MSD Oncology

# KEYTRUDA® (pembrolizumab) + Lenvima® (lenvatinib) in the treatment of adults with advanced/recurrent endometrial cancer that has progressed on or following prior treatment with platinum-containing therapy in any setting, and who are not candidates for curative surgery or radiation



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**Please refer to the full Summary of Product Characteristics for KEYTRUDA, and patient-targeted Risk Minimisation Materials, before prescribing KEYTRUDA.**

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: 020 8 154 8000). By clicking the above link, you will be taken to the MHRA website.

**FOR UK HEALTHCARE PROFESSIONALS ONLY**

**Please click the following links for the KEYTRUDA Prescribing Information: Great Britain; Northern Ireland.**
**Please click the following links for the Lenvima Prescribing Information: Great Britain and Northern Ireland.**

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Job code: GB-KLE-00179. Date of preparation: November 2023.



MSD Eisai

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# Slide deck navigation

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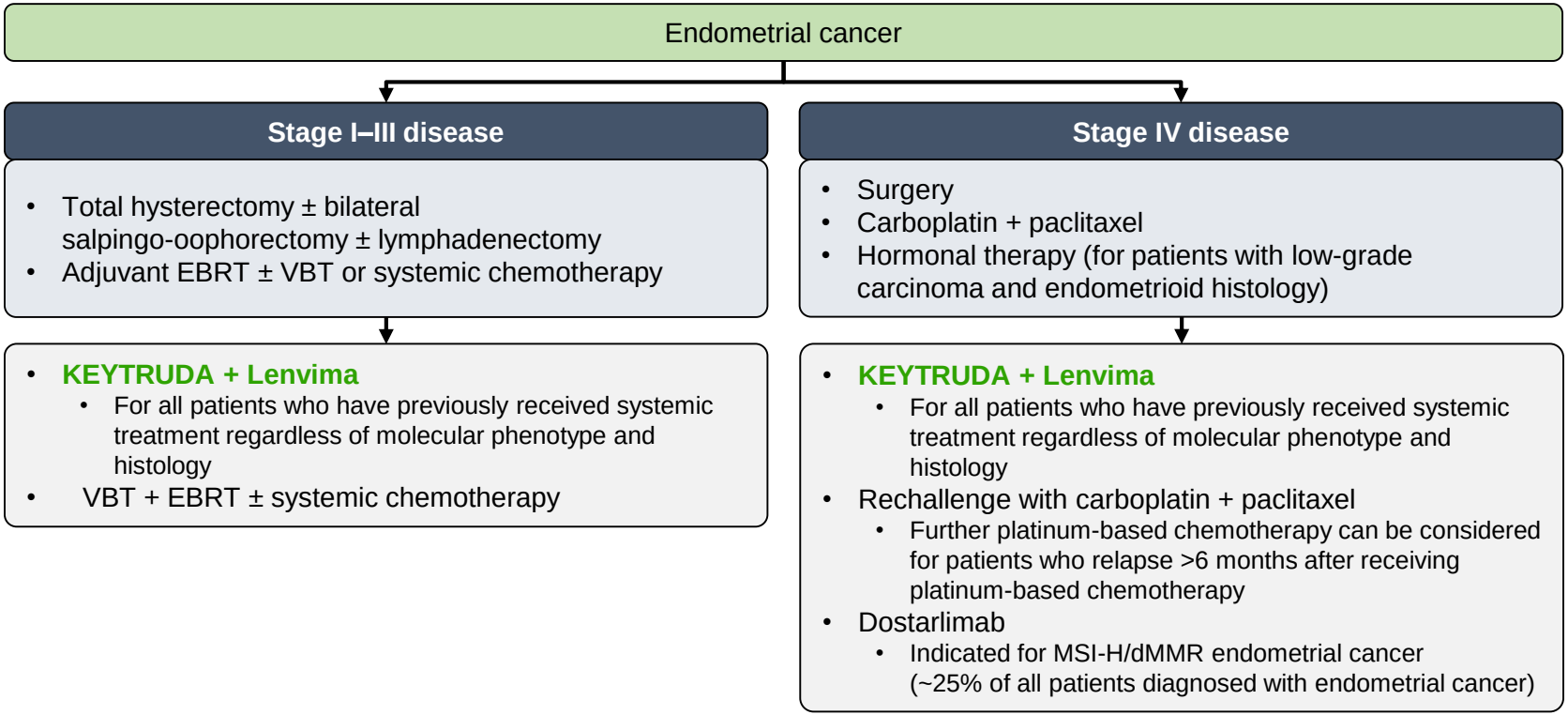
# Overview of KEYTRUDA + Lenvima in advanced/recurrent endometrial cancer

Click the links below to navigate to the section of interest

**The current treatment pathway in endometrial cancer**

# The current treatment pathway in endometrial cancer[1,2]




dMMR, mismatch repair deficient; EBRT, external beam radiotherapy; MSI-H, microsatellite instability-high; VBT, vaginal brachytherapy.

1. Oaknin A et al. *Ann Oncol* 2022;S0923–7534:01207–01208; 2. Ryan N et al. *Genet Med* 2019;21:2167–2180.

**Prescribing Information:** KEYTRUDA GB; KEYTRUDA NI; Lenvima

# KEYNOTE-775: Overview

Click the links below to navigate to the section of interest

**Study design**

**Baseline characteristics in the ITT population**

ITT, intention-to-treat.

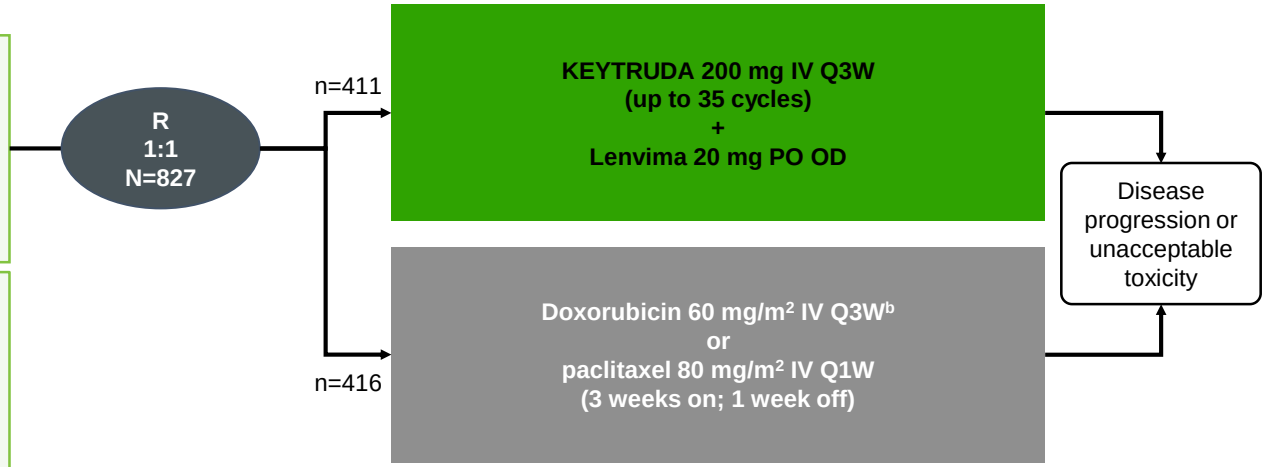
# KEYNOTE-775: Study design

Randomised, open-label, Phase 3 study

**Key eligibility criteria**
- Advanced, metastatic or recurrent endometrial cancer
- One prior platinum-based chemotherapy[a]
- ECOG PS 0–1
- Measurable disease per BICR
- Tissue available for MMR testing

**Stratification factors**
- MMR status (pMMR vs dMMR) and further stratification within pMMR by:
  - Region 1: Europe, USA, Canada, Australia, New Zealand and Israel, Region 2: rest of world
  - ECOG PS (0 vs 1)
  - Prior history of pelvic radiation (yes vs no)

**Endpoints**
- Primary: PFS per BICR, OS
- Secondary: ORR, HRQoL, PK, safety
- Exploratory: DOR




[a]Patients could receive up to two prior platinum-based chemotherapy regimens if one was given in the neoadjuvant or adjuvant setting; [b]Maximum cumulative dose of 500 mg/m².

BICR, blinded independent central review; dMMR, mismatch repair deficient; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQoL, health-related quality of life; IV, intravenous; MMR, mismatch repair; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; pMMR, mismatch repair proficient; PO, orally; Q1W, every week; Q3W, every 3 weeks; OD, once daily; R, randomisation.

Makker V et al. *N Engl J Med* 2022;386:437–448.

# KEYNOTE-775: Baseline characteristics in the ITT population

| Characteristic, n (%)[a] | KEYTRUDA + Lenvima (n=411) | Chemotherapy (n=416) |
|---|---|---|
| Age | | |
| Median (range), years | 64 (30–82) | 65 (35–86) |
| <65 years | 206 (50.1) | 204 (49.0) |
| Race[b] | | |
| White | 261 (63.5) | 246 (59.1) |
| Black | 17 (4.1) | 14 (3.4) |
| Asian | 85 (20.7) | 92 (22.1) |
| Geographic region | | |
| Region 1[c] | 234 (56.9) | 240 (57.7) |
| Region 2[d] | 177 (43.1) | 176 (42.3) |
| MMR status | | |
| pMMR | 346 (84.2) | 351 (84.4) |
| dMMR | 65 (15.8) | 65 (15.6) |

| Characteristic, n (%) | KEYTRUDA + Lenvima (n=411) | Chemotherapy (n=416) |
|---|---|---|
| ECOG PS | | |
| 0 | 246 (59.9) | 241 (57.9) |
| 1 | 164 (39.9) | 175 (42.1) |
| History of pelvic radiation | 174 (42.3) | 186 (44.7) |
| Histological features at initial diagnosis | | |
| Endometrioid carcinoma | 243 (59.1) | 254 (61.1) |
| High grade | 94 (22.9) | 90 (21.6) |
| Low grade | 59 (14.4) | 54 (13.0) |
| Not specified[e] | 90 (21.9) | 110 (26.4) |
| Serous carcinoma | 103 (25.1) | 115 (27.6) |
| Clear cell carcinoma | 30 (7.3) | 17 (4.1) |
| Mixed features | 22 (5.4) | 16 (3.8) |

[a]Unless stated otherwise; [b]Race was reported by the patient. Data on race were missing for 36 patients (8.8%) in the KEYTRUDA + Lenvima group and 44 (10.6%) in the chemotherapy group. Other races or ethnic groups (reported by 12 patients [2.9%] in the KEYTRUDA + Lenvima group and by 20 [4.8%] in the chemotherapy group) included American Indian or Alaska Native, Native Hawaiian or other Pacific Islander and multiple; [c]Europe, USA, Canada, Australia, New Zealand and Israel; [d]Rest of world; [e]Included endometrioid carcinoma (grade not specified) and endometrioid carcinoma with squamous differentiation. Table adapted from Makker V et al. *N Engl J Med* 2022.

dMMR, mismatch repair deficient; ECOG PS, Eastern Cooperative Oncology Group performance status; ITT, intention-to-treat; pMMR, mismatch repair proficient.

