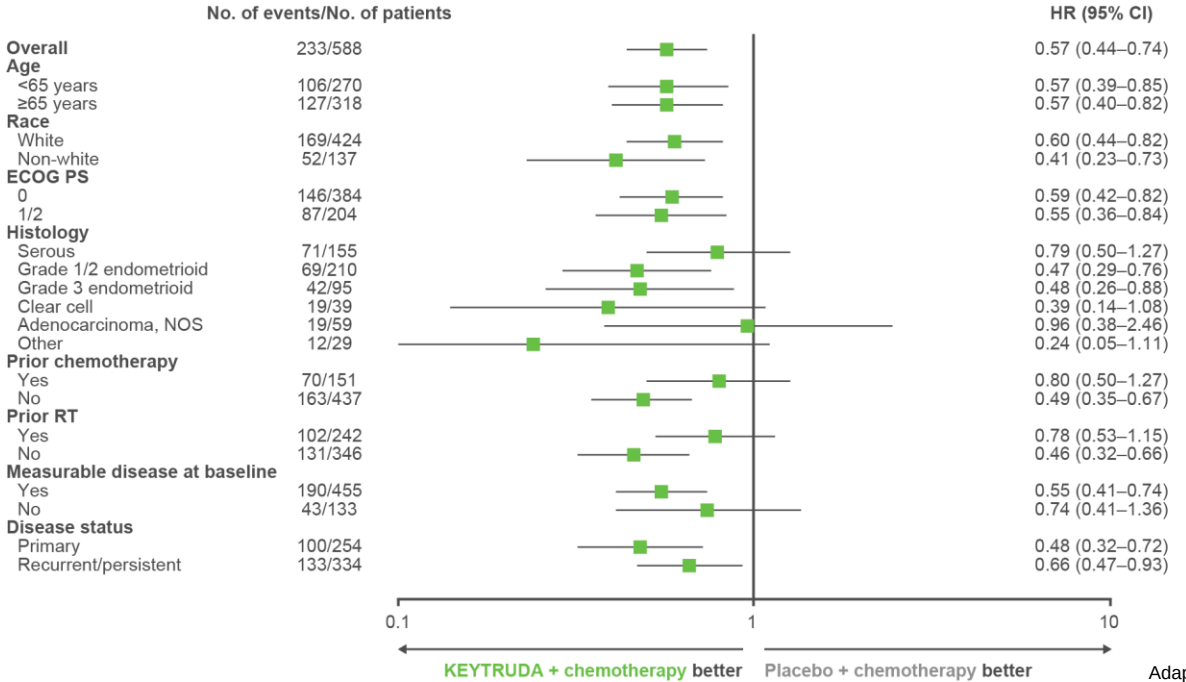
In the dMMR population:
KEYTRUDA + chemotherapy followed by KEYTRUDA maintenance resulted in a 66% relative risk reduction of disease progression or death compared with placebo + chemotherapy followed by placebo maintenance (HR[a] for progression or death: 0.34; 95% CI: 0.22–0.53; p<0.0001[b])

Adapted from Eskander RN et al. *Nat Med* 2025.

Analysis cutoff date: 16 December 2022. Tick-marks indicate censored data.
[a]Stratified HR for progression or death, based on a stratified Cox regression model; [b]Based on a one-sided stratified log-rank test (compared to an alpha boundary of 0.00207 for dMMR).
CI, confidence interval; dMMR, mismatch repair deficient; HR, hazard ratio; NR, not reached; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

Exploratory endpoint: pMMR population – PFS by investigator per RECIST v1.1 | Interim analysis

pMMR



This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Subgroup analysis results by PD-L1 expression are shown in the appendix. Click here to view.

Adapted from Eskander RN et al. *Nat Med* 2025.

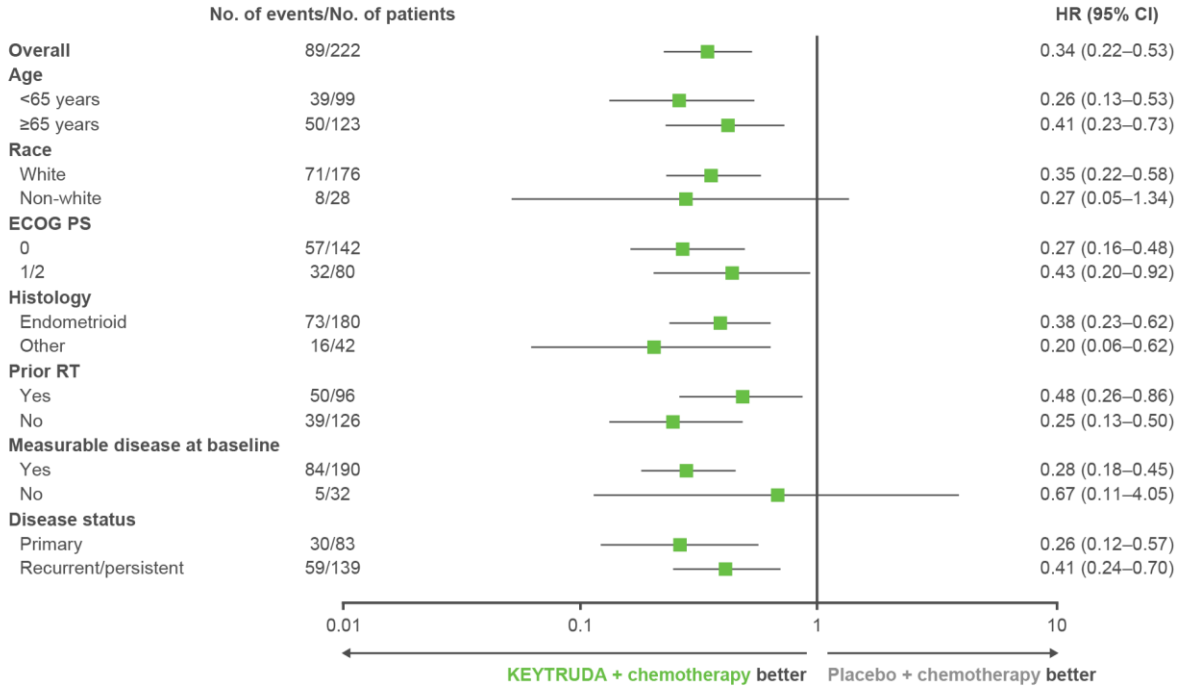
Analysis cutoff date: 6 December 2022.

CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; NOS, not otherwise specified; PD-L1, programmed death ligand-1; PFS, progression-free survival; pMMR, mismatch repair proficient; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1; RT, radiotherapy.

Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

Exploratory endpoint: dMMR population – PFS by investigator per RECIST v1.1 | Interim analysis

dMMR



This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Subgroup analysis results by PD-L1 expression and methylation status are shown in the appendix. Click the links to view.

Adapted from Eskander RN et al. *Nat Med* 2025.

Analysis cutoff date: 16 December 2022.

CI, confidence interval; dMMR, mismatch repair deficient; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; PD-L1, programmed death ligand-1; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1; RT, radiotherapy.

Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

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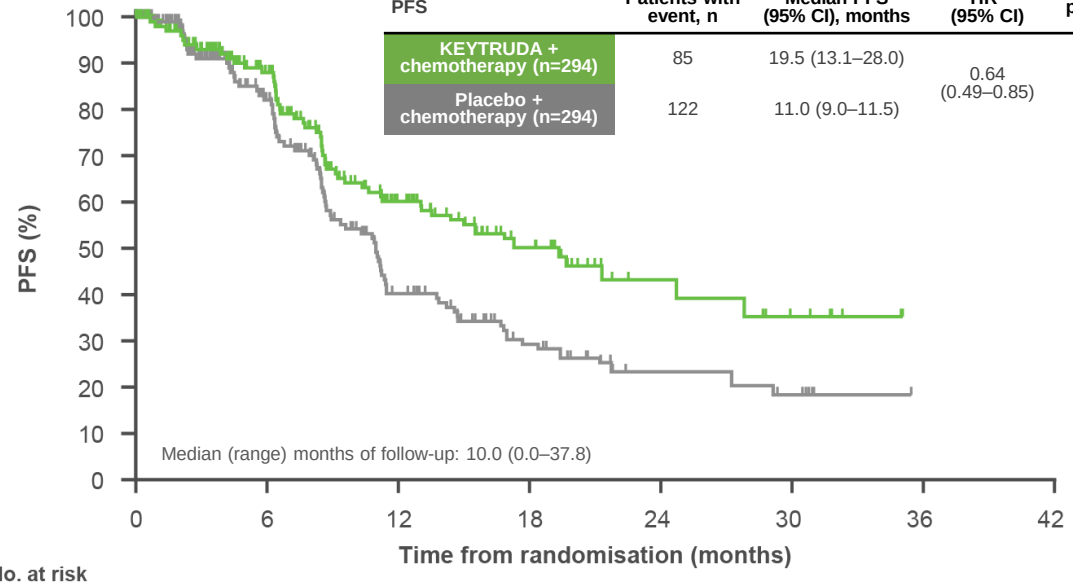
Exploratory endpoint: pMMR population – PFS per RECIST v1.1 by BICR | Interim analysis

pMMR

PFS	Patients with event, n	Median PFS (95% CI), months	HR[a] (95% CI)	p-value[b]
KEYTRUDA + chemotherapy (n=294)	85	19.5 (13.1–28.0)	0.64 (0.49–0.85)	0.0008
Placebo + chemotherapy (n=294)	122	11.0 (9.0–11.5)		



No. at risk								
KEYTRUDA + chemotherapy	294	167	64	34	11	7	0	0
Placebo + chemotherapy	294	155	48	23	9	6	0	0

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Adapted from Eskander RN et al. *Nat Med* 2025.

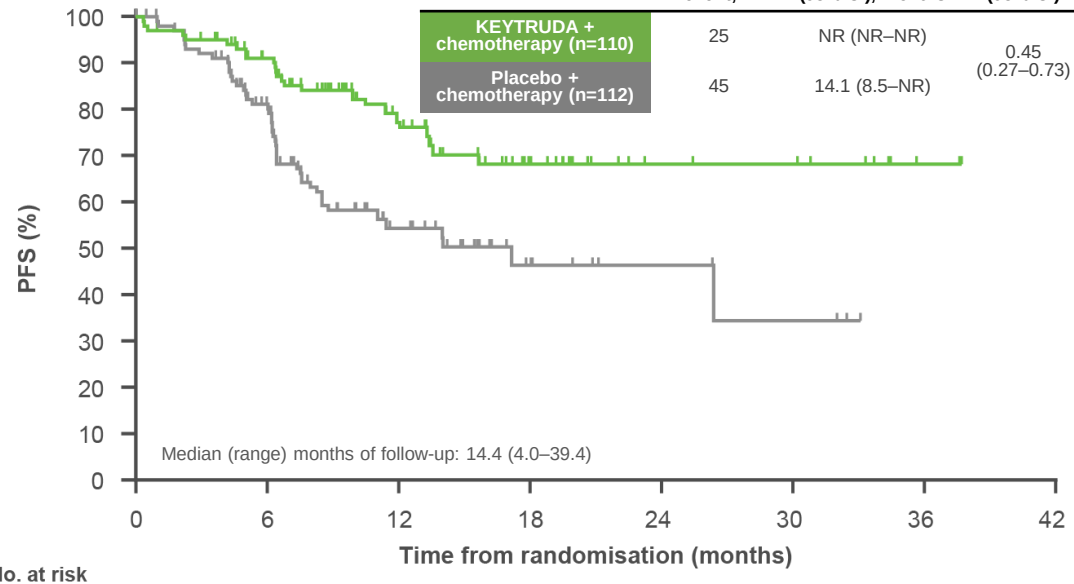
Analysis cutoff date: 6 December 2022. Tick-marks indicate censored data.

[a]Based on a Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by prior chemotherapy; [b]One-sided nominal p-value based on log-rank test stratified by prior chemotherapy.
BICR, blind independent central review; CI, confidence interval; HR, hazard ratio; PFS, progression-free survival; pMMR, mismatch repair proficient;
RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

Exploratory endpoint: dMMR population – PFS per RECIST v1.1 by BICR | Interim analysis

dMMR

PFS	Patients with event, n	Median PFS (95% CI), months	HR[a] (95% CI)	p-value[b]
KEYTRUDA + chemotherapy (n=110)	25	NR (NR–NR)	0.45 (0.27–0.73)	0.0005
Placebo + chemotherapy (n=112)	45	14.1 (8.5–NR)		



No. at risk								
KEYTRUDA + chemotherapy	110	85	48	26	10	9	2	0
Placebo + chemotherapy	112	75	31	10	5	3	0	0

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Adapted from Eskander RN et al. *Nat Med* 2025.

Analysis cutoff date: 16 December 2022. Tick-marks indicate censored data.

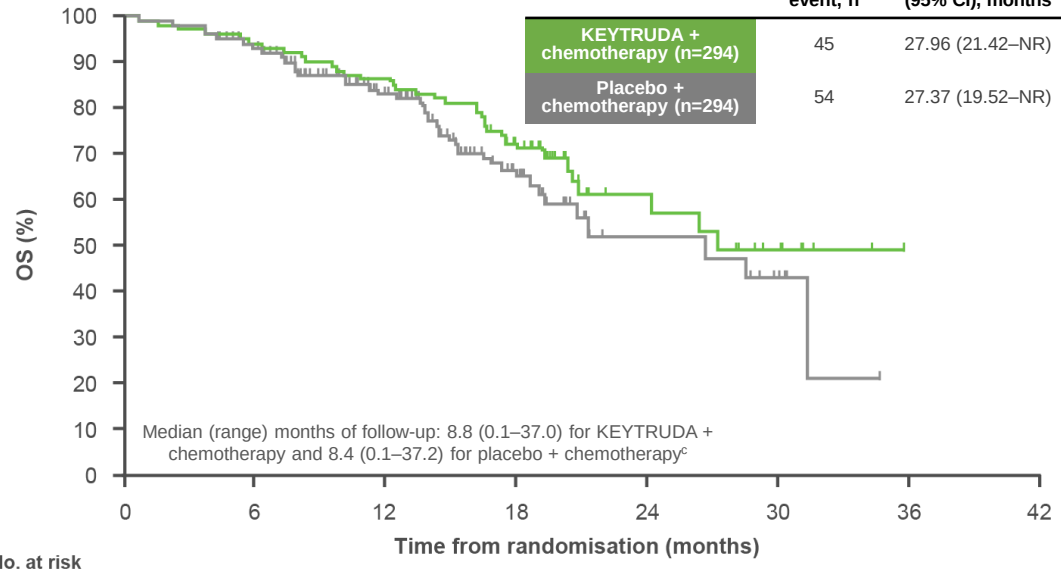
[a]Based on a Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by prior chemotherapy; [b]One-sided nominal p-value based on log-rank test stratified by prior chemotherapy.
BICR, blind independent central review; CI, confidence interval; dMMR, mismatch repair deficient; HR, hazard ratio; NR, not reached; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1.

Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

Secondary endpoint: pMMR population – OS | Interim analysis

pMMR

OS	Patients with event, n	Median OS (95% CI), months	HR[a] (95% CI)	p-value[b]
KEYTRUDA + chemotherapy (n=294)	45	27.96 (21.42–NR)	0.79 (0.53–1.17)	0.1157
Placebo + chemotherapy (n=294)	54	27.37 (19.52–NR)		



No. at risk								
KEYTRUDA + chemotherapy	294	179	97	51	16	10	1	0
Placebo + chemotherapy	294	174	94	46	11	7	0	0

OS data were immature at interim analysis and analysis of OS is ongoing.[1] OS endpoint was not formally assessed within the multiplicity control.[2] Results should be interpreted with caution

In the pMMR population:
OS maturity (percentage of patients with event) at interim analysis was 16.8%[2]

Adapted from Eskander RN et al. *Nat Med* 2025.

Analysis cutoff date: 6 December 2022. **Tick-marks indicate censored data.**
[a]Based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by prior chemotherapy;[1] [b]One-sided nominal p-value based on log-rank test stratified by prior chemotherapy;[1]
[c]Follow-up duration is the time from randomisation to the date of death or the analysis cut-off if the participant is still alive.[1]
CI, confidence interval; HR, hazard ratio; NR, not reached; OS, overall survival; pMMR, mismatch repair proficient.
1. Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1; 2. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed May 2025.

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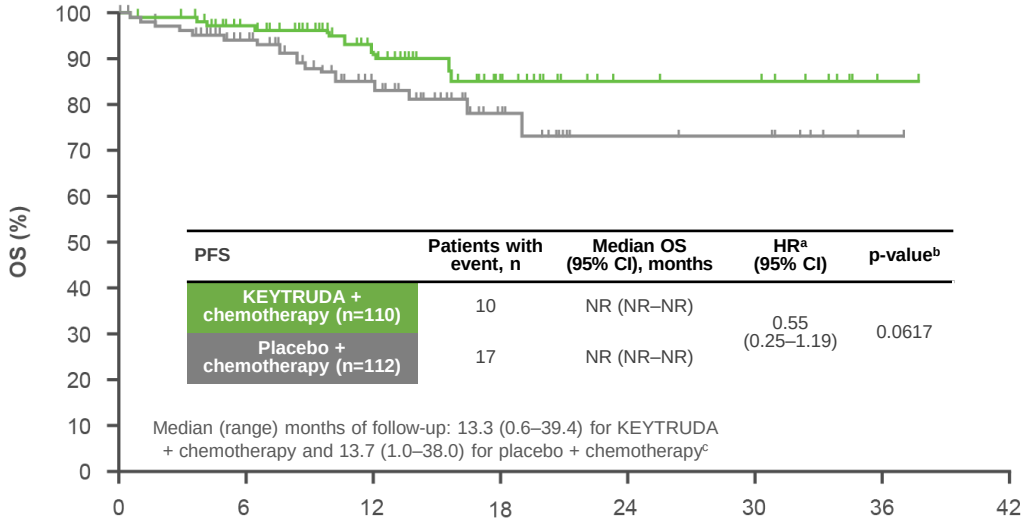
Secondary endpoint: dMMR population – OS | Interim analysis

dMMR



PFS	Patients with event, n	Median OS (95% CI), months	HR[a] (95% CI)	p-value[b]
KEYTRUDA + chemotherapy (n=110)	10	NR (NR–NR)	0.55 (0.25–1.19)	0.0617
Placebo + chemotherapy (n=112)	17	NR (NR–NR)		

Median (range) months of follow-up: 13.3 (0.6–39.4) for KEYTRUDA + chemotherapy and 13.7 (1.0–38.0) for placebo + chemotherapy[c]

No. at risk								
KEYTRUDA + chemotherapy	110	88	55	29	12	11	2	0
Placebo + chemotherapy	112	87	52	18	8	7	1	0

OS data were immature at interim analysis and analysis of OS is ongoing.[1] OS endpoint was not formally assessed within the multiplicity control.[2] Results should be interpreted with caution

In the dMMR population:
OS maturity (percentage of patients with event) at interim analysis was 12.2%[2]

Adapted from Eskander RN et al. *Nat Med* 2025.

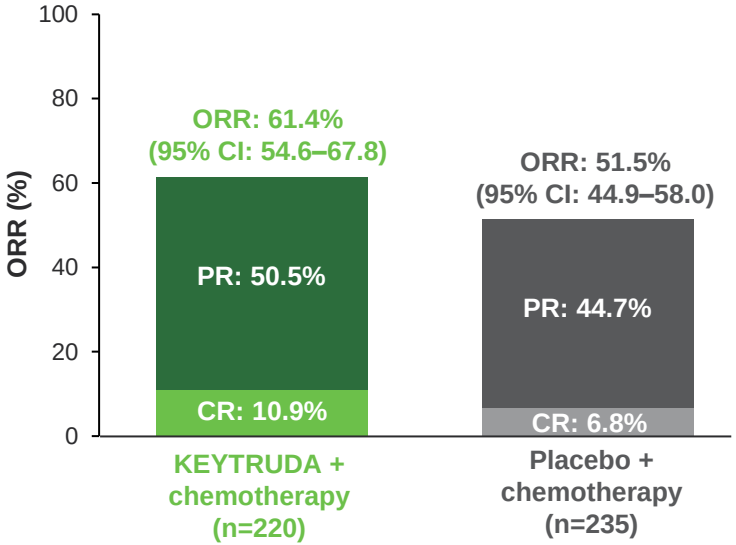
Analysis cutoff date: 16 December 2022. Tick-marks indicate censored data.
[a]Based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by prior chemotherapy;[1] [b]One-sided nominal p-value based on log-rank test stratified by prior chemotherapy;[1]
[c]Follow-up duration is the time from randomisation to the date of death or the analysis cut-off date if the participant is still alive.[1]
CI, confidence interval; dMMR, mismatch repair deficient; HR, hazard ratio; NR, not reached; OS, overall survival.
1. Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1; 2. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed May 2025.

UK Prescribing Information

Secondary endpoint: pMMR population – ORR and DOR | Interim analysis

pMMR

Investigator-assessed ORR and BOR per RECIST v1.1 (patients with measurable disease at baseline; n=455)[1]



DOR (n=455)[1,2]

	KEYTRUDA + chemotherapy (n=220)	Placebo + chemotherapy (n=235)
Median DOR (range), months[a]	7.1 (0.0+ to 32.8+)	6.4 (0.0+ to 20.1+)
DOR ≥12 months, %[b2]	35	16

Median (range) months of follow-up: 10.0 (0.0–37.8)

Adapted from Eskander RN et al. *Nat Med* 2025.

Not all patients had post-baseline assessment available at interim analysis. This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

A tabular view of ORR and BOR is shown in the appendix. Click here to view.

Analysis cutoff date: 6 December 2022.

[a]'+' indicates no PD by the time of last disease assessment;[1] [b]Based on Ianlan–Meier estimation.[2]

BOR, best objective response; CI, confidence interval; CR, complete response; DOR, duration of response; ORR, objective response rate; PD, progressive disease; pMMR, mismatch repair proficient; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1.

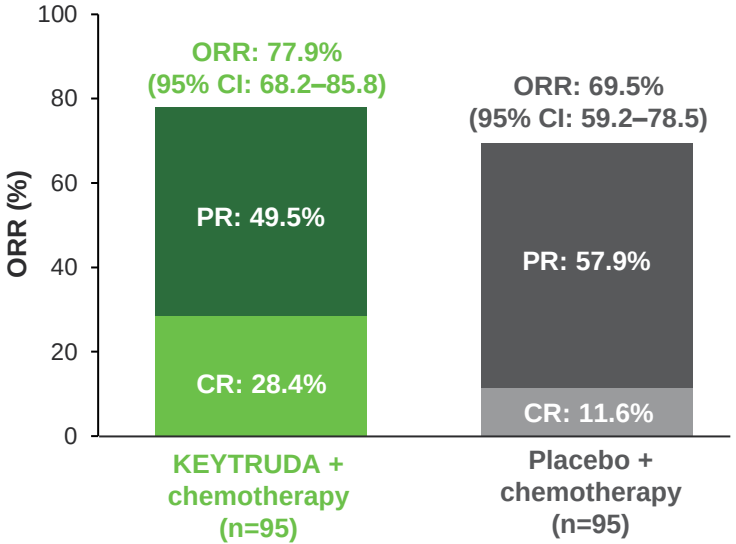
1. Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1; 2. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed May 2025.

UK Prescribing Information

Secondary endpoint: dMMR population – ORR and DOR | Interim analysis

dMMR

Investigator-assessed ORR and BOR per RECIST v1.1 (patients with measurable disease at baseline; n=190)[1]



DOR (n=190)[1,2]

	KEYTRUDA + chemotherapy (n=95)	Placebo + chemotherapy (n=95)
Median DOR (range), months[a]	NR (0.0+ to 33.0+)	4.4 (0.0+ to 32.8+)
DOR ≥12 months, %[b2]	79	21

Median (range) months of follow-up: 14.4 (4.0–39.4)

Adapted from Eskander RN et al. *Nat Med* 2025.

Not all patients had post-baseline assessment available at interim analysis. This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

A tabular view of ORR and BOR is shown in the appendix. Click here to view.

Analysis cutoff date: 16 December 2022.

[a]'+' indicates no PD by the time of last disease assessment;[1] [b]Based on Kaplan-Meier estimation.[2]

BOR, best objective response; CI, confidence interval; CR, complete response; dMMR, mismatch repair deficient; DOR, duration of response; NR, not reached; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1.

1. Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1; 2. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed May 2025.

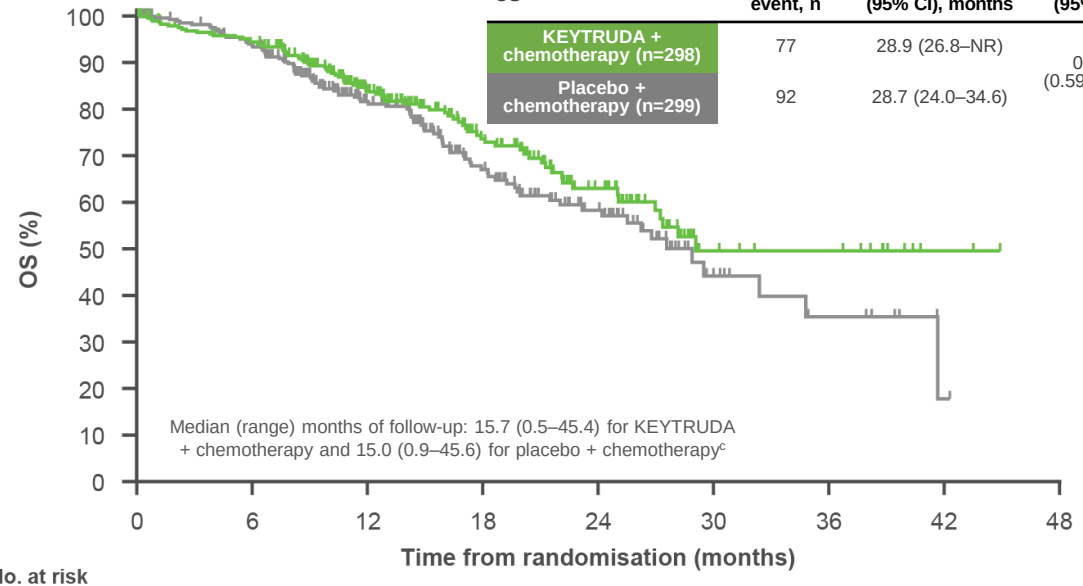
UK Prescribing Information

Efficacy results: *Ad hoc* analysis

Secondary endpoint: pMMR population – OS | *Ad hoc* analysis

pMMR

OS	Patients with event, n	Median OS (95% CI), months	HR[a] (95% CI)	p-value[b]
KEYTRUDA + chemotherapy (n=298)	77	28.9 (26.8–NR)	0.80 (0.59–1.08)	0.0683
Placebo + chemotherapy (n=299)	92	28.7 (24.0–34.6)		



No. at risk									
KEYTRUDA + chemotherapy	298	271	169	94	49	14	11	3	0
Placebo + chemotherapy	299	268	159	89	47	13	7	2	0

OS data were immature at the *ad hoc* analysis and OS analysis is ongoing. OS endpoint was not formally assessed within the multiplicity control. Results should be interpreted with caution

Adapted from Eskander RN et al. *Nat Med* 2025.