Makker V et al. *N Engl J Med* 2022;386:437–448.

# KEYNOTE-775: Results (interim analysis)

Click the links below to navigate to the section of interest

**KEYTRUDA + Lenvima demonstrated superior PFS vs chemotherapy in all patients**

**KEYTRUDA + Lenvima demonstrated superior PFS vs chemotherapy in patients who were pMMR**

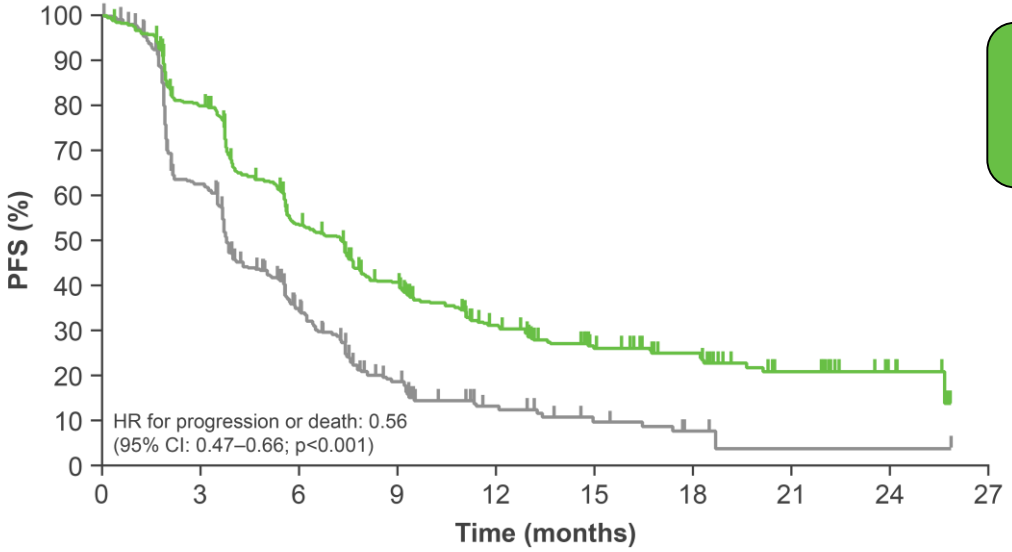
**KEYTRUDA + Lenvima demonstrated superior OS vs chemotherapy in all patients**

**KEYTRUDA + Lenvima demonstrated superior OS vs chemotherapy in patients who were pMMR**

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

# KEYNOTE-775: KEYTRUDA + Lenvima demonstrated superior PFS vs chemotherapy in all patients (interim analysis)[a,1,2]

| Treatment arm | Median (95% CI), months | HR (95% CI) | p value |
|---|---|---|---|
| KEYTRUDA + Lenvima | 7.2 (5.7–7.6) | 0.56 (0.47–0.66) | <0.001 |
| Chemotherapy | 3.8 (3.6–4.2) | – | – |




| No. at risk | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| KEYTRUDA + Lenvima | 411 | 316 | 202 | 144 | 86 | 56 | 43 | 17 | 6 | 0 |
| Chemotherapy | 416 | 214 | 95 | 42 | 18 | 10 | 4 | 1 | 1 | 0 |

A **44% reduction in the risk of progression or death** was observed with KEYTRUDA + Lenvima vs chemotherapy in the ITT population (HR 0.56, 95% CI: 0.47–0.66; p<0.001)

**The forest plot for PFS in patients who were pMMR and in key subgroups is shown in the appendix. Click here to view.**

**Analysis cut-off date: 26 October 2020.**

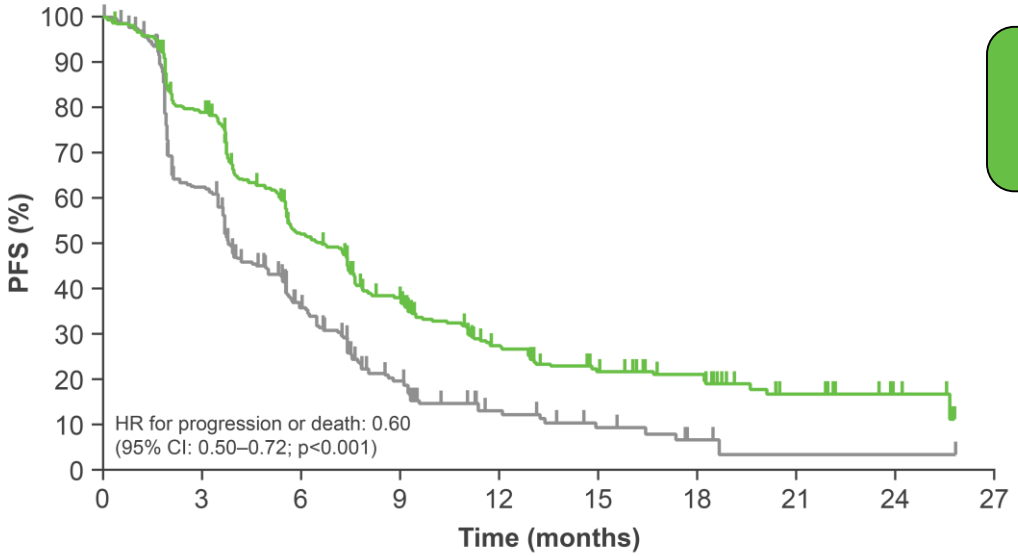
[a]By BICR per RECIST v1.1. Figure adapted from Makker V et al. *N Engl J Med* 2022. Tick marks indicate censored data.

BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; mo, month; PFS, progression-free survival; pMMR, mismatch repair proficient; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1.

1. Makker V et al. *N Engl J Med* 2022;386:437–448; 2. KEYTRUDA (pembrolizumab) SmPC. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed November 2023.

# KEYNOTE-775: KEYTRUDA + Lenvima demonstrated superior PFS vs chemotherapy in patients who were pMMR (interim analysis)[a,1,2]

| Treatment arm | Median (95% CI), months | HR (95% CI) | p value |
|---|---|---|---|
| KEYTRUDA + Lenvima | 6.6 (5.6–7.4) | 0.60 (0.50–0.72) | <0.001 |
| Chemotherapy | 3.8 (3.6–5.0) | – | – |




| No. at risk | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| KEYTRUDA + Lenvima | 346 | 264 | 165 | 112 | 60 | 39 | 30 | 12 | 5 | 0 |
| Chemotherapy | 351 | 177 | 83 | 37 | 15 | 8 | 3 | 1 | 1 | 0 |

A **40% reduction in the risk of progression or death** was observed with KEYTRUDA + Lenvima vs chemotherapy in the pMMR population (HR 0.60, 95% CI: 0.50–0.72; p<0.001)

**Analysis cut-off date: 26 October 2020.**

[a]By BICR per RECIST v1.1. Figure adapted from Makker V et al. *N Engl J Med* 2022. Tick marks indicate censored data.

BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; mo, month; PFS, progression-free survival; pMMR, mismatch repair proficient; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1.

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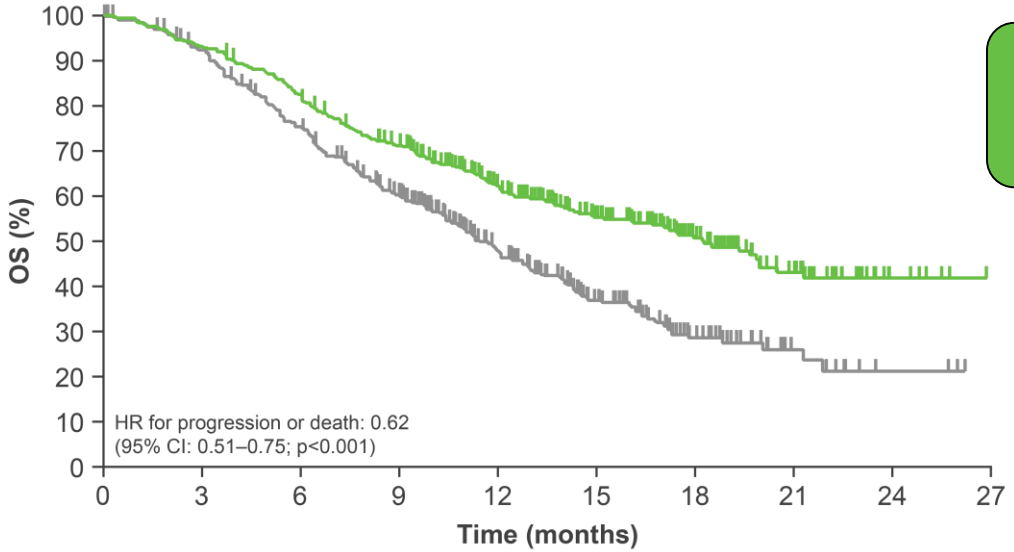
# KEYNOTE-775: KEYTRUDA + Lenvima demonstrated superior OS vs chemotherapy in all patients (interim analysis)[1,2]

| Treatment arm | Median (95% CI), months | HR (95% CI) | p value |
|---|---|---|---|
| KEYTRUDA + Lenvima | 18.3 (15.2–20.5) | 0.62 (0.51–0.75) | <0.001 |
| Chemotherapy | 11.4 (10.5–12.9) | – | – |




| No. at risk | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| KEYTRUDA + Lenvima | 411 | 383 | 337 | 282 | 198 | 136 | 81 | 40 | 7 | 0 |
| Chemotherapy | 416 | 373 | 300 | 228 | 138 | 80 | 40 | 11 | 3 | 0 |