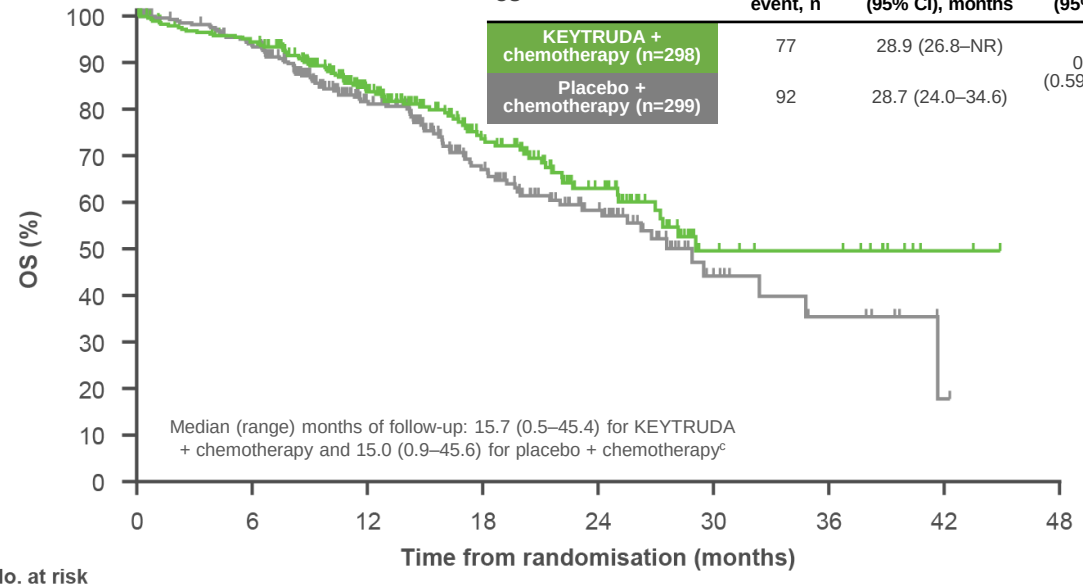
Analysis cutoff date: 18 August 2023. Tick-marks indicate censored data. The study was unblinded after meeting its primary endpoint of investigator-assessed PFS at interim analysis (analysis cut-off dates 6 December 2022 and 16 December 2022 for pMMR and dMMR populations, respectively).

[a]Based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by prior chemotherapy; [b]One-sided nominal p-value based on log-rank test stratified by prior chemotherapy;
[c]Follow-up duration is defined as the time from randomisation to the date of death or the database cutoff date if the participant is still alive.
CI, confidence interval; dMMR, mismatch repair deficient; HR, hazard ratio; NR, not reached; OS, overall survival; pMMR, mismatch repair proficient.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

Secondary endpoint: pMMR population – OS | *Ad hoc* analysis

pMMR

OS	Patients with event, n	Median OS (95% CI), months	HR[a] (95% CI)	p-value[b]
KEYTRUDA + chemotherapy (n=298)	77	28.9 (26.8–NR)	0.80 (0.59–1.08)	0.0683
Placebo + chemotherapy (n=299)	92	28.7 (24.0–34.6)		



No. at risk									
KEYTRUDA + chemotherapy	298	271	169	94	49	14	11	3	0
Placebo + chemotherapy	299	268	159	89	47	13	7	2	0

An ad hoc sensitivity analysis was conducted to account for post-study subsequent immunotherapy therapy with an analysis cut-off date 18 August 2023

Please refer to the Eskander RN et al. 2025 publication for the corresponding Kaplan–Meier curve estimates of this analysis

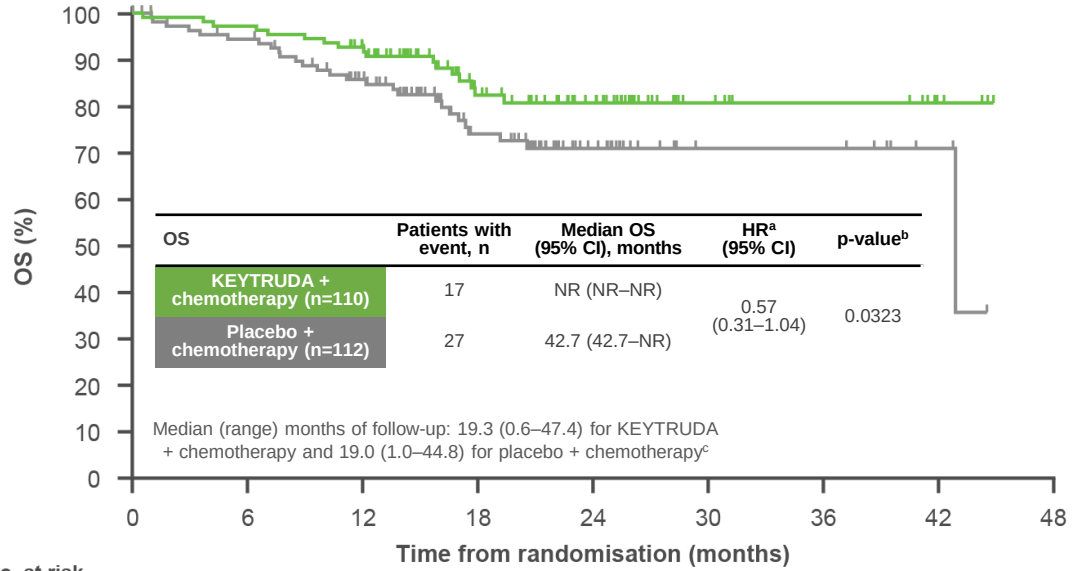
Figure and table adapted from Eskander RN et al. 2025.

Analysis cutoff date: 18 August 2023. Tick-marks indicate censored data. The study was unblinded after meeting its primary endpoint of investigator-assessed PFS at interim analysis (analysis cut-off dates of 6 December 2022 and 16 December 2022 for pMMR and dMMR populations, respectively).

[a]Based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by prior chemotherapy; [b]One-sided nominal p-value based on log-rank test stratified by prior chemotherapy;
[c]Follow-up duration is defined as the time from randomisation to the date of death or the database cutoff date if the participant is still alive.
CI, confidence interval; dMMR, mismatch repair deficient; HR, hazard ratio; NR, not reached; OS, overall survival; pMMR, mismatch repair proficient.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

Secondary endpoint: dMMR population – OS | *Ad hoc* analysis

dMMR



OS	Patients with event, n	Median OS (95% CI), months	HR[a] (95% CI)	p-value[b]
KEYTRUDA + chemotherapy (n=110)	17	NR (NR–NR)	0.57 (0.31–1.04)	0.0323
Placebo + chemotherapy (n=112)	27	42.7 (42.7–NR)		

OS data were immature at the *ad hoc* analysis and OS analysis is ongoing. OS endpoint was not formally assessed within the multiplicity control. Results should be interpreted with caution

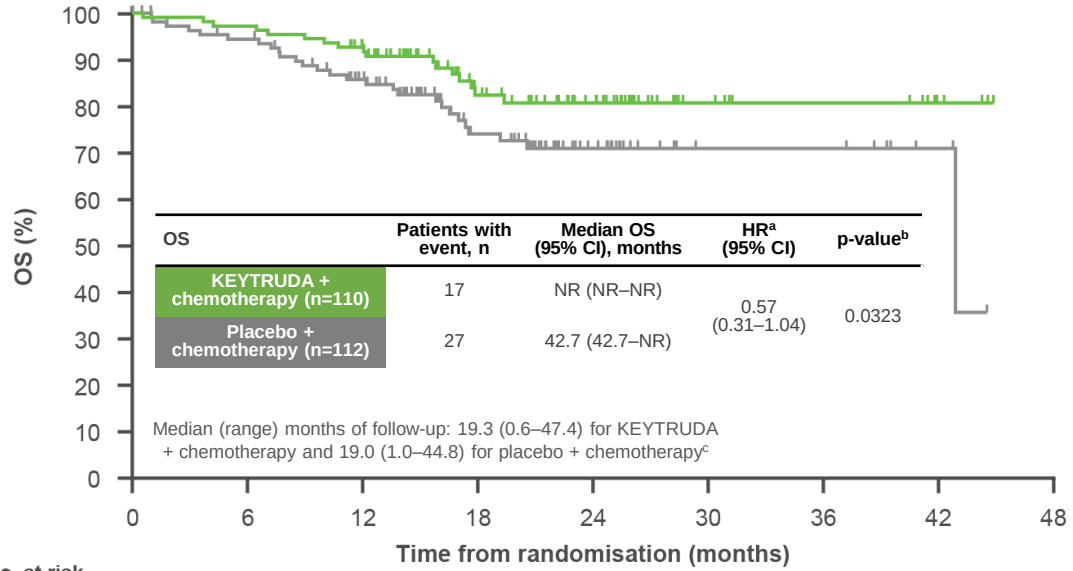
Adapted from Eskander RN et al. *Nat Med* 2025.

Analysis cutoff date: 18 August 2023. Tick-marks indicate censored data. The study was unblinded after meeting its primary endpoint of investigator-assessed PFS at interim analysis (analysis cut-off dates 6 December 2022 and 16 December 2022 for pMMR and dMMR populations, respectively).

[a]Based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by prior chemotherapy; [b]One-sided nominal p-value based on log-rank test stratified by prior chemotherapy;
[c]Follow-up duration is defined as the time from randomisation to the date of death or the database cutoff date if the participant is still alive.
CI, confidence interval; dMMR, mismatch repair deficient; HR, hazard ratio; NR, not reached; OS, overall survival; pMMR, mismatch repair proficient.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

Secondary endpoint: dMMR population – OS | *Ad hoc* analysis

dMMR



OS	Patients with event, n	Median OS (95% CI), months	HR[a] (95% CI)	p-value[b]
KEYTRUDA + chemotherapy (n=110)	17	NR (NR–NR)	0.57 (0.31–1.04)	0.0323
Placebo + chemotherapy (n=112)	27	42.7 (42.7–NR)		

Median (range) months of follow-up: 19.3 (0.6–47.4) for KEYTRUDA + chemotherapy and 19.0 (1.0–44.8) for placebo + chemotherapy[c]

No. at risk									
KEYTRUDA + chemotherapy	110	106	93	53	35	14	10	6	0
Placebo + chemotherapy	112	100	82	50	24	8	8	4	0

- An ad hoc sensitivity analysis was conducted to account for post-study subsequent immunotherapy therapy with an analysis cut-off date 18 August 2023
- Due to sparse OS events in the dMMR population with/without subsequent anti-PD-1/PD-L1 therapies with or without lenvatinib, the model and bootstrap samples were not stable for the dMMR population during the first-stage parametric survival model
- Consequently, the two-stage model result for the dMMR population is not presented

Please refer to the Eskander RN et al. 2025 publication for the corresponding Kaplan–Meier curve estimates of this analysis

Adapted from Eskander RN et al. *Nat Med* 2025.

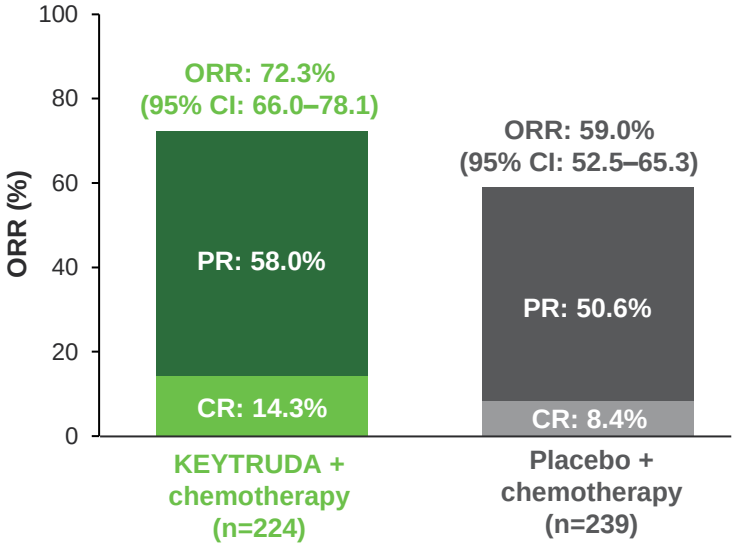
Analysis cutoff date: 18 August 2023. Tick-marks indicate censored data. The study was unblinded after meeting its primary endpoint of investigator-assessed PFS at interim analysis (analysis cut-off dates 6 December 2022 and 16 December 2022 for pMMR and dMMR populations, respectively).

[a]Based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by prior chemotherapy; [b]One-sided nominal p-value based on log-rank test stratified by prior chemotherapy;
[c]Follow-up duration is defined as the time from randomisation to the date of death or the database cutoff date if the participant is still alive.
CI, confidence interval; dMMR, mismatch repair deficient; HR, hazard ratio; NR, not reached; OS, overall survival; pMMR, mismatch repair proficient.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

Secondary endpoint: pMMR population – ORR and DOR | *Ad hoc* analysis

pMMR

Investigator-assessed ORR and BOR per RECIST v1.1 (patients with measurable disease at baseline; n=463)[a]



DOR (n=463)

	KEYTRUDA + chemotherapy (n=224)	Placebo + chemotherapy (n=239)
Median DOR (range), months[b]	8.1 (0.0+ to 40.9+)	6.4 (0.0+ to 28.3+)

Median (range) months of follow-up: 20.8 (7.9–46.2)

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

A tabular view of ORR and BOR is shown in the appendix. Click here to view.

Adapted from Eskander RN et al. *Nat Med* 2025.

Analysis cutoff date: 18 August 2023.

[a]Analysis included patients in the intention-to-treat population with measurable disease at baseline. Data shown are the mean ORR and 95% CI based on the binomial exact method; [b]'+' indicates no PD by the time of last disease assessment.

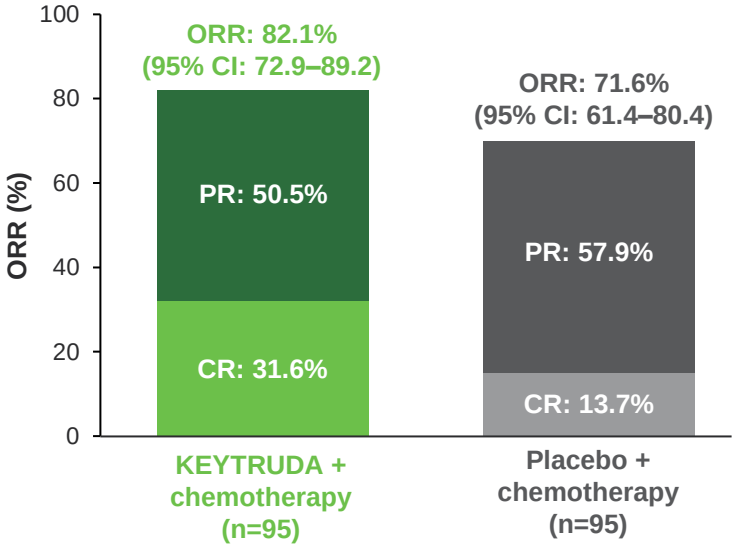
BOR, best objective response; CI, confidence interval; CR, complete response; DOR, duration of response; ORR, objective response rate; PD, progressive disease; pMMR, mismatch repair proficient; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1.

Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

Secondary endpoint: dMMR population – ORR and DOR | *Ad hoc* analysis

dMMR

Investigator-assessed ORR and BOR per RECIST v1.1 (patients with measurable disease at baseline; n=190)[a]



DOR (n=190)

	KEYTRUDA + chemotherapy (n=95)	Placebo + chemotherapy (n=95)
Median DOR (range), months[b]	NR (0.0+ to 41.8+)	4.8 (0.0+ to 42.2+)

Median (range) months of follow-up: 22.5 (12.0–47.4)

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

A tabular view of ORR and BOR is shown in the appendix. Click here to view.

Adapted from Eskander RN et al. *Nat Med* 2025.

Analysis cutoff date: 18 August 2023.

[a]Analysis included patients in the intention-to-treat population with measurable disease at baseline. Data shown are the mean ORR and 95% CI based on the binomial exact method; [b]'+' indicates no PD by the time of last disease assessment.
BOR, best objective response; CI, confidence interval; CR, complete response; dMMR, mismatch repair deficient; DOR, duration of response; NR, not reached; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1.

Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

Safety results: Interim analysis

Safety data: pMMR and dMMR populations – AEs of any cause | Interim analysis

AE of any cause, n (%)	pMMR		dMMR	
	KEYTRUDA + chemotherapy (n=276)	Placebo + chemotherapy (n=274)	KEYTRUDA + chemotherapy (n=109)	Placebo + chemotherapy (n=106)
Any AE	258 (93.5)	256 (93.4)	107 (98.2)	105 (99.1)
Grade ≥3	152 (55.1)	124 (45.3)	69 (63.3)	50 (47.2)
AE leading to death (Grade 5)	6 (2.2)[a]	2 (0.7)[a]	1 (0.9)[b]	2 (1.9)[b]

Adapted from Eskander RN et al. *N Engl J Med* 2023.

Total Grade ≥3 AEs of any cause were more frequent with KEYTRUDA + chemotherapy vs placebo + chemotherapy regardless of MMR status

For further information on the safety of KEYTRUDA, please refer to the SmPC: United Kingdom

Analysis cutoff date: 6 December 2022 for pMMR and 16 December for dMMR.

[a]Included sepsis in four patients, cardiac arrest in two patients and small intestinal obstruction or sudden death not otherwise specified in one patient each. Grade 5 cardiac arrest was deemed to be possibly related to KEYTRUDA in one patient in the pMMR population; [b]Included one each of cardiac arrest, sepsis and lower gastrointestinal haemorrhage.

AE, adverse event; dMMR, mismatch repair deficient; MMR, mismatch repair; pMMR, mismatch repair proficient; SmPC, Summary of Product Characteristics.

Eskander RN et al. *N Engl J Med* 2023;388:2159–2170.

Safety data: pMMR and dMMR populations – AEs of interest | Interim analysis

	pMMR				dMMR			
	KEYTRUDA + chemotherapy (n=276)		Placebo + chemotherapy (n=274)		KEYTRUDA + chemotherapy (n=109)		Placebo + chemotherapy (n=106)	
	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
AE of interest, n (%)	92 (33.3)	10 (3.6)	54 (19.7)	7 (2.6)	42 (38.5)	9 (8.3)	28 (26.4)	6 (5.7)
Infusion reaction	41 (14.9)	4 (1.4)	35 (12.8)	5 (1.8)	16 (14.7)	4 (3.7)	16 (15.1)	3 (2.8)
Hypothyroidism	37 (13.4)	0 (0)	7 (2.6)	0 (0)	14 (12.8)	0 (0)	10 (9.4)	0 (0)
Hyperthyroidism	16 (5.8)	0 (0)	10 (3.6)	0 (0)	10 (9.2)	0 (0)	1 (0.9)	0 (0)
Colitis	4 (1.4)	0 (0)	4 (1.5)	1 (0.4)	7 (6.4)	0 (0)	0 (0)	0 (0)
Pneumonitis	2 (0.7)	0 (0)	1 (0.4)	0 (0)	3 (2.8)	2 (1.8)	2 (1.9)	1 (0.9)
Glucose intolerance	0 (0)	0 (0)	0 (0)	0 (0)	2 (1.8)	0 (0)	0 (0)	0 (0)
Acute kidney injury	5 (1.8)	5 (1.8)	1 (0.4)	1 (0.4)	2 (1.8)	2 (1.8)	2 (1.9)	2 (1.9)
Hepatic failure	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.9)	1 (0.9)	0 (0)	0 (0)
Myositis	1 (0.4)	0 (0)	0 (0)	0 (0)	1 (0.9)	0 (0)	1 (0.9)	0 (0)
Hypophysitis	2 (0.7)	2 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Pancreatitis	1 (0.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Adrenal insufficiency	4 (1.4)	0 (0)	1 (0.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Adapted from Eskander RN et al. *N Engl J Med* 2023.

The events of interest are those with a possible immune-related cause and are considered regardless of attribution by the investigator. Some patients may have had more than one AE of interest. The events are listed in descending order of frequency in the KEYTRUDA group in the dMMR population.

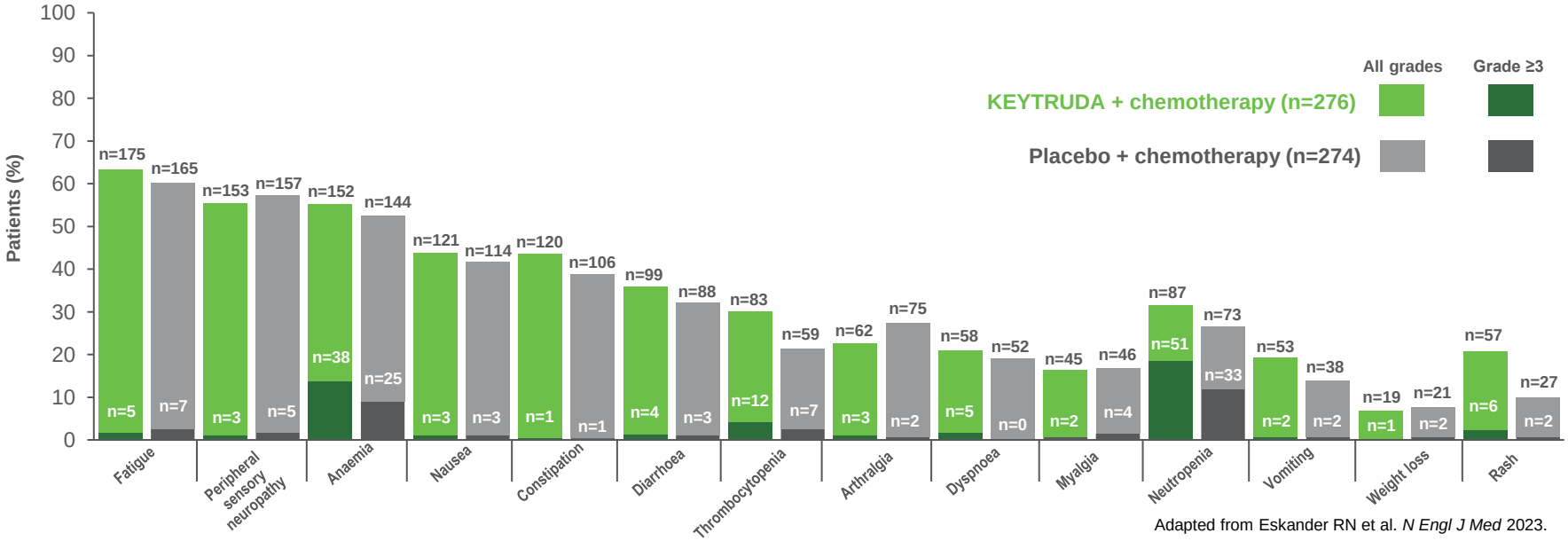
For further information on the safety of KEYTRUDA, please refer to the SmPC: United Kingdom

Analysis cutoff date: 6 December 2022 for pMMR and 16 December for dMMR.
AE, adverse event; dMMR, mismatch repair deficient; pMMR, mismatch repair proficient; SmPC, Summary of Product Characteristics.
Eskander RN et al. *N Engl J Med* 2023;388:2159–2170.

Safety data: pMMR population – AEs of any cause with ≥15% rounded incidence | Interim analysis

pMMR

Median follow-up: 7.9 months



Adapted from Eskander RN et al. *N Engl J Med* 2023.

For further information on the safety of KEYTRUDA, please refer to the SmPC: United Kingdom

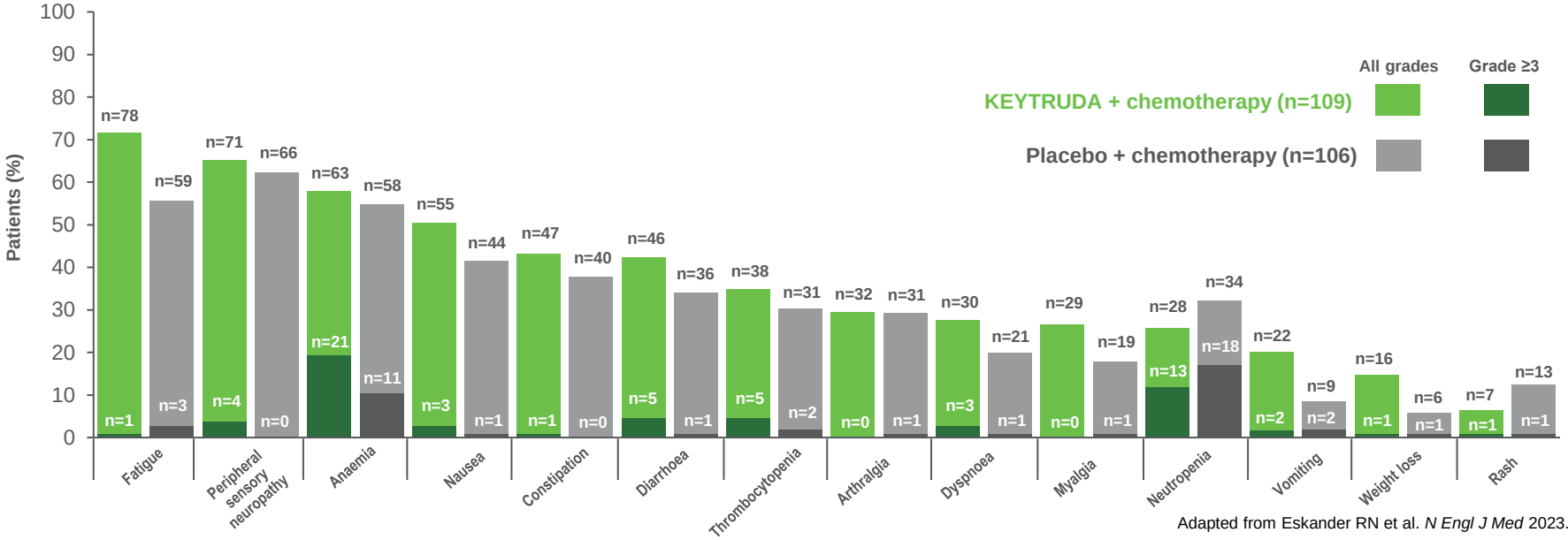
Analysis cutoff date: 6 December 2022.
AE, adverse event; pMMR, mismatch repair proficient; SmPC, Summary of Product Characteristics.
Eskander RN et al. *N Engl J Med* 2023;388:2159–2170.

UK Prescribing Information

Safety data: dMMR population – AEs of any cause with ≥15% rounded incidence | Interim analysis

dMMR

Median follow-up: 12 months



Adapted from Eskander RN et al. *N Engl J Med* 2023.