A **38% reduction in the risk of death** was observed with KEYTRUDA + Lenvima vs chemotherapy in the ITT population (HR 0.62, 95% CI: 0.51–0.75; p<0.001)

**The forest plot for OS in patients who were pMMR and in key subgroups is shown in the appendix. Click here to view.**

**Analysis cut-off date: 26 October 2020.**

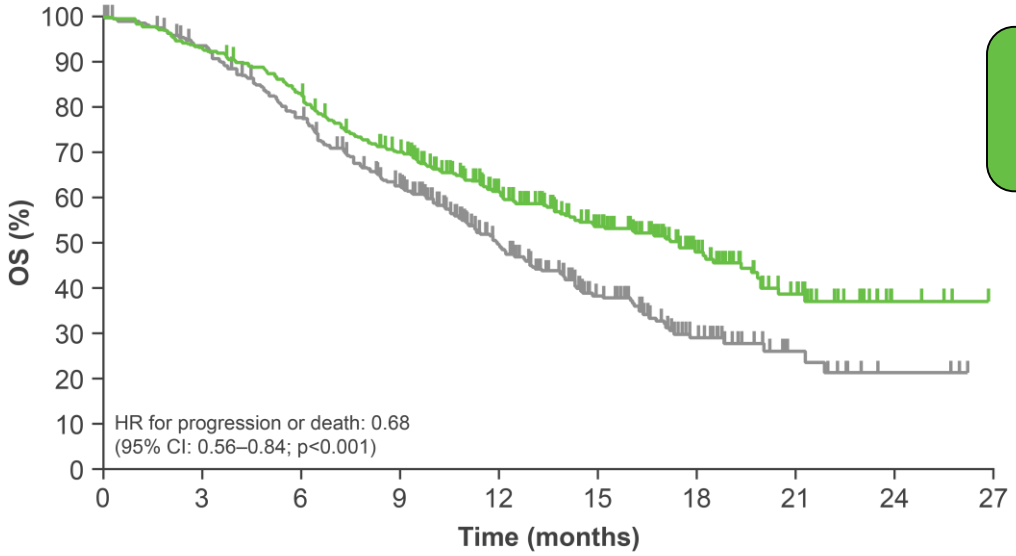
Figure adapted from Makker V et al. *N Engl J Med* 2022. Tick marks indicate censored data.

CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; mo, month; OS, overall survival; pMMR, mismatch repair proficient.

1. Makker V et al. *N Engl J Med* 2022;386:437–448; 2. KEYTRUDA (pembrolizumab) SmPC. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed November 2023.

# KEYNOTE-775: KEYTRUDA + Lenvima demonstrated superior OS vs chemotherapy in patients who were pMMR (interim analysis)[1,2]

| Treatment arm | Median (95% CI), months | HR (95% CI) | p value |
|---|---|---|---|
| KEYTRUDA + Lenvima | 17.4 (14.2–19.9) | 0.68 (0.56–0.84) | <0.001 |
| Chemotherapy | 12.0 (10.8–13.3) | – | – |




| No. at risk | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| KEYTRUDA + Lenvima | 346 | 322 | 285 | 232 | 160 | 109 | 62 | 28 | 5 | 0 |
| Chemotherapy | 351 | 319 | 262 | 201 | 120 | 70 | 33 | 11 | 3 | 0 |

A **32% reduction in the risk of death** was observed with KEYTRUDA + Lenvima vs chemotherapy in the pMMR population (HR 0.68, 95% CI: 0.56–0.84; p<0.001)

**Analysis cut-off date: 26 October 2020.**

Figure adapted from Makker V et al. *N Engl J Med* 2022. Tick marks indicate censored data.

CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; mo, month; OS, overall survival; pMMR, mismatch repair proficient..

1. Makker V et al. *N Engl J Med* 2022;386:437–448; 2. KEYTRUDA (pembrolizumab) SmPC. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed November 2023.

# KEYNOTE-775: Results (final analysis)

Click the links below to navigate to the section of interest


KEYTRUDA + Lenvima presented superior PFS vs chemotherapy in all patients

KEYTRUDA + Lenvima presented superior PFS vs chemotherapy in patients who were pMMR

KEYTRUDA + Lenvima presented superior OS vs chemotherapy in all patients

KEYTRUDA + Lenvima presented superior OS vs chemotherapy in patients who were pMMR

KEYTRUDA + Lenvima presented superior ORR and DOR vs chemotherapy in all patients

KEYTRUDA + Lenvima presented superior ORR and DOR vs chemotherapy in patients who were pMMR

Summary of AEs in all treated patients

AEs with ≥25% incidence in either arm

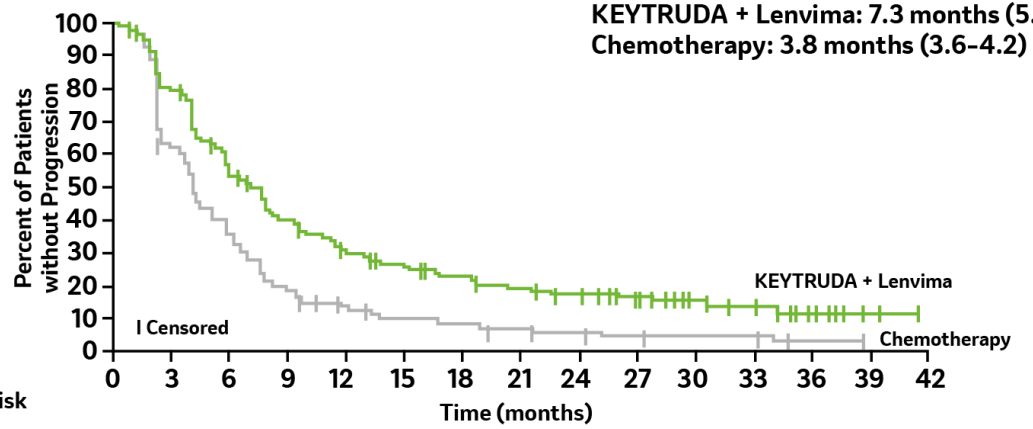
TEAEs with ≥10% incidence in either arm


AE, adverse event; DOR, duration of response; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; pMMR, mismatch repair proficient; TEAE, treatment-emergent adverse event.

# KEYNOTE-775: KEYTRUDA + Lenvima presented superior PFS vs chemotherapy in all patients at the final analysis (nominal p-value)[a,1,2]

## All-Comer Population

**Median Progression-free Survival (95% CI)**
**KEYTRUDA + Lenvima: 7.3 months (5.7–7.6)**
**Chemotherapy: 3.8 months (3.6–4.2)**




| No. at risk | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| KEYTRUDA + Lenvima | 411 | 317 | 203 | 148 | 109 | 87 | 79 | 65 | 57 | 45 | 35 | 23 | 10 | 4 | 0 |
| Chemotherapy | 416 | 214 | 95 | 43 | 27 | 19 | 15 | 11 | 8 | 6 | 5 | 5 | 1 | 0 | 0 |

A **44% reduction in the risk of progression or death** was presented with KEYTRUDA + Lenvima vs chemotherapy in the ITT population (HR 0.56, 95% CI: 0.48–0.66; **nomina**l p-value<0.0001)

**Analysis cut-off date: 1 March 2022.**

[a]By BICR per RECIST v1.1. Figure adapted from Makker V et al. *Presented at ESMO* 2022. Tick marks indicate censored data.

BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; mo, month; PFS, progression-free survival; pMMR, mismatch repair proficient; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1.

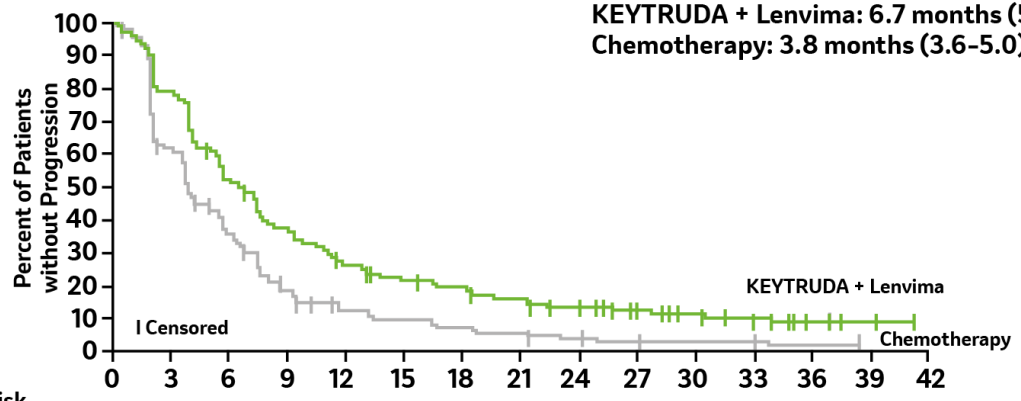
1. Makker V et al. Slide deck presented at: European Society for Medical Oncologists (ESMO) Virtual Annual Meeting; September 9-13, 2022; 2. MSD data on file.

**Prescribing Information:** KEYTRUDA GB; KEYTRUDA NI; Lenvima

# KEYNOTE-775: KEYTRUDA + Lenvima presented superior PFS vs chemotherapy in patients who were pMMR at the final analysis (nominal p-value)[a,1,2]

## pMMR Population

**Median Progression-free Survival (95% CI)**
**KEYTRUDA + Lenvima: 6.7 months (5.6–7.4)**
**Chemotherapy: 3.8 months (3.6–5.0)**




| No. at risk | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| KEYTRUDA + Lenvima | 346 | 265 | 166 | 116 | 80 | 61 | 55 | 43 | 36 | 24 | 18 | 14 | 6 | 4 | 0 |
| Chemotherapy | 351 | 177 | 83 | 38 | 23 | 16 | 12 | 9 | 6 | 4 | 3 | 3 | 1 | 0 | 0 |

A **40% reduction in the risk of progression or death** was presented with KEYTRUDA + Lenvima vs chemotherapy in the pMMR population (HR 0.60, 95% CI: 0.50–0.72; **nomina**l p-value<0.0001)

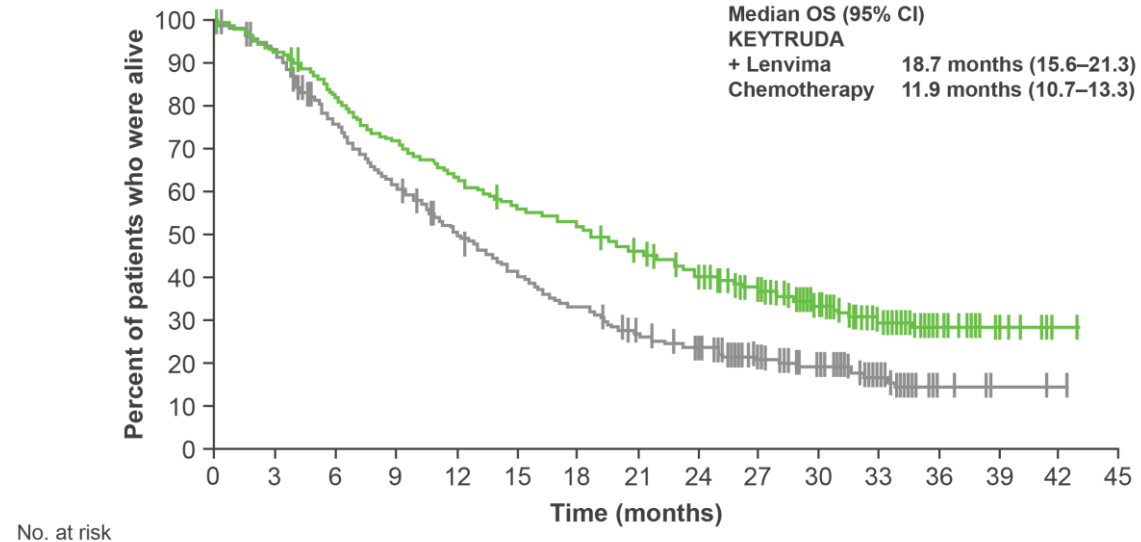
**Analysis cut-off date: 1 March 2022.**

[a]By BICR per RECIST v1.1. Figure adapted from Makker V et al. *Presented at ESMO* 2022. Tick marks indicate censored data.

BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; mo, month; PFS, progression-free survival; pMMR, mismatch repair proficient; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1.

1. Makker V et al. Slide deck presented at: European Society for Medical Oncologists (ESMO) Virtual Annual Meeting; September 9-13, 2022; 2. MSD data on file.

# KEYNOTE-775: KEYTRUDA + Lenvima presented superior OS vs chemotherapy in all patients at the final analysis (nominal p-value)[1–3]




A **35% reduction in the risk of death** was presented with KEYTRUDA + Lenvima vs chemotherapy in the ITT population (HR 0.65, 95% CI: 0.55–0.77; **nominal** p-value<0.0001)

**Analysis cut-off date: 1 March 2022.**

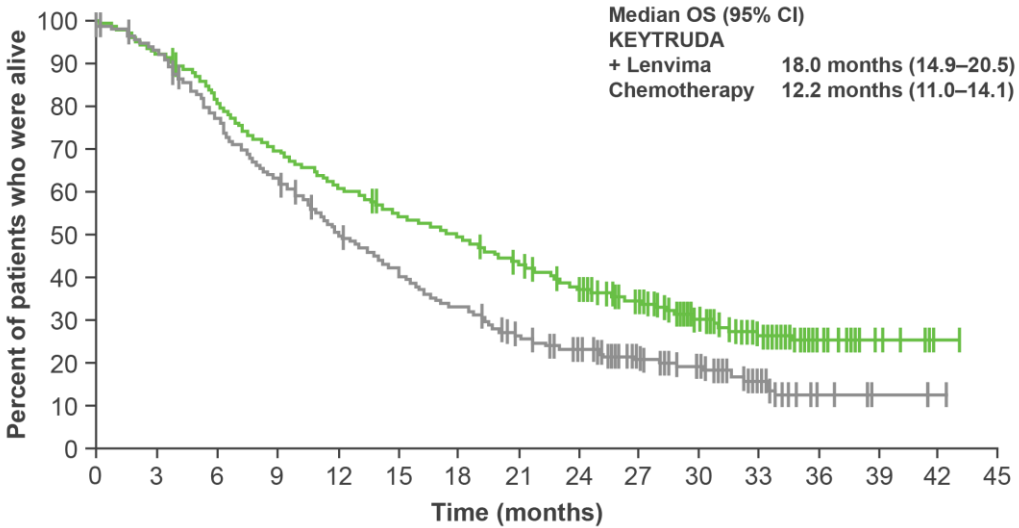
Figure adapted from Makker V et al. *Presented at ESMO* 2022. Tick marks indicate censored data.

CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; mo, month; OS, overall survival; pMMR, mismatch repair proficient.

1. Makker V et al. *N Engl J Med* 2022;386:437–448; 2. KEYTRUDA (pembrolizumab) SmPC. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed November 2023; 3. MSD data on file.

**Prescribing Information:** KEYTRUDA GB; KEYTRUDA NI; Lenvima

# KEYNOTE-775: KEYTRUDA + Lenvima presented superior OS vs chemotherapy in patients who were pMMR at the final analysis (nominal p-value)[1–3]




A **30% reduction in the risk of death** was presented with KEYTRUDA + Lenvima vs chemotherapy in the pMMR population (HR 0.70, 95% CI: 0.58–0.83; **nominal** p-value<0.0001)

**Analysis cut-off date: 1 March 2022.**

Figure adapted from Makker V et al. *Presented at ESMO* 2022. Tick marks indicate censored data.

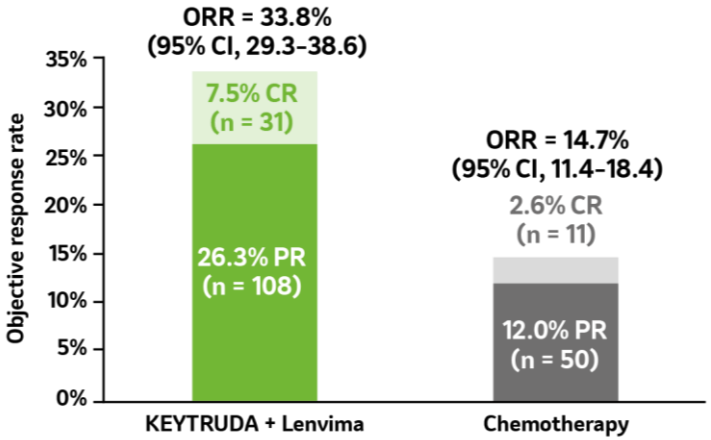
CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; mo, month; OS, overall survival; pMMR, mismatch repair proficient..

1. Makker V et al. *N Engl J Med* 2022;386:437–448; 2. KEYTRUDA (pembrolizumab) SmPC. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed November 2023; 3. MSD data on file.

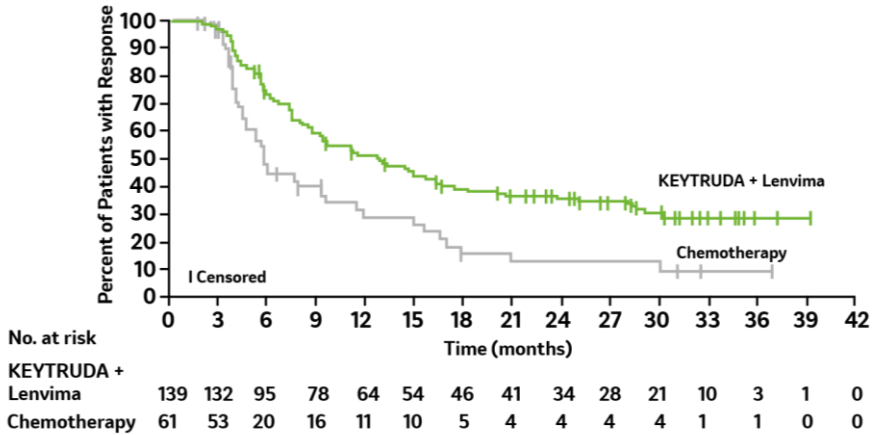
**Prescribing Information:** KEYTRUDA GB; KEYTRUDA NI; Lenvima

# KEYNOTE-775: KEYTRUDA + Lenvima presented superior ORR and DOR vs chemotherapy in all patients (final analysis)

## All-comer ORR[a]




## All-comer DOR[b]




**33.8% of patients achieved an objective response with KEYTRUDA + Lenvima vs 14.7% of patients receiving chemotherapy**

**Median DOR was 12.9 months (95% CI: 1.6–39.5) with KEYTRUDA + Lenvima vs 5.7 months (95% CI: 0.0–37.1) with chemotherapy**

**A tabular view of objective responses and duration of response is shown in the appendix. Click here to view.**

**Analysis cut-off date: 1 March 2022.**

Figures adapted from Makker V et al. *Presented at ESMO* 2022. Tick marks indicate censored data.