For further information on the safety of KEYTRUDA, please refer to the SmPC: United Kingdom

Analysis cutoff date: 16 December 2022.
AE, adverse event; dMMR, mismatch repair deficient; SmPC, Summary of Product Characteristics.
Eskander RN et al. *N Engl J Med* 2023;388:2159–2170.

UK Prescribing Information

Safety data: pMMR and dMMR populations – Treatment discontinuation | Interim analysis

	pMMR		dMMR	
	KEYTRUDA + chemotherapy	Placebo + chemotherapy	KEYTRUDA + chemotherapy	Placebo + chemotherapy
Treated, n	275	272	107	105
Discontinued treatment, n	145	169	47	77
Reason for discontinuing treatment, n				
PD	80	99	18	48
AEs	36	17	17	6
Patient withdrawal	11	11	6	4
Death	6	2	1	2
Other[a]	12	40	5	17

Disease progression was the primary reason for treatment discontinuation in both the pMMR and dMMR populations, and across both treatment arms

For further information on the safety of KEYTRUDA, please refer to the SmPC: United Kingdom

Analysis cutoff date: 6 December 2022 for pMMR and 16 December for dMMR.

[a]Includes alternative therapy (in absence of progression), off treatment due to other complicating disease, symptomatic deterioration and other (not otherwise specified).

AE, adverse event; dMMR, mismatch repair deficient; PD, progressive disease; pMMR, mismatch repair proficient; SmPC, Summary of Product Characteristics.

Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

UK Prescribing Information

Safety results: *Ad hoc* analysis

Safety data: Combined pMMR and dMMR population – AEs of any cause | *Ad hoc* analysis

AE	pMMR and dMMR	
	KEYTRUDA + chemotherapy (n=391)	Placebo + chemotherapy (n=388)
Any AE, n (%)	388 (99.2)	387 (99.7)
Grade ≥3, %	65.7	49.2
TRAE, n (%)	379 (96.9)	373 (96.1)
Grade ≥3, %	49.9	34.0
AE leading to treatment discontinuation, %	71 (18.2)	28 (7.2)

Adapted from Eskander RN et al. *Nat Med* 2025.

Safety at the *ad hoc* analysis was assessed in the combined population in all randomised and treated patients

For further information on the safety of KEYTRUDA, please refer to the SmPC: United Kingdom

Analysis cutoff date: 18 August 2023.
AE, adverse event; dMMR, mismatch repair deficient; pMMR, mismatch repair proficient; SmPC, Summary of Product Characteristics; TRAE, treatment-related adverse event.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

Safety data: Combined pMMR and dMMR population – Immune-mediated AEs | *Ad hoc* analysis

	pMMR and dMMR	
	KEYTRUDA + chemotherapy (n=391)	Placebo + chemotherapy (n=388)
Any grade, n (%)	155 (39.6)	102 (26.3)
Grade ≥3, %	9.7	4.1
AEs of interest, n (%)		
Infusion reaction	74 (18.9)	72 (18.6)
Hypothyroidism	54 (13.8)	15 (3.9)
Hyperthyroidism	32 (8.2)	10 (2.6)
Severe skin reactions	15 (3.8)	6 (1.5)
Colitis	8 (2.0)	3 (0.8)
Adrenal insufficiency	5 (1.3)	1 (0.3)
Pneumonitis	5 (1.3)	2 (0.5)
Myositis	3 (0.8)	1 (0.3)
Uveitis	3 (0.8)	1 (0.3)

	pMMR and dMMR	
	KEYTRUDA + chemotherapy (n=391)	Placebo + chemotherapy (n=388)
Gastritis	2 (0.5)	0 (0)
Hypophysitis	2 (0.5)	0 (0)
Myasthenic syndrome	2 (0.5)	0 (0)
Nephritis	2 (0.5)	0 (0)
Type 1 diabetes mellitus	2 (0.5)	0 (0)
Thyroiditis	2 (0.5)	0 (0)
Vasculitis	2 (0.5)	1 (0.3)
Encephalitis	1 (0.3)	0 (0)
Guillain-Barre syndrome	1 (0.3)	0 (0)
Myocarditis	1 (0.3)	0 (0)
Pancreatitis	1 (0.3)	0 (0)
Sarcoidosis	1 (0.3)	0 (0)

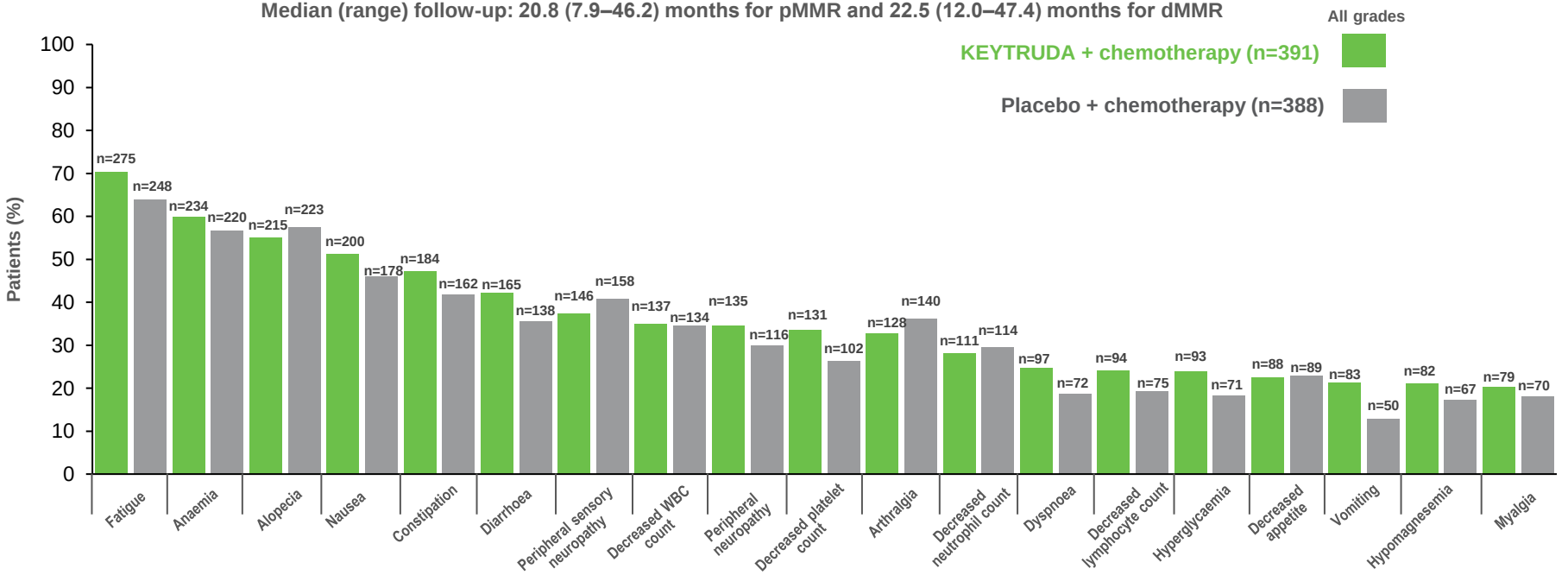
Adapted from Eskander RN et al. *Nat Med* 2025.

For further information on the safety of KEYTRUDA, please refer to the SmPC: United Kingdom

Analysis cutoff date: 18 August 2023.
AE, adverse event; dMMR, mismatch repair deficient; pMMR, mismatch repair proficient; SmPC, Summary of Product Characteristics.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

UK Prescribing Information

Safety data: Combined pMMR and dMMR population – AEs of any cause with ≥20% incidence | *Ad hoc* analysis



Adapted from Eskander RN et al. *Nat Med* 2025.

For further information on the safety of KEYTRUDA, please refer to the SmPC: United Kingdom

Analysis cutoff date: 18 August 2023.
AE, adverse event; dMMR, mismatch repair deficient; pMMR, mismatch repair proficient; WBC, white blood cell.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

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All patients:
Safety data –Treatment discontinuation | *Ad hoc* analysis

	pMMR		dMMR	
	KEYTRUDA + chemotherapy	Placebo + chemotherapy	KEYTRUDA + chemotherapy	Placebo + chemotherapy
Treated, n	284	283	107	105
Discontinued treatment, n	215	275	56	104
Reason for discontinuing treatment, n				
PD	124	115	23	53
AEs	50	22	21	6
Patient withdrawal	13	12	6	4
Death	9	2	1	2
Other[a]	19	124	5	39

Adapted from Eskander RN et al. *Nat Med* 2025.

Treatment was discontinued because of AEs in 18.2% (71/391) and 7.2% (28/388) of patients in the KEYTRUDA + chemotherapy and placebo + chemotherapy groups, respectively

For further information on the safety of KEYTRUDA, please refer to the SmPC: United Kingdom

Analysis cutoff date: 18 August 2023.

[a]Includes alternative therapy (in absence of progression), off treatment due to other complicating disease, symptomatic deterioration and other (not otherwise specified).

AE, adverse event; dMMR, mismatch repair deficient; PD, progressive disease; pMMR, mismatch repair proficient; SmPC, Summary of Product Characteristics.

Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

UK Prescribing Information

Dosing and administration

KEYTRUDA dosing in combination with chemotherapy

For first-line treatment of primary advanced or recurrent endometrial carcinoma, the recommended dose of KEYTRUDA is 200 mg Q3W for 6 cycles in combination with chemotherapy, followed by KEYTRUDA 400 mg Q6W for up to 14 cycles as monotherapy

KEYTRUDA dosing

Administered as an IV infusion

Over 30 minutes

KEYTRUDA was administered with paclitaxel (175 mg/m^2) and carboplatin (AUC 5 mg/ml/min) in the combination phase of the KEYNOTE-868 (NRG-GY018) trial

Patients should be treated with KEYTRUDA until disease progression or unacceptable toxicity

Atypical responses (i.e. an initial transient increase in tumour size or new small lesions within the first few months, followed by tumour shrinkage) have been observed

It is recommended to continue treatment in clinically stable patients with initial evidence of disease progression until disease progression is confirmed

No dose reductions of KEYTRUDA are recommended. KEYTRUDA should be withheld or discontinued to manage AEs as described within the SmPC

When administering KEYTRUDA in combination with IV chemotherapy, KEYTRUDA should be administered first

Consult the full KEYTRUDA SmPC for guidance on dosing. For use in combination, see the KEYTRUDA SmPC for concomitant therapies

Chemotherapy refers to carboplatin + paclitaxel.

AE, adverse event; AUC, area under the curve; IV, intravenous; Q3W, every 3 weeks; Q6W, every 6 weeks; SmPC, Summary of Product Characteristics.

KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed May 2025.

Summary of efficacy and safety results

KEYNOTE-868 (NRG-GY018): Summary of efficacy data

Primary endpoint: PFS results (interim analysis)

KEYTRUDA + chemotherapy, followed by KEYTRUDA maintenance, demonstrated a statistically significant improvement vs placebo + chemotherapy, followed by placebo maintenance, in investigator-assessed PFS (per RECIST v1.1) in pMMR and dMMR adult patients with primary advanced or recurrent endometrial carcinoma

- **pMMR**: Median PFS for KEYTRUDA + chemotherapy, followed by KEYTRUDA maintenance, was 13.1 months and 8.7 months for placebo + chemotherapy, followed by placebo maintenance (HR: 0.57; 95% CI: 0.44–0.74; p<0.0001)
- **dMMR:** Median PFS was not reached for KEYTRUDA + chemotherapy, followed by KEYTRUDA maintenance, and was 8.3 months for placebo + chemotherapy, followed by placebo maintenance (HR: 0.34; 95% CI: 0.22–0.53; p<0.0001)

Secondary endpoint: OS results[a]

OS data are immature and further analysis is required

Interim analysis

- Interim results suggested a trend favouring KEYTRUDA + chemotherapy vs placebo + chemotherapy, regardless of MMR status
  - pMMR: HR (95% CI) was 0.79 (0.53–1.17), p=0.1157[b]
  - dMMR: HR (95% CI) was 0.55 (0.25–1.19), p=0.0617[b]

Ad hoc analysis

- The trend favouring KEYTRUDA + chemotherapy vs placebo + chemotherapy was maintained at the *ad hoc* analysis regardless of MMR status
  - pMMR: HR (95% CI) was 0.80 (0.59–1.08), p=0.0683[b]
  - dMMR: HR (95% CI) was 0.57 (0.31–1.04), p=0.0323[b]

[a]OS data were immature at the interim and *ad hoc* analyses, and OS analysis is ongoing; [b]OS endpoint was not formally assessed within the multiplicity control and p-values are nominal.
CI, confidence interval; dMMR, mismatch repair deficient; HR, hazard ratio; MMR, mismatch repair; OS, overall survival; PFS, progression-free survival; pMMR, mismatch repair proficient; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

KEYNOTE-868 (NRG-GY018): Summary of safety data

Interim analysis[1]

- **dMMR:** Grade ≥3 AEs occurred in 63.3% of patients treated with KEYTRUDA + chemotherapy and 47.2% of those treated with placebo + chemotherapy
- **pMMR:** Grade ≥3 AEs occurred in 55.1% of patients treated with KEYTRUDA + chemotherapy and 45.3% of those treated with placebo + chemotherapy
- The incidence of immune-mediated AEs or infusion reactions was similar to that reported in previous studies of KEYTRUDA monotherapy in endometrial cancer[3]

Ad hoc combined pMMR and dMMR analysis[2]

- Grade ≥3 AEs occurred in 65.7% of patients treated with KEYTRUDA + chemotherapy and 49.2% of those treated with placebo + chemotherapy
- The incidence of immune-mediated AEs and infusion reactions was higher for KEYTRUDA + chemotherapy vs placebo + chemotherapy (39.6% vs 26.3%, respectively)

AE, adverse event; dMMR, mismatch repair deficient; pMMR, mismatch repair proficient.