[a]95% CI based on binomial exact CI method. Only confirmed CRs and PRs are included in ORR.. DCR: KEYTRUDA + Lenvima 72.3 (67.7–76.5), chemotherapy 46.6 (41.8–51.6). At the interim analysis, 18 (KEYTRUDA + Lenvima) and 9 (chemotherapy) patients with pMMR tumours had a CR of 27 (KEYTRUDA + Lenvima) and 11 (chemotherapy) patients in the all-comer population had a CR; [b]Median DOR is derived from product-limit KM method for censored data and includes patients with CR or PR. Median TTR (for patients with CR or PR): KEYTRUDA + Lenvima 2.1 (1.5–23.3), chemotherapy 2.1 (1.0–7.4).

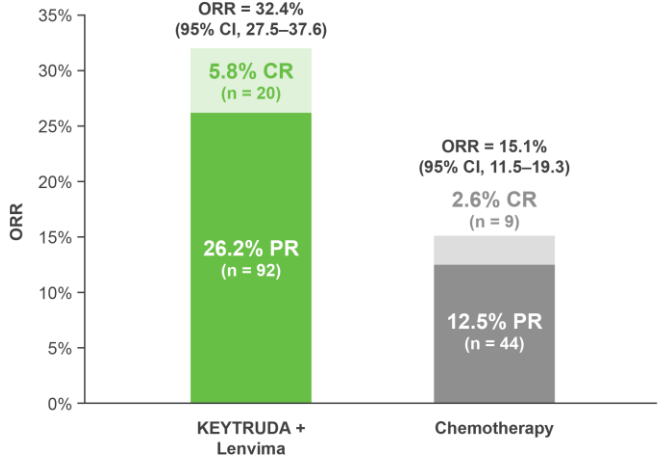
BOR, best objective response; CI, confidence interval; CR, complete response; DCR, sum of the complete, partial and stable disease rates; DOR, duration of response; ORR, objective response rate; PR, partial response; SD, stable disease; TTR, time to response.

Makker V et al. Slide deck presented at: European Society for Medical Oncologists (ESMO) Virtual Annual Meeting; September 9-13, 2022.

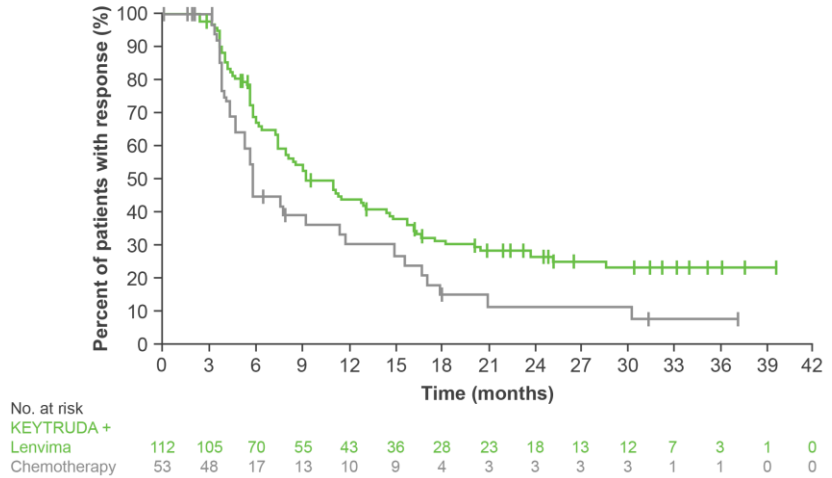
**Prescribing Information: KEYTRUDA GB; KEYTRUDA NI; Lenvima**

# KEYNOTE-775: KEYTRUDA + Lenvima presented superior ORR and DOR vs chemotherapy in patients who were pMMR (final analysis)

## pMMR ORR[a]




## pMMR DOR[b]




**32.4% of patients achieved an objective response with KEYTRUDA + Lenvima vs 15.1% of patients receiving chemotherapy**

**Median DOR was 9.3 months (95% CI: 1.6–39.5) with KEYTRUDA + Lenvima vs 5.7 months (95% CI: 0.0–37.1) with chemotherapy**

**A tabular view of objective responses and duration of response is shown in the appendix. Click here to view.**

**Analysis cut-off date: 1 March 2022.**

Figures adapted from Makker V et al. *Presented at ESMO* 2022. Tick marks indicate censored data.

[a]95% CI based on binomial exact CI method. Only confirmed CRs and PRs are included in ORR. DCR (BOR of CR, PR or SD at 7 weeks or more after randomisation): KEYTRUDA + Lenvima ,72.0 (66.9–76.6), chemotherapy 46.4 (41.1–51.8). DCR: KEYTRUDA + Lenvima 72.3 (67.7–76.5), chemotherapy 46.6 (41.8–51.6) At the interim analysis, 18 (KEYTRUDA + Lenvima) and 9 (chemotherapy) patients with pMMR tumours had a CR of 27 (KEYTRUDA + Lenvima) and 11 (chemotherapy) patients in the all-comer population had a CR; [b]Median DOR is derived from product-limit KM method for censored data and includes patients with CR or PR. Median TTR (for patients with CR or PR): KEYTRUDA + Lenvima 2.1 (1.5–23.0), chemotherapy 3.5 (1.0–7.4).

CI, confidence interval; CR, complete response; DOR, duration of response; ORR, objective response rate; PR, partial response; SD, stable disease; TTR, time to response.

Makker V et al. Slide deck presented at: European Society for Medical Oncologists (ESMO) Virtual Annual Meeting; September 9-13, 2022.

**Prescribing Information: KEYTRUDA GB; KEYTRUDA NI; Lenvima**

# KEYNOTE-775: Summary of AEs in all treated patients

| AE, n (%) | KEYTRUDA + Lenvima (n=406) | Chemotherapy (n=388) |
|---|---|---|
| Any AE | 405 (99.8) | 386 (99.5) |
| Grade ≥3 | 361 (88.9) | 282 (72.7) |
| Serious AEs | 214 (52.7) | 118 (30.4) |
| AE leading to dose reductions[a] | 270 (66.5) | 50 (12.9) |
| AE leading to treatment interruption[b] | 281 (69.2) | 105 (27.1) |
| KEYTRUDA[c] | 203 (50.0) | – |
| Lenvima[c] | 238 (58.6) | – |
| KEYTRUDA + Lenvima | 125 (30.8) | – |
| AE leading to discontinuation | 134 (33.0) | 31 (8.0) |
| KEYTRUDA[c] | 76 (18.7) | – |
| Lenvima[c] | 125 (30.8) | – |
| KEYTRUDA + Lenvima | 57 (14.0) | – |
| AE leading to death | 23 (5.7) | 19 (4.9) |

For further information on the safety of KEYTRUDA + Lenvima, please refer to the SmPC: Great Britain, Northern Ireland.

**Analysis cut-off date: 26 October 2020.**

[a]Includes Lenvima only or chemotherapy; [b]Includes KEYTRUDA or Lenvima; [c]Regardless of the action taken with the other drug in the combination arm. Table adapted from Makker V et al. *N Engl J Med* 2022 (and supplementary appendix).

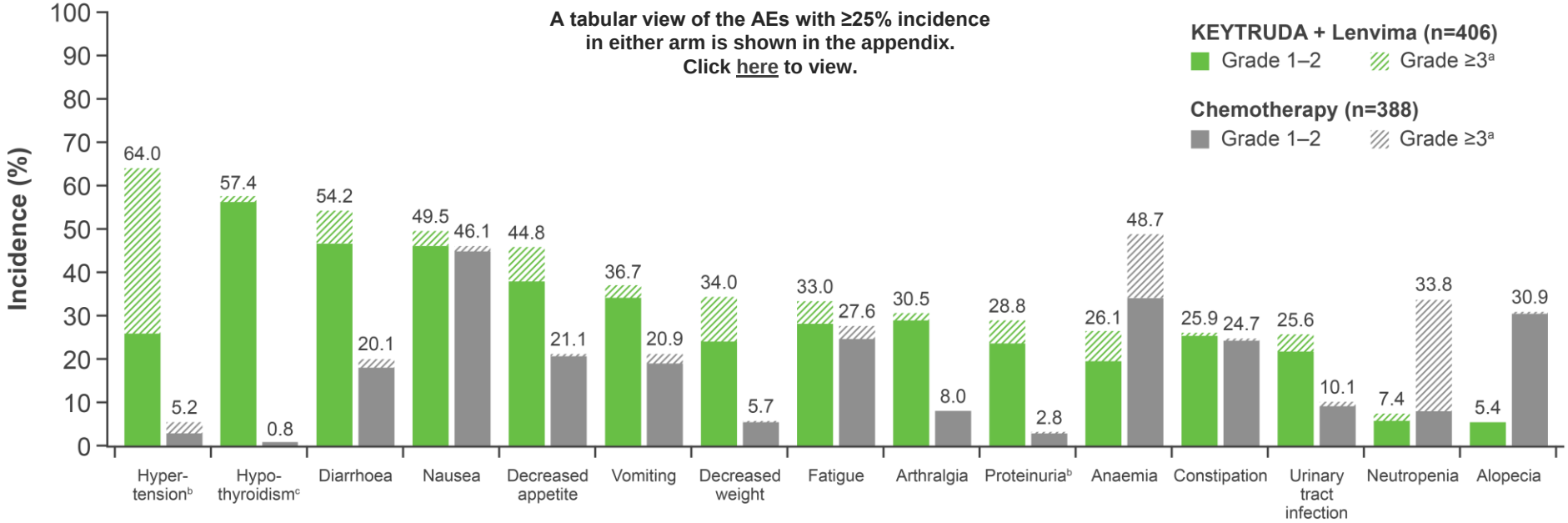
AE, adverse event; SmPC, Summary of Product Characteristics.