1. Eskander RN et al. *N Engl J Med* 2023;388:2159–2170; 2. Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1; 3. O'Malley DM et al. *J Clin Oncol 2022;*40:752–761.

Appendix: Data analysis considerations

KEYNOTE-868 (NRG-GY018): Definitions of the interim and *ad hoc* analyses

Analysis	Total number of randomised patients (N) and analysis cut-off date	Population for the analysis of the endpoints	Median (range) follow-up, months
Interim	**N=810** **Analysis cut-off date pMMR:** 6 December 2022 (n=588) **Analysis cut-off date dMMR:** 16 December 2022 (n=222)	The primary endpoint was assessed separately for pMMR and dMMR in the interim analysis Secondary and exploratory endpoints were assessed separately in the pMMR and dMMR populations except for safety (combined population)	**pMMR:** 10.0 (0.0–37.8) **dMMR:** 14.4 (4.0–39.4)
Ad hoc	**N=819** **Analysis cut-off date:** 18 August 2023 – included ~9 months of additional follow-up (pMMR n=597; dMMR n=222)		**pMMR:** 20.8 (7.9–46.2) **dMMR:** 22.5 (12.0–47.4)

Additional considerations

- As the analysis cut-off date was in close proximity to the last patient enrolled and not all patients were randomised at this stage, some patients in the study did not have a post-baseline assessment available for response evaluation at the analysis cut-off dates used for the interim analysis. An *ad hoc* analysis was therefore conducted with ~9 additional months of follow-up
- At the end of randomisation, 819 patients had been randomised in the study, of which nine patients in the pMMR population were randomised after the 6 December 2022 analysis cut-off date and therefore were not included in both the current and previous PFS and OS analyses using the interim analysis cut-off dates, but are included in the *ad hoc* analyses (analysis cut-off date 18 August 2023)
- The study was unblinded after meeting its primary endpoint of investigator-assessed PFS at interim analysis (analysis cut-off dates 6 December 2022 and 16 December 2022 for pMMR and dMMR populations, respectively). Investigators were informed of patients' assigned treatment and patients were made aware of the study outcome and their treatment assignment. Consequently, nearly all patients (>99%) in the placebo + chemotherapy group discontinued study treatment by the time of the *ad hoc* analysis (analysis cut-off date 18 August 2023), with some participants subsequently receiving immunotherapy outside the study

dMMR, mismatch repair deficient; OS, overall survival; PFS, progression-free survival; pMMR, mismatch repair proficient.

Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

KEYNOTE-868 (NRG-GY018): Differences in the analysis methodology between published interim analyses[1,2]

pMMR and dMMR categorisation

- In the interim analysis presented in Eskander RN et al. 2023, central MMR status was used, if available, with local MMR status being used in the absence of central results[1]
  - Patients with indeterminate central MMR status were excluded as per protocol
- In the interim analysis and *ad hoc* analyses presented in Eskander RN et al. 2025, patients were categorised based on the MMR stratification status used for randomisation, which could have been based on either central or local MMR results[2]
- Differences in classification did not result in meaningful differences in numerical values or study conclusions[2]

dMMR, mismatch repair deficient; MMR, mismatch repair; pMMR, mismatch repair proficient.

1. Eskander RN et al. *N Engl J Med* 2023;388:2159–2170; 2. Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

Appendix: Baseline patient demographics and disease characteristics at the *ad hoc* analysis

KEYNOTE-868 (NRG-GY018): Baseline patient demographics and disease characteristics | *Ad hoc* analysis (1/2)

Baseline characteristics	pMMR			dMMR		
	KEYTRUDA + chemotherapy (n=298)	Placebo + chemotherapy (n=299)	All (n=597)	KEYTRUDA + chemotherapy (n=110)	Placebo + chemotherapy (n=112)	All (n=222)
Median age (range), years	66.2 (31.0–94.0)	66.0 (29.0–91.0)	66.1 (29.0–94.0)	67.2 (39.0–82.0)	66.1 (37.0–86.0)	66.1 (37.0–86.0)
Race/ethnicity, n (%)						
White	216 (72.5)	215 (71.9)	431 (72.2)	91 (82.7)	85 (75.9)	176 (79.3)
Black	46 (15.4)	51 (17.1)	97 (16.2)	10 (9.1)	9 (8.0)	19 (8.6)
Asian	17 (5.7)	15 (5.0)	32 (5.4)	3 (2.7)	4 (3.6)	7 (3.2)
Hispanic	23 (7.7)	15 (5.0)	38 (6.4)	4 (3.6)	7 (6.3)	11 (5.0)
ECOG PS, n (%)						
0	200 (67.1)	201 (67.2)	401 (67.2)	70 (63.6)	72 (64.3)	142 (64.0)
1	89 (29.9)	89 (29.8)	178 (29.8)	39 (35.5)	35 (31.3)	74 (33.3)
2	9 (3.0)	9 (3.0)	18 (3.0)	1 (0.9)	5 (4.5)	6 (2.7)

Adapted from Eskander RN et al. *Nat Med* 2025.

Analysis cutoff date: 18 August 2023.

dMMR, mismatch repair deficient; ECOG PS, Eastern Cooperative Oncology Group performance status; MMR, mismatch repair; pMMR, mismatch repair proficient.

Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

KEYNOTE-868 (NRG-GY018): Baseline patient demographics and disease characteristics | *Ad hoc* analysis (2/2)

MMR status

Baseline characteristics	pMMR			dMMR		
	KEYTRUDA + chemotherapy (n=298)	Placebo + chemotherapy (n=299)	All (n=597)	KEYTRUDA + chemotherapy (n=110)	Placebo + chemotherapy (n=112)	All (n=222)
Previous therapy, n (%)						
Adjuvant chemotherapy	75 (25.2)	77 (25.8)	152 (25.5)	4 (3.6)	8 (7.1)	12 (5.4)
Radiotherapy	120 (40.3)	126 (42.1)	246 (41.2)	42 (38.2)	54 (48.2)	96 (43.2)
Surgery	269 (90.3)	253 (84.6)	522 (87.4)	97 (88.2)	104 (92.9)	201 (90.5)
Histologic subtype, n (%)						
Endometrioid carcinoma						
Grade 1	56 (18.8)	46 (15.4)	102 (17.1)	20 (18.2)	34 (30.4)	54 (24.3)
Grade 2	52 (17.4)	59 (19.7)	111 (18.6)	52 (47.3)	43 (38.4)	95 (42.8)
Grade 3	53 (17.8)	45 (15.1)	98 (16.4)	15 (13.6)	16 (14.3)	31 (14.0)
Serous	81 (27.2)	77 (25.8)	158 (26.5)	4 (3.6)	1 (0.9)	5 (2.3)
Adenocarcinoma NOS	24 (8.1)	35 (11.7)	59 (9.9)	12 (10.9)	12 (10.7)	24 (10.8)
Clear cell carcinoma	19 (6.4)	20 (6.7)	39 (6.5)	0 (0)	0 (0)	0 (0)
Other	13 (4.4)[a]	17 (5.7)[a]	30 (5.0)[a]	7 (6.4)[a]	6 (5.4)[a]	13 (5.9)[a]

Adapted from Eskander RN et al. *Nat Med* 2025.

Analysis cutoff date: 18 August 2023.

[a]Including mixed epithelial, dedifferentiated/undifferentiated and missing.

dMMR, mismatch repair deficient; MMR, mismatch repair; NOS, not otherwise specified; pMMR, mismatch repair proficient.

Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

Appendix: Selected secondary and exploratory endpoints

Secondary endpoint: pMMR population – Investigator-assessed ORR and BOR per RECIST v1.1 (tabular view) | Interim analysis

pMMR

Patients with measurable disease at baseline (n=455)
Median (range) months of follow-up: 10.0 (0.0–37.8)

	KEYTRUDA + chemotherapy (n=220)	Placebo + chemotherapy (n=235)
ORR, n (%) [95% CI]	135 (61.4) [54.6–67.8]	121 (51.5) [44.9–58.0]
BOR, n (%)		
CR	24 (10.9)	16 (6.8)
PR	111 (50.5)	105 (44.7)
SD	29 (13.2)	52 (22.1)
PD	12 (5.5)	19 (8.1)
Not evaluable[a]	2 (0.9)	2 (0.9)
No assessment[b]	42 (19.1)	41 (17.4)
Median TTR (range), months	2.3 (1.9–19.6)	2.3 (1.0–7.1)
Median DOR (range)[c], months	7.1 (0.0+ to 32.8+)	6.4 (0.0+ to 20.1+)

Adapted from Eskander RN et al. *Nat Med* 2025.

Not all patients had post-baseline assessment available at interim analysis.
Statistical analyses for secondary and exploratory endpoints are descriptive in nature

Analysis cutoff date: 6 December 2022.
[a]Post-baseline assessment available but not evaluable; [b]No post-baseline assessment available for response evaluation; [c]'+' indicates no PD by the time of last disease assessment.
BOR, best objective response; CI, confidence interval; CR, complete response; DOR, duration of response; ORR, objective response rate; PD, progressive disease; pMMR, mismatch repair proficient; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1; SD, stable disease; TTR, time to response.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

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Secondary endpoint: dMMR population – Investigator-assessed ORR and BOR per RECIST v1.1 (tabular view) | Interim analysis

dMMR

Patients with measurable disease at baseline (n=190)
Median (range) months of follow-up: 14.4 (4.0–39.4)

	KEYTRUDA + chemotherapy (n=95)	Placebo + chemotherapy (n=95)
ORR, n (%) [95% CI]	74 (77.9) [68.2–85.8]	66 (69.5) [59.2–78.5]
BOR, n (%)		
CR	27 (28.4)	11 (11.6)
PR	47 (49.5)	55 (57.9)
SD	10 (10.5)	17 (17.9)
PD	5 (5.3)	3 (3.2)
Not evaluable[a]	0	1 (1.1)
No assessment[b]	6 (6.3)	8 (8.4)
Median TTR (range), months	2.3 (1.3–11.5)	2.2 (2.0–6.2)
Median DOR (range)[c], months	NR (0.0+ to 33.0+)	4.4 (0.0+ to 32.8+)

Adapted from Eskander RN et al. *Nat Med* 2025.

Not all patients had post-baseline assessment available at interim analysis.
Statistical analyses for secondary and exploratory endpoints are descriptive in nature

Analysis cutoff date: 16 December 2022.
[a]Post-baseline assessment available but not evaluable; [b]No post-baseline assessment available for response evaluation; [c]'+' indicates no PD by the time of last disease assessment.
BOR, best objective response; CI, confidence interval; CR, complete response; dMMR, mismatch repair deficient; DOR, duration of response; NR, not reached; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1; SD, stable disease; TTR, time to response.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

Secondary endpoint: pMMR population – Investigator-assessed ORR and BOR per RECIST v1.1 (tabular view) | *Ad hoc* analysis

pMMR

Patients with measurable disease at baseline (n=463)

Median (range) months of follow-up: 20.8 (7.9–46.2)

	KEYTRUDA + chemotherapy (n=224)	Placebo + chemotherapy (n=239)
ORR[a], n (%) [95% CI]	162 (72.3) [66.0–78.1]	141 (59.0) [52.5–65.3]
BOR, n (%)		
CR	32 (14.3)	20 (8.4)
PR	130 (58.0)	121 (50.6)
SD	26 (11.6)	55 (23.0)
PD	16 (7.1)	19 (7.9)
Not evaluable[b]	2 (0.9)	3 (1.3)
No assessment[c]	18 (8.0)	21 (8.8)
Median TTR (range), months	2.3 (1.9–19.6)	2.3 (1.0–7.1)
Median DOR (range)[d], months	8.1 (0.0+ to 40.9+)	6.4 (0.0+ to 28.3+)

Adapted from Eskander RN et al. *Nat Med* 2025.

Statistical analyses for secondary and exploratory endpoints are descriptive in nature

Analysis cutoff date: 18 August 2023. This analysis was conducted after unblinding and subsequent initiation of post-study immunotherapy in the placebo arm. This might have introduced bias in the estimation of HRs favouring the placebo arm, thus limiting interpretability of the *ad hoc* analysis.

[a]Analysis included patients in the intention-to-treat population with measurable disease at baseline. Data shown are the mean ORR and 95% CI based on the binomial exact method; [b]Post-baseline assessment available but not evaluable; [c]No post-baseline assessment available for response evaluation; [d]'+' indicates no PD by the time of last disease assessment.

BOR, best objective response; CI, confidence interval; CR, complete response; DOR, duration of response; HR, hazard ratio; ORR, objective response rate; PD, progressive disease; pMMR, mismatch repair proficient; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1; SD, stable disease; TTR, time to response.

Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

UK Prescribing Information

Secondary endpoint: dMMR population – Investigator-assessed ORR and BOR per RECIST v1.1 (tabular view) | *Ad hoc* analysis

dMMR

Patients with measurable disease at baseline (n=190)

Median (range) months of follow-up: 22.5 (12.0–47.4)

	KEYTRUDA + chemotherapy (n=95)	Placebo + chemotherapy (n=95)
ORR[a], n (%) [95% CI]	78 (82.1) [72.9–89.2]	68 (71.6) [61.4–80.4]
BOR, n (%)		
CR	30 (31.6)	13 (13.7)
PR	48 (50.5)	55 (57.9)
SD	7 (7.4)	16 (16.8)
PD	4 (4.2)	3 (3.2)
Not evaluable[b]	0	0
No assessment[c]	6 (6.3)	8 (8.4)
Median TTR (range), months	2.3 (1.6–11.6)	2.3 (2.0–14.5)
Median DOR (range)[d], months	NR (0.0+ to 41.8+)	4.8 (0.0+ to 42.2+)

Adapted from Eskander RN et al. *Nat Med* 2025.