Makker V et al. *N Engl J Med* 2022;386:437–448 (and supplementary appendix).

**Prescribing Information:** KEYTRUDA GB; KEYTRUDA NI; Lenvima

# KEYNOTE-775: AEs with ≥25% incidence in either arm

**A tabular view of the AEs with ≥25% incidence in either arm is shown in the appendix. Click here to view.**

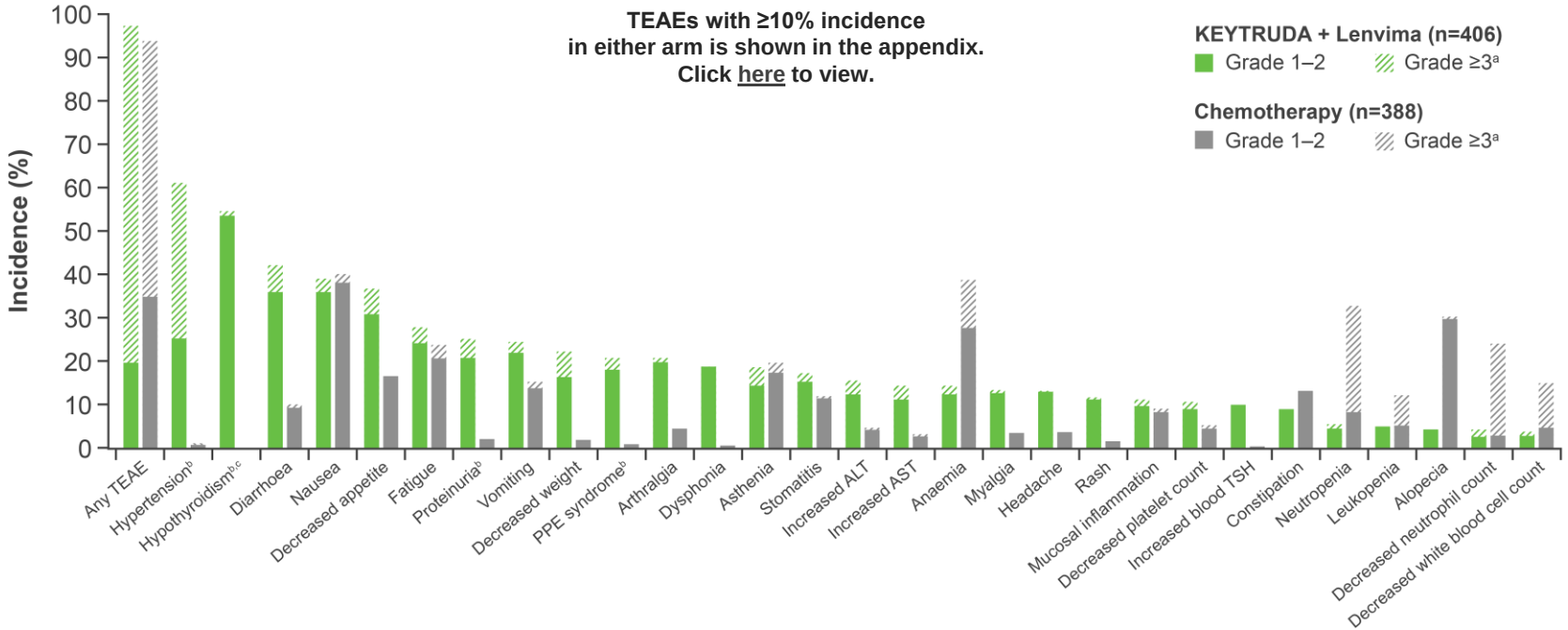



For further information on the safety of KEYTRUDA + Lenvima, please refer to the SmPC: Great Britain, Northern Ireland.

**Analysis cut-off date: 26 October 2020.** [a]Among patients who received KEYTRUDA + Lenvima, 5.7% died due to Grade 5 AEs (GI disorder in 1.2% of patients, cardiac disorder in 0.5%, general disorder in 1.5%, infection in 0.7%, decreased appetite in 0.2%, and neoplasms, nervous system disorder, psychiatric disorder, renal disorder, reproductive disorder or respiratory disorder in 0.2% each). Among patients who received chemotherapy, 4.9% died due to Grade 5 AEs (cardiac disorder in 1.0%, general disorder in 1.3%, infection in 1.5%, subdural haematoma in 0.3% and respiratory disorder in 0.8%); [b]Clinically significant AE with Lenvima; [c]AE of interest with KEYTRUDA.
Figure adapted from Makker V et al. *N Engl J Med* 2022.
AE, adverse event; GI, gastrointestinal; SmPC, Summary of Product Characteristics.
Makker V et al. *N Engl J Med* 2022;386:437–448.

**Prescribing Information: KEYTRUDA GB; KEYTRUDA NI; Lenvima**

# KEYNOTE-775: Treatment-emergent adverse events with ≥10% incidence in either arm




For further information on the safety of KEYTRUDA + Lenvima, please refer to the SmPC: Great Britain, Northern Ireland.

**Analysis cut-off date: 26 October 2020.**

[a]TEAEs led to death in 1.5% of patients in the KEYTRUDA + Lenvima group (cardiac disorder [n=1]; gastrointestinal disorder [n=1]; general disorders and administration site conditions [n=2]; benign, malignant and unspecified neoplasms [n=1]; nervous system disorders [n=1]), and 2.1% of patients in the chemotherapy group (cardiac disorders [n=3]; infections and infestations [n=3]; respiratory, thoracic, mediastinal disorders [n=2]); [b]Clinically significant AEs for Lenvima in all patients; [c]AE of interest for KEYTRUDA in all patients. Figure adapted from Makker V et al. *N Engl J Med* 2022 (supplementary appendix).

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; PPE, palmar–plantar erythrodysesthesia; SmPC, Summary of Product Characteristics; TEAE, treatment-emergent adverse event; TSH, thyroid-stimulating hormone

Makker V et al. *N Engl J Med* 2022;386:437–448.

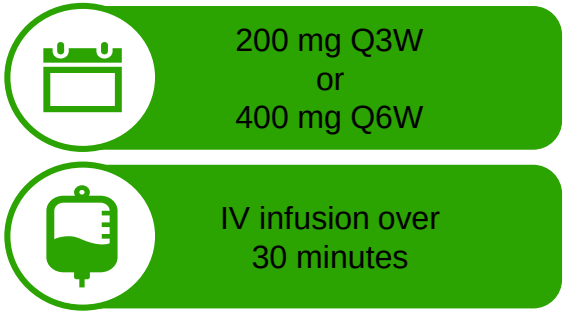
**Prescribing Information: KEYTRUDA GB; KEYTRUDA NI; Lenvima**

# Implementing KEYTRUDA + Lenvima for the treatment of adults with advanced/recurrent endometrial cancer

**Prescribing Information:** KEYTRUDA GB; KEYTRUDA NI; Lenvima

# KEYTRUDA + Lenvima dosing

**KEYTRUDA[1]**




- Continue treatment with KEYTRUDA until disease progression or unacceptable toxicity occurs
- No dose reductions of KEYTRUDA are recommended. KEYTRUDA should be withheld or discontinued to manage AEs as described in the SmPC
- Immune-related AEs, including severe and fatal cases, have occurred in patients receiving KEYTRUDA
  - Please refer to the SmPC for further information on KEYTRUDA dosing: Great Britain, Northern Ireland

**Lenvima[2]**


- Continue treatment with Lenvima for as long as there is clinical benefit or until unacceptable toxicity occurs
- For AEs thought to be related to Lenvima, upon resolution/improvement of an AE to Grade 0–1 or baseline, treatment should be resumed at a reduced dose of Lenvima
  - Please refer to the SmPC for further information on Lenvima dosing: Great Britain; Northern Ireland

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

1. KEYTRUDA (pembrolizumab) SmPC. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed November 2023;
2. LENVIMA (lenvatinib) SmPC. Available at: https://www.medicines.org.uk/emc/product/6840/smpc. Accessed November 2023.

**Prescribing Information: KEYTRUDA GB; KEYTRUDA NI; Lenvima**

# KEYNOTE-775: Summary

# KEYNOTE-775: Summary of efficacy and safety in the ITT population

**KEYTRUDA + Lenvima showed statistically significant (interim analysis), clinically meaningful improvements in PFS and OS vs chemotherapy in all patients with advanced, metastatic or recurrent endometrial cancer**

**KEYTRUDA + Lenvima presented a higher PFS vs chemotherapy (final analysis)**

- Median (95% CI) PFS: 7.3 (5.7–7.6) months with KEYTRUDA + Lenvima vs 3.8 (3.6–4.2) months with chemotherapy (HR 0.56, 95% CI: 0.48–0.66; nominal p-value<0.0001)

**KEYTRUDA + Lenvima presented a higher OS vs chemotherapy (final analysis)**

- Median (95% CI) OS: 18.7 (15.6–21.3) months with KEYTRUDA + Lenvima vs 11.9 (10.7–13.3) months with chemotherapy (HR 0.65, 95% CI: 0.55–0.77; nominal p-value<0.0001)

**Safety data were generally consistent with the known AE profiles of each agent (final analysis)**

- Grade ≥3 AEs occurred in 88.9% of patients in the KEYTRUDA + Lenvima arm and 72.7% of patients in the chemotherapy arm
- Of those treated, patients in the KEYTRUDA + Lenvima arm had a higher proportion of discontinuations of any trial agent (33.0%) compared with patients in the chemotherapy arm (8.0%)
    - The main reason for discontinuation in both treatment arms was disease progression

AE, adverse event; CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; OS, overall survival; PFS, progression-free survival.

Makker V et al. *N Engl J Med* 2022;386:437–448.

**Prescribing Information:** KEYTRUDA GB; KEYTRUDA NI; Lenvima

# KEYNOTE-775: Appendix

Click the links below to navigate to the section of interest

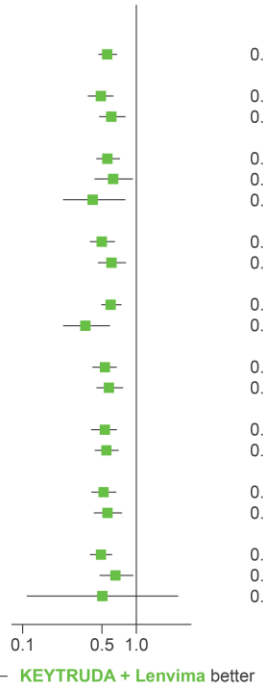

- PFS in key subgroups (ITT population)
- PFS in key subgroups (pMMR population)
- OS in key subgroups (ITT population)
- OS in key subgroups (pMMR population)
- Objective responses in the ITT and pMRR populations
- Objective responses in the dMMR population
- AEs with ≥25% incidence in either arm
- TEAEs with ≥10% incidence in either arm (1)
- TEAEs with ≥10% incidence in either arm (2)
- QoL


AE, adverse event; dMMR, mismatch repair deficient; ITT, intention-to-treat; OS, overall survival; PFS, progression-free survival; pMMR, mismatch repair proficient; QoL, quality of life.

# KEYNOTE-775: PFS in key subgroups (ITT population)

**No formal statistical analysis was performed for the subgroup analyses and no clinical conclusions can be drawn**

| Subgroup | KEYTRUDA + Lenvima<br>No. of events/N | Chemotherapy<br>No. of events/N | HR (95% CI) |
|---|---|---|---|
| **Overall** | 281/411 | 286/416 | 0.56 (0.47–0.66) |
| **Age, yr** | | | |
| <65 | 138/206 | 146/204 | 0.49 (0.38–0.62) |
| ≥65 | 143/205 | 140/212 | 0.61 (0.48–0.78) |
| **Race** | | | |
| White | 177/261 | 163/246 | 0.56 (0.45–0.70) |
| Asian | 59/85 | 62/92 | 0.63 (0.44–0.91) |
| Other | 20/29 | 28/34 | 0.42 (0.23–0.78) |
| **Region** | | | |
| Region 1[a] | 160/234 | 169/240 | 0.50 (0.40–0.63) |
| Region 2[b] | 121/177 | 117/176 | 0.61 (0.47–0.79) |
| **MMR status** | | | |
| pMMR | 247/346 | 238/351 | 0.60 (0.50–0.72) |
| dMMR | 34/65 | 48/65 | 0.36 (0.23–0.57) |
| **ECOG PS** | | | |
| 0 | 166/246 | 162/241 | 0.53 (0.42–0.66) |
| 1 | 115/164 | 124/175 | 0.58 (0.45–0.75) |
| **Prior history of pelvic radiation** | | | |
| Yes | 114/174 | 123/186 | 0.53 (0.41–0.69) |
| No | 167/237 | 163/230 | 0.55 (0.44–0.68) |
| **Histology** | | | |
| Endometrioid | 150/243 | 173/254 | 0.52 (0.41–0.65) |
| Non-endometrioid | 131/168 | 113/162 | 0.56 (0.43–0.73) |
| **Prior lines of therapy** | | | |
| 1 | 207/297 | 203/277 | 0.49 (0.40–0.60) |
| 2 | 71/103 | 79/126 | 0.66 (0.48–0.92) |
| ≥3 | 3/11 | 4/13 | 0.51 (0.11–2.30) |




**Analysis cut-off date: 26 October 2020.**

[a]Europe, USA, Canada, Australia, New Zealand and Israel; [b]Rest of world. Figures adapted from Makker V et al. *N Engl J Med* 2022.

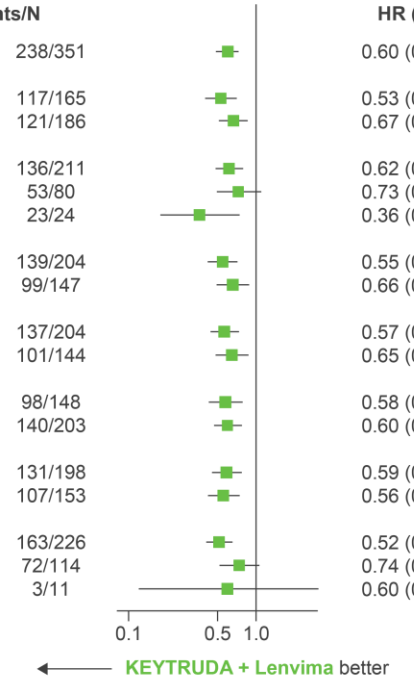
CI, confidence interval; dMMR, mismatch repair deficient; ECOG PS, Eastern Cooperative Oncology Group performance status; ITT, intention-to-treat; PFS, progression-free survival; MMR, mismatch repair; pMMR, mismatch repair proficient.

Makker V et al. *N Engl J Med* 2022;386:437–448 (supplementary appendix).

# KEYNOTE-775: PFS in key subgroups (pMMR population)

**No formal statistical analysis was performed for the subgroup analyses and no clinical conclusions can be drawn**

| Subgroup | KEYTRUDA + Lenvima No. of events/N | Chemotherapy No. of events/N | HR (95% CI) |
|---|---|---|---|
| **Overall** | 247/346 | 238/351 | 0.60 (0.50–0.72) |
| **Age, yr** | | | |
| <65 | 118/171 | 117/165 | 0.53 (0.41–0.69) |
| ≥65 | 129/175 | 121/186 | 0.67 (0.52–0.86) |
| **Race** | | | |
| White | 154/220 | 136/211 | 0.62 (0.49–0.78) |
| Asian | 55/74 | 53/80 | 0.73 (0.50–1.08) |
| Other | 16/23 | 23/24 | 0.36 (0.18–0.73) |
| **Region** | | | |
| Region 1[a] | 144/202 | 139/204 | 0.55 (0.43–0.70) |
| Region 2[b] | 103/144 | 99/147 | 0.66 (0.50–0.87) |
| **ECOG PS** | | | |
| 0 | 149/212 | 137/204 | 0.57 (0.45–0.72) |
| 1 | 98/133 | 101/144 | 0.65 (0.49–0.86) |
| **Prior history of pelvic radiation** | | | |
| Yes | 97/142 | 98/148 | 0.58 (0.43–0.77) |
| No | 150/204 | 140/203 | 0.60 (0.48–0.76) |
| **Histology** | | | |
| Endometrioid | 122/188 | 131/198 | 0.59 (0.46–0.76) |
| Non-endometrioid | 125/158 | 107/153 | 0.56 (0.43–0.73) |
| **Prior lines of therapy** | | | |
| 1 | 177/244 | 163/226 | 0.52 (0.42–0.65) |
| 2 | 67/92 | 72/114 | 0.74 (0.53–1.04) |
| ≥3 | 3/10 | 3/11 | 0.60 (0.12–3.07) |




**Analysis cut-off date: 26 October 2020.**

[a]Europe, USA, Canada, Australia, New Zealand and Israel; [b]Rest of world. Figures adapted from Makker V et al. *N Engl J Med* 2022.

CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; PFS, progression-free survival; pMMR, mismatch repair proficient.

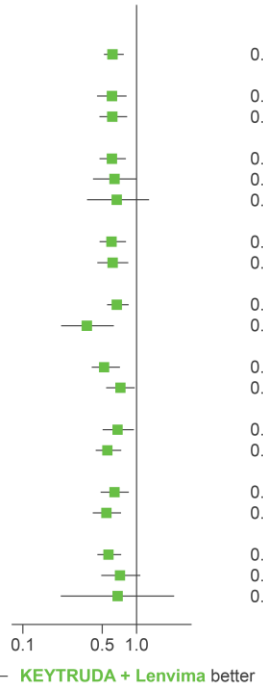
Makker V et al. *N Engl J Med* 2022;386:437–448 (supplementary appendix).

**Prescribing Information: KEYTRUDA GB; KEYTRUDA NI; Lenvima**

# KEYNOTE-775: OS in key subgroups (ITT population)

**No formal statistical analysis was performed for the subgroup analyses and no clinical conclusions can be drawn**

| Subgroup | KEYTRUDA + Lenvima No. of events/N | Chemotherapy No. of events/N | HR (95% CI) |
|---|---|---|---|
| **Overall** | 188/411 | 245/416 | 0.62 (0.51–0.75) |
| **Age, yr** | | | |
| <65 | 89/206 | 116/204 | 0.61 (0.46–0.80) |
| ≥65 | 99/205 | 129/212 | 0.62 (0.48–0.81) |
| **Race** | | | |
| White | 117/261 | 141/246 | 0.61 (0.48–0.79) |
| Asian | 36/85 | 51/92 | 0.65 (0.42–0.99) |
| Other | 19/29 | 25/34 | 0.68 (0.37–1.26) |
| **Region** | | | |
| Region 1[a] | 110/234 | 145/240 | 0.61 (0.48–0.79) |
| Region 2[b] | 78/177 | 100/176 | 0.62 (0.46–0.84) |
| **MMR status** | | | |
| pMMR | 165/346 | 203/351 | 0.68 (0.56–0.84) |
| dMMR | 23/65 | 42/65 | 0.37 (0.22–0.62) |
| **ECOG PS** | | | |
| 0 | 91/246 | 131/241 | 0.53 (0.41–0.70) |
| 1 | 96/164 | 114/175 | 0.73 (0.55–0.95) |
| **Prior history of pelvic radiation** | | | |
| Yes | 77/174 | 99186 | 0.69 (0.51–0.93) |
| No | 111/237 | 146/230 | 0.56 (0.44–0.72) |
| **Histology** | | | |
| Endometrioid | 95/243 | 127/254 | 0.65 (0.49–0.84) |
| Non-endometrioid | 93/168 | 118/162 | 0.55 (0.42–0.72) |
| **Prior lines of therapy** | | | |
| 1 | 136/297 | 172/277 | 0.57 (0.46–0.72) |
| 2 | 47/103 | 65/126 | 0.72 (0.50–1.06) |
| ≥3 | 5/11 | 8/13 | 0.69 (0.22–2.10) |




**Analysis cut-off date: 26 October 2020.**

[a]Europe, USA, Canada, Australia, New Zealand and Israel. [b]Rest of world. Figures adapted from Makker V et al. *N Engl J Med* 2022.