Statistical analyses for secondary and exploratory endpoints are descriptive in nature

Analysis cutoff date: 18 August 2023. This analysis was conducted after unblinding and subsequent initiation of post-study immunotherapy in the placebo arm. This might have introduced bias in the estimation of HRs favouring the placebo arm, thus limiting interpretability of the *ad hoc* analysis.

[a]Analysis included patients in the intention-to-treat population with measurable disease at baseline. Data shown are the mean ORR and 95% CI based on the binomial exact method; [b]Post-baseline assessment available but not evaluable; [c]No post-baseline assessment available for response evaluation; [d]'+' indicates no PD by the time of last disease assessment.

BOR, best objective response; CI, confidence interval; CR, complete response; dMMR, mismatch repair deficient; DOR, duration of response; NR, not reached; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1; SD, stable disease; TTR, time to response.

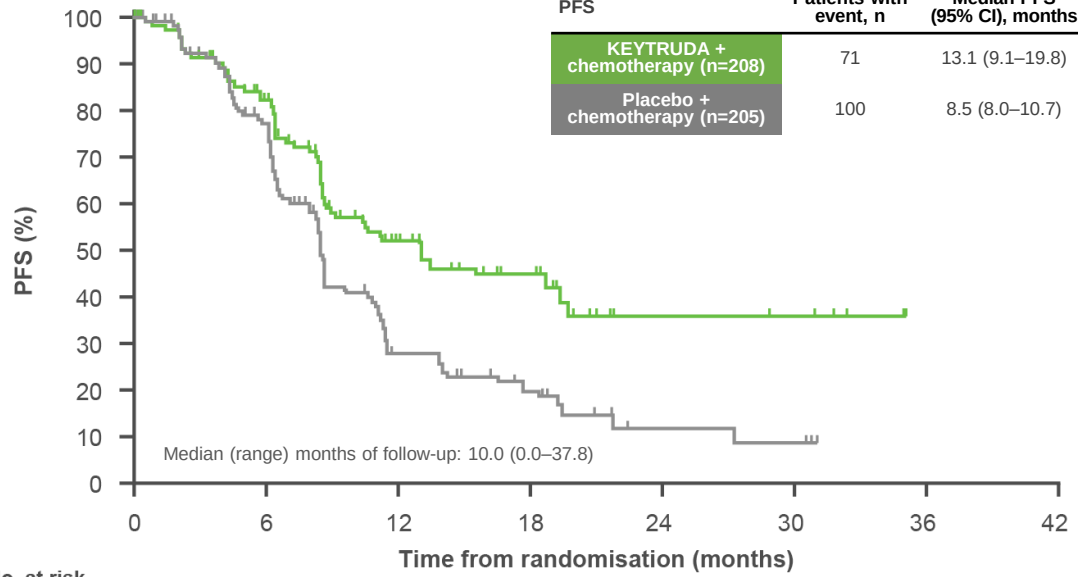
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

UK Prescribing Information

Exploratory endpoint: pMMR population – PFS by investigator per RECIST v1.1 (PD-L1 CPS ≥1) | Interim analysis

pMMR

PFS	Patients with event, n	Median PFS (95% CI), months	HR (95% CI)
KEYTRUDA + chemotherapy (n=208)	71	13.1 (9.1–19.8)	0.59 (0.43–0.80)
Placebo + chemotherapy (n=205)	100	8.5 (8.0–10.7)	



No. at risk								
KEYTRUDA + chemotherapy	208	115	36	20	6	5	0	0
Placebo + chemotherapy	205	101	23	13	4	3	0	0

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

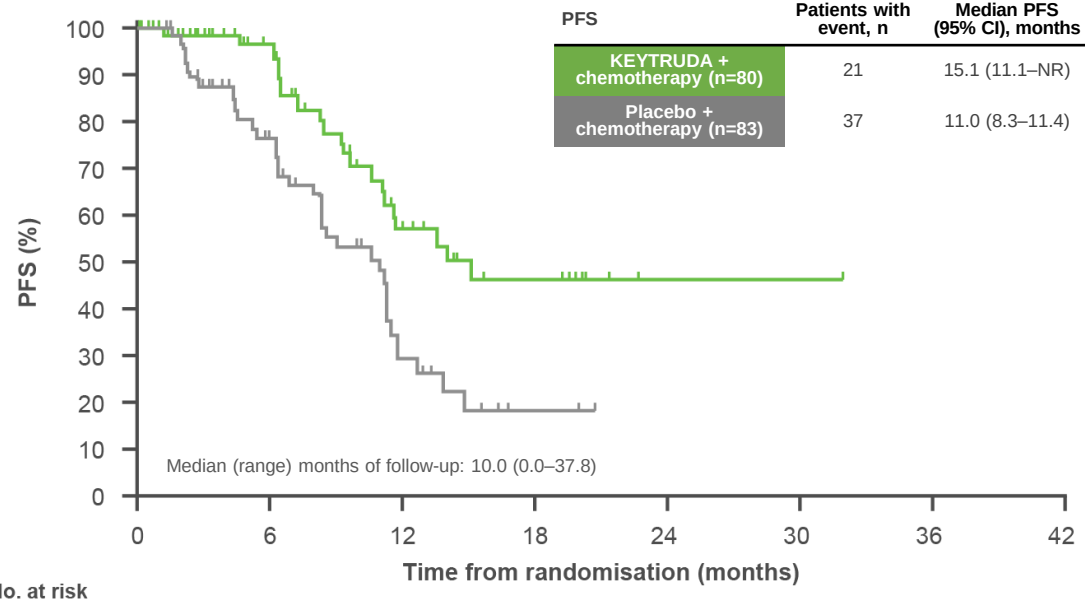
Adapted from Eskander RN et al. *Nat Med* 2025.

Analysis cutoff date: 6 December 2022. Tick-marks indicate censored data.
CI, confidence interval; CPS, combined positive score; HR, hazard ratio; PD-L1, programmed death ligand-1; PFS, progression-free survival; pMMR, mismatch repair proficient; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

UK Prescribing Information

Exploratory endpoint: pMMR population – PFS by investigator per RECIST v1.1 (PD-L1 CPS <1) | Interim analysis

pMMR



PFS	Patients with event, n	Median PFS (95% CI), months	HR (95% CI)
KEYTRUDA + chemotherapy (n=80)	21	15.1 (11.1–NR)	0.44 (0.26–0.75)
Placebo + chemotherapy (n=83)	37	11.0 (8.3–11.4)	

No. at risk								
KEYTRUDA + chemotherapy	80	45	21	9	1	1	0	0
Placebo + chemotherapy	83	39	11	2	0	0	0	0

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

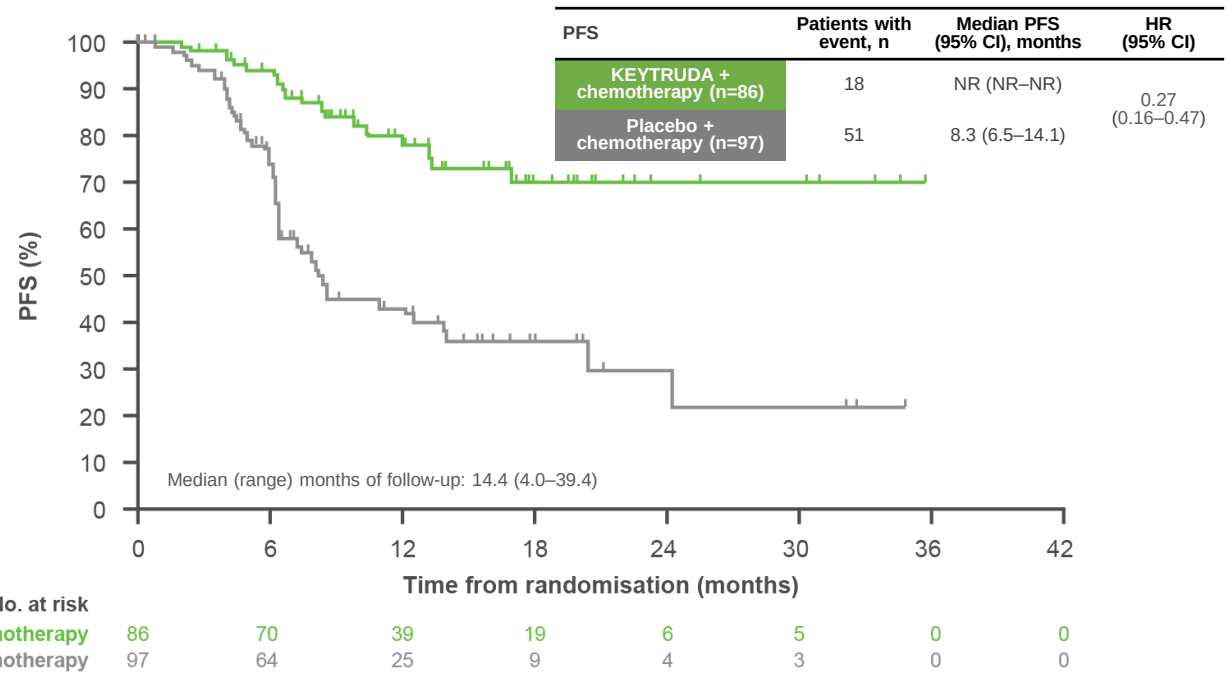
Adapted from Eskander RN et al. *Nat Med* 2025.

Analysis cutoff date: 6 December 2022. Tick-marks indicate censored data.
CI, confidence interval; CPS, combined positive score; HR, hazard ratio; NR, not reached; PD-L1, programmed death ligand-1; PFS, progression-free survival; pMMR, mismatch repair proficient; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

UK Prescribing Information

Exploratory endpoint: dMMR population – PFS by investigator per RECIST v1.1 (PD-L1 CPS ≥1) | Interim analysis

dMMR



PFS	Patients with event, n	Median PFS (95% CI), months	HR (95% CI)
KEYTRUDA + chemotherapy (n=86)	18	NR (NR–NR)	0.27 (0.16–0.47)
Placebo + chemotherapy (n=97)	51	8.3 (6.5–14.1)	

No. at risk								
KEYTRUDA + chemotherapy	86	70	39	19	6	5	0	0
Placebo + chemotherapy	97	64	25	9	4	3	0	0

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Adapted from Eskander RN et al. *Nat Med* 2025.

Analysis cutoff date: 16 December 2022. Tick-marks indicate censored data.
CI, confidence interval; CPS, combined positive score; dMMR, mismatch repair deficient; HR, hazard ratio; NR, not reached; PD-L1, programmed death ligand-1; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

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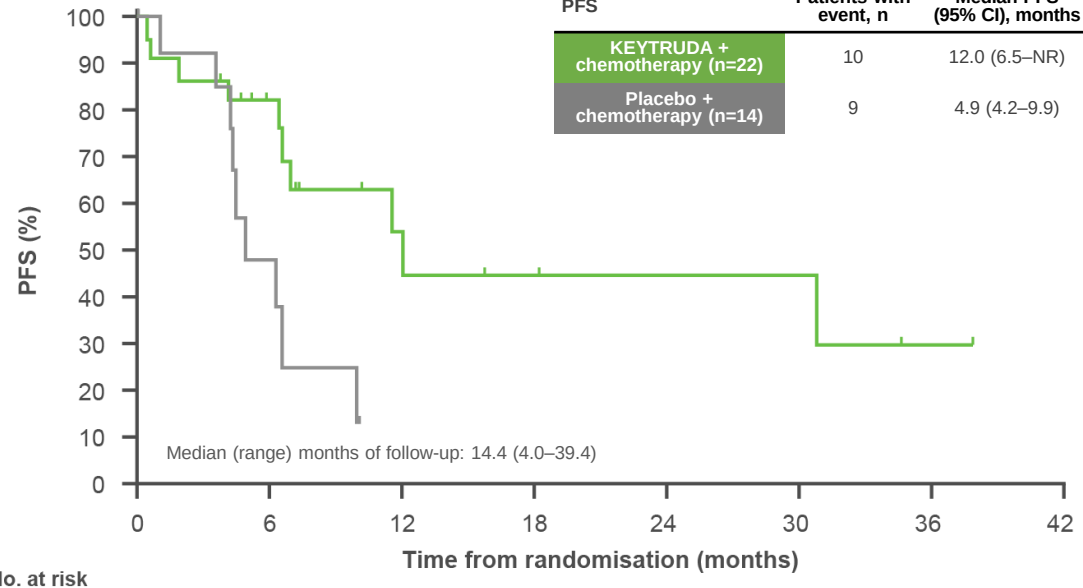
Exploratory endpoint: dMMR population – PFS by investigator per RECIST v1.1 (PD-L1 CPS <1) | Interim analysis

dMMR

PFS	Patients with event, n	Median PFS (95% CI), months	HR (95% CI)
KEYTRUDA + chemotherapy (n=22)	10	12.0 (6.5–NR)	0.30 (0.11–0.83)
Placebo + chemotherapy (n=14)	9	4.9 (4.2–9.9)	



No. at risk								
KEYTRUDA + chemotherapy	22	14	5	4	3	3	1	0
Placebo + chemotherapy	14	5	0	0	0	0	0	0

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Adapted from Eskander RN et al. *Nat Med* 2025.

Analysis cutoff date: 16 December 2022. Tick-marks indicate censored data.
CI, confidence interval; CPS, combined positive score; dMMR, mismatch repair deficient; HR, hazard ratio; NR, not reached; PD-L1, programmed death ligand-1; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

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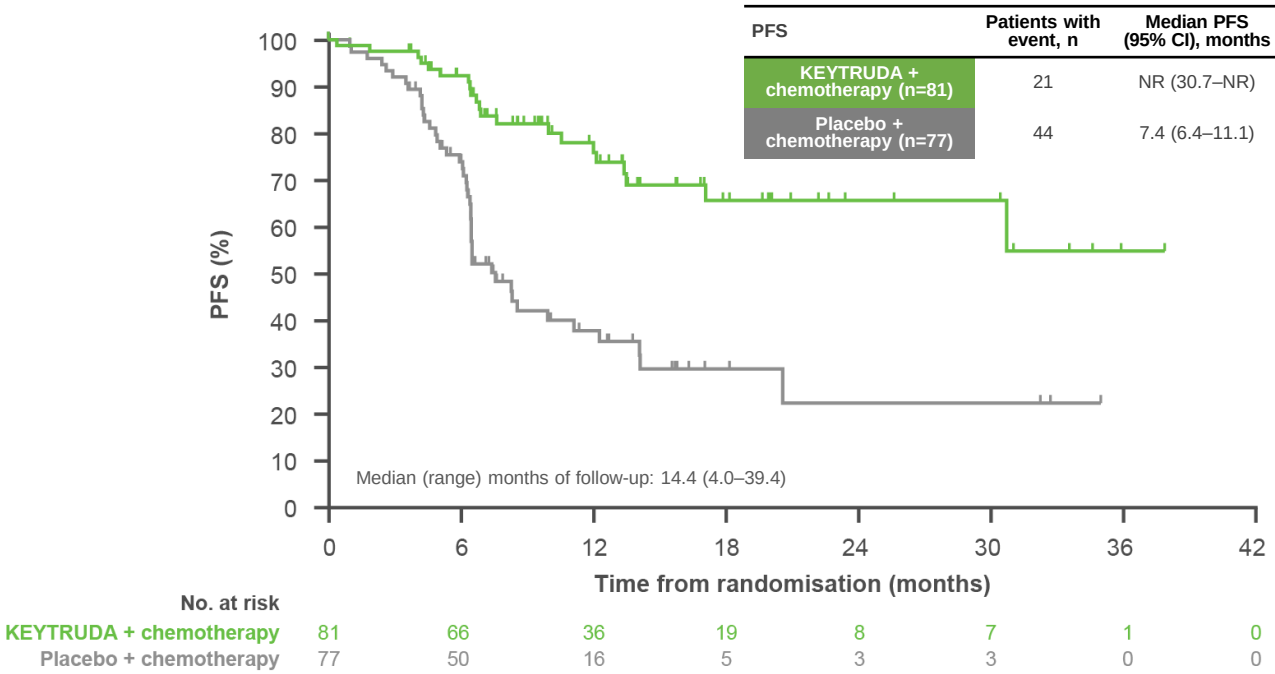
Exploratory endpoint: dMMR population – PFS by investigator per RECIST v1.1 (with methylation) | Interim analysis

dMMR



PFS	Patients with event, n	Median PFS (95% CI), months	HR (95% CI)
KEYTRUDA + chemotherapy (n=81)	21	NR (30.7–NR)	0.30 (0.18–0.50)
Placebo + chemotherapy (n=77)	44	7.4 (6.4–11.1)	

No. at risk								
KEYTRUDA + chemotherapy	81	66	36	19	8	7	1	0
Placebo + chemotherapy	77	50	16	5	3	3	0	0

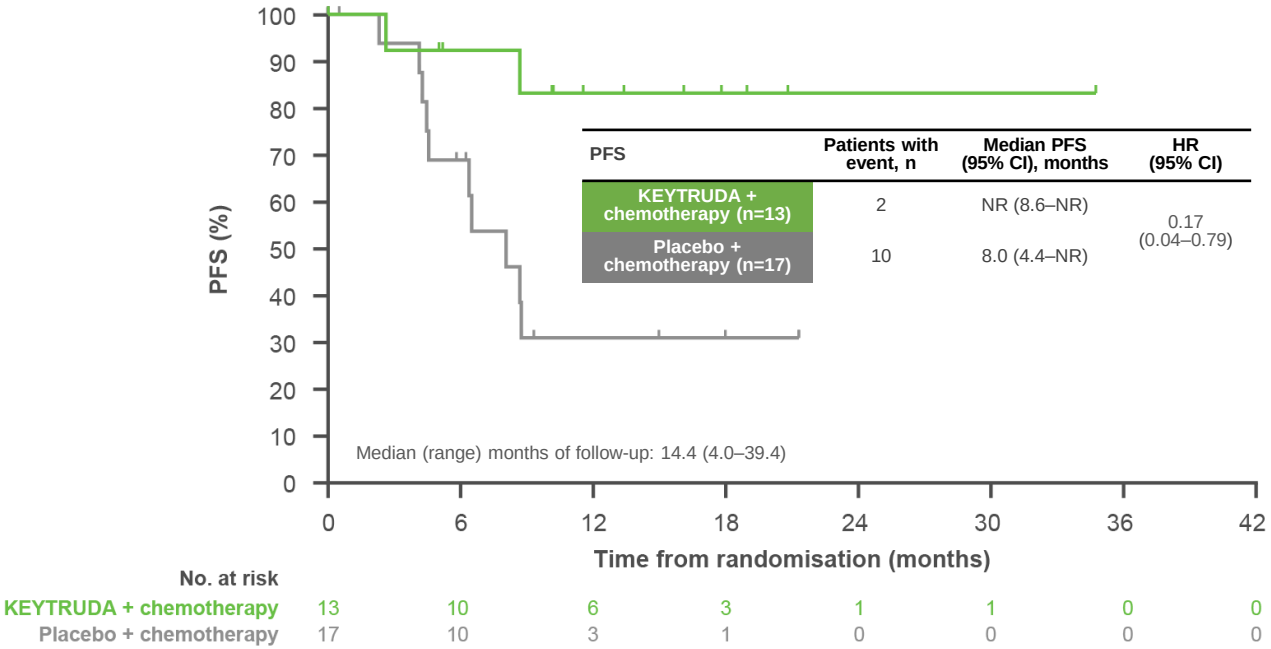
This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Adapted from Eskander RN et al. *Nat Med* 2025.

Analysis cutoff date: 16 December 2022. Tick-marks indicate censored data.
CI, confidence interval; dMMR, mismatch repair deficient; HR, hazard ratio; NR, not reached; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

Exploratory endpoint: dMMR population – PFS by investigator per RECIST v1.1 (without methylation) | Interim analysis

dMMR



PFS	Patients with event, n	Median PFS (95% CI), months	HR (95% CI)
KEYTRUDA + chemotherapy (n=13)	2	NR (8.6–NR)	0.17 (0.04–0.79)
Placebo + chemotherapy (n=17)	10	8.0 (4.4–NR)	

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Adapted from Eskander RN et al. *Nat Med* 2025.

Analysis cutoff date: 16 December 2022. Tick-marks indicate censored data.
CI, confidence interval; dMMR, mismatch repair deficient; HR, hazard ratio; NR, not reached; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1.
Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

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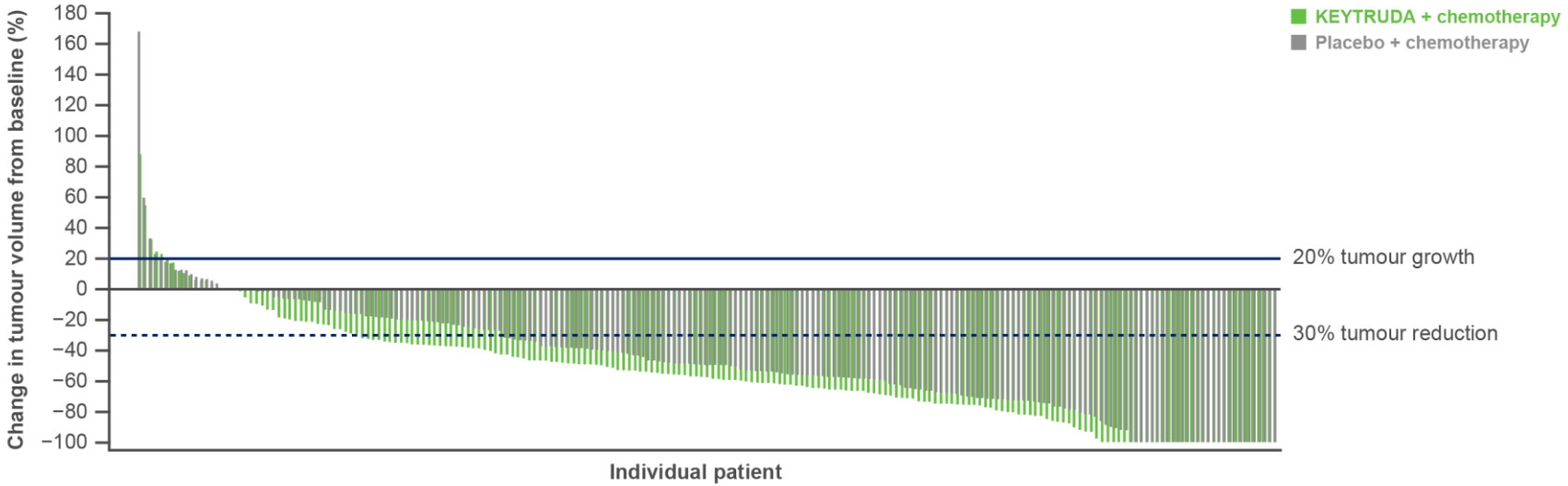
Exploratory endpoint: pMMR population – Maximum change in tumour measurement from baseline | *Ad hoc* analysis

Median (range) months of follow-up: 20.8 (7.9–46.2)

pMMR



Adapted from Eskander RN et al. *Nat Med* 2025.

Analysis cutoff date: 18 August 2023. This analysis was conducted after unblinding and subsequent initiation of post-study immunotherapy in the placebo arm. This might have introduced bias in the estimation of HRs favouring the placebo arm, thus limiting interpretability of the *ad hoc* analysis.

HR, hazard ratio; pMMR, mismatch repair proficient.

Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

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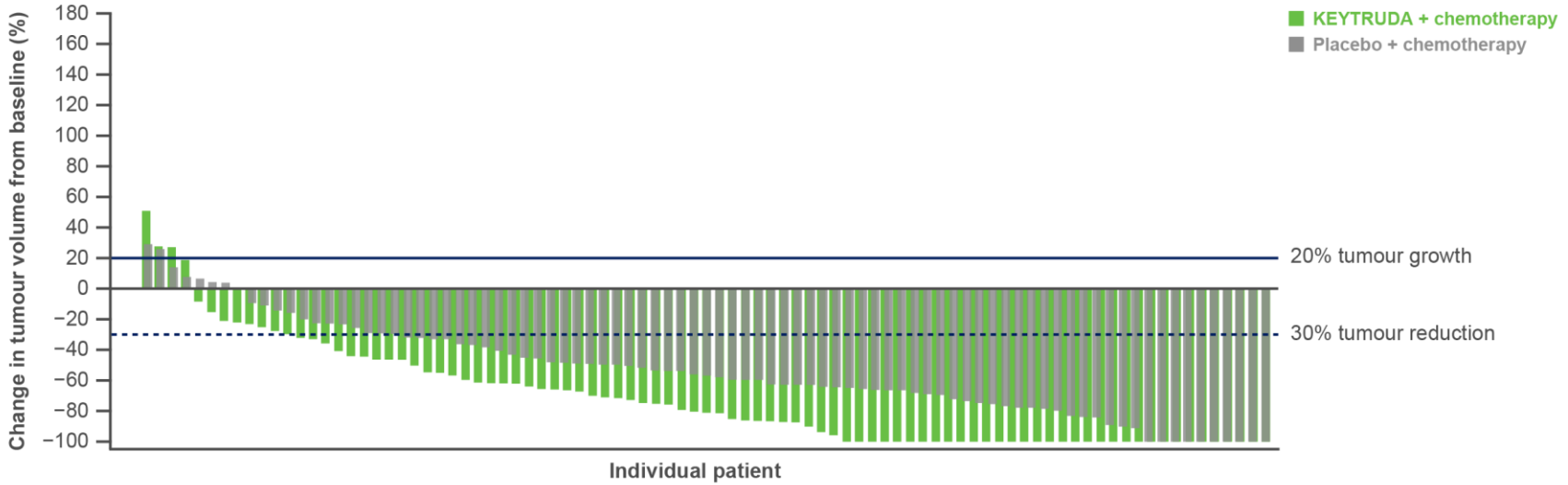
Exploratory endpoint: dMMR population – Maximum change in tumour measurement from baseline | *Ad hoc* analysis

Median (range) months of follow-up: 22.5 (12.0–47.4)

dMMR



Adapted from Eskander RN et al. *Nat Med* 2025.

Analysis cutoff date: 18 August 2023. This analysis was conducted after unblinding and subsequent initiation of post-study immunotherapy in the placebo arm. This might have introduced bias in the estimation of HRs favouring the placebo arm, thus limiting interpretability of the *ad hoc* analysis.

dMMR, mismatch repair deficient; HR, hazard ratio.

Eskander RN et al. *Nat Med* 2025. https://doi.org/10.1038/s41591-025-03566-1.

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