CI, confidence interval; dMMR, mismatch repair deficient; ECOG PS, Eastern Cooperative Oncology Group performance status; ITT, intention-to-treat; MMR, mismatch repair; OS, overall survival; pMMR, mismatch repair proficient.

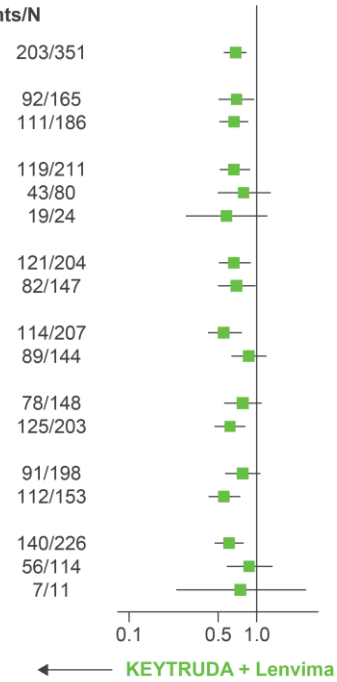
Makker V et al. *N Engl J Med* 2022;386:437–448 (supplementary appendix).

**Prescribing Information: KEYTRUDA GB; KEYTRUDA NI; Lenvima**

# KEYNOTE-775: OS in key subgroups (pMMR population)

**No formal statistical analysis was performed for the subgroup analyses and no clinical conclusions can be drawn**

| Subgroup | KEYTRUDA + Lenvima No. of events/N | Chemotherapy No. of events/N | HR (95% CI) |
|---|---|---|---|
| **Overall** | 165/346 | 203/351 | 0.68 (0.56–0.84) |
| **Age, yr** | | | |
| <65 | 78/171 | 92/165 | 0.70 (0.51–0.94) |
| ≥65 | 87/175 | 111/186 | 0.67 (0.51–0.89) |
| **Race** | | | |
| White | 102/220 | 119/211 | 0.62 (0.52–0.88) |
| Asian | 34/74 | 43/80 | 0.79 (0.50–1.24) |
| Other | 15/23 | 19/24 | 0.58 (0.28–1.18) |
| **Region** | | | |
| Region 1[a] | 98/202 | 121/204 | 0.67 (0.51–0.88) |
| Region 2[b] | 67/144 | 82/147 | 0.70 (0.50–0.96) |
| **ECOG PS** | | | |
| 0 | 82/212 | 114/207 | 0.56 (0.42–0.75) |
| 1 | 82/133 | 89/144 | 0.87 (0.64–1.18) |
| **Prior history of pelvic radiation** | | | |
| Yes | 66/142 | 78/148 | 0.78 (0.56–1.08) |
| No | 99/204 | 125/203 | 0.62 (0.47–0.80) |
| **Histology** | | | |
| Endometrioid | 76/188 | 91/198 | 0.78 (0.57–1.05) |
| Non-endometrioid | 89/158 | 112/153 | 0.56 (0.42–0.74) |
| **Prior lines of therapy** | | | |
| 1 | 114/244 | 140/226 | 0.61 (0.47–0.78) |
| 2 | 46/92 | 56/114 | 0.88 (0.59–1.30) |
| ≥3 | 5/10 | 7/11 | 0.75 (0.24–2.37) |




**Analysis cut-off date: 26 October 2020.**

[a]Europe, USA, Canada, Australia, New Zealand and Israel. [b]Rest of world. Figures adapted from Makker V et al. *N Engl J Med* 2022.

CI, confidence interval; dMMR, mismatch repair deficient; ECOG PS, Eastern Cooperative Oncology Group performance status; ITT, intention-to-treat; OS, overall survival; pMMR, mismatch repair proficient.

Makker V et al. *N Engl J Med* 2022;386:437–448 (supplementary appendix).

**Prescribing Information: KEYTRUDA GB; KEYTRUDA NI; Lenvima**

# KEYNOTE-775: Objective responses in the pMMR and all-comers populations (final analysis)

| | pMMR population | | All-comer population | |
|---|---|---|---|---|
| **Endpoint** | **KEYTRUDA + Lenvima (n=346)** | **Chemotherapy (n=351)** | **KEYTRUDA + Lenvima (n=411)** | **Chemotherapy (n=416)** |
| ORR difference %, (95% CI)[a] | 17.2 (11.0–23.5) | | 19.2 (13.4–24.9) | |
| % (95% CI) [b] | 32.4 (27.5–37.6) | 15.1 (11.5–19.3) | 33.8 (39.3–38.6) | 14.7 (11.4–18.4) |
| BOR, % (95% CI) [a] | | | | |
| CR[c] | 5.8 (3.6–8.8) | 2.6 (1.2–4.8) | 7.5 (5.2–10.5) | 2.6 (1.3–4.7) |
| PR[c] | 26.6 (22.0–31.6) | 12.5 (9.3–16.5) | 26.3 (22.1–30.8) | 12.0 (9.1–15.5) |
| SD | 46.5 (41.2–51.9) | 39.6 (34.4–44.9) | 45.0 (40.1–50.0) | 40.1 (35.4–45.0) |
| PD | 15.6 (11.9–19.9) | 30.8 (26.0–35.9) | 14.8 (11.5–18.7) | 29.6 (25.2–34.2) |
| NE[d] | 0.6 (0.1–2.1) | 2.0 (0.8–4.1) | 1.2 (0.4–2.8) | 1.9 (0.8–3.8) |
| NA[e] | 4.9 (2.9–7.8) | 12.5 (9.3–16.5) | 5.1 (3.2–7.7) | 13.7 (10.5–17.4) |
| Disease control rate, % (95% CI) [a,f] | 72.0 (66.9–76.6) | 46.4 (41.1–51.8) | 72.3 (67.7–76.5) | 46.6 (41.8–51.6) |
| Median DOR[g,h] | 9.3 (1.6–39.5) | 5.7 (0.0–37.1) | 12.9 (1.6–39.5) | 5.7 (0.0–37.1) |
| Median TTR[h] | 2.1 (1.5–23.0) | 3.5 (1.0–7.4) | 2.1 (1.5–23.0) | 2.1 (1.0–7.4) |

**Analysis cut-off date: 1 March 2022.**

a95% CI based on binomial exact CI method; bbased on Miettinen & Nurminen method stratified by MMR status; ECOG PS, geographic region and prior history of pelvic radiation (for all-comer population and pMMR populations; cFor best OR of CR or PR, only confirmed responses are included; dPost-baseline assessment(s) available, but NE; eNo post-baseline assessment available for response evaluation; fDefined as BOR of CR, PR or SD at 7 weeks or more after randomisation; gFrom product-limit (Kaplan—Meier) method for censored data;hIncludes participants with CR or PR.

BOR, best overall response; CI, confidence interval; CR, complete response; DOR, duration of response; ITT, intention-to-treat; mo, months; MMR, mismatch repair; NA, not assessed; NE, not estimable; ORR, objective respor PD, progressive disease; PR, partial response; SD, stable disease; TTR, time to response.

Makker V et al. Slide deck presented at: European Society for Medical Oncologists (ESMO) Virtual Annual Meeting; September 9-13, 2022.

**Prescribing Information:** KEYTRUDA GB; KEYTRUDA NI; Lenvima

# KEYNOTE-775: Objective responses in the dMMR population

| Endpoint | KEYTRUDA + Lenvima (n=411) | Chemotherapy (n=416) |
|---|---|---|
| ORR | | |
| n | 26 | 8 |
| % (95% CI) | 40 (28–53) | 12 (5–23) |
| BOR | | |
| CR | | |
| n | 9 | 2 |
| % (95% CI) | 14 (7–25) | 3 (<1–11) |
| PR | | |
| n | 17 | 6 |
| % (95% CI) | 26 (16–39) | 9 (3–19) |
| SD | | |
| n | 25 | 28 |
| % (95% CI) | 38 (27–51) | 43 (31–56) |

| Endpoint | KEYTRUDA + Lenvima (n=411) | Chemotherapy (n=416) |
|---|---|---|
| BOR (continued) | | |
| PD | | |
| n | 7 | 15 |
| % (95% CI) | 11 (4–21) | 23 (14–35) |
| NE | | |
| n | 3 | 1 |
| % (95% CI) | 5 (1–13) | 2 (0–8) |
| NA | | |
| n | 4 | 13 |
| % (95% CI) | 6 (2–15) | 20 (11–32) |
| Median DOR (range), mo | NR (2.1–20.4) | 4.1 (1.9–15.6) |
| Median TTR (range), mo | 2.9 (1.7–16.3) | 1.9 (1.8–3.7) |
| Disease control | | |
| n | 48 | 31 |
| % (95% CI) | 74 (61–84) | 48 (35–60) |

**Analysis cut-off date: 1 March 2022.**

Table adapted from Makker V et al. *N Engl J Med* 2022.

BOR, best overall response; CI, confidence interval; CR, complete response; dMMR, mismatch repair deficient; DOR, duration of response; mo, months; NA, not assessed; NE, not estimable; NR, not reached; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; TTR, time to response.

Makker V et al. *N Engl J Med* 2022;386:437–448.

**Prescribing Information:** KEYTRUDA GB; KEYTRUDA NI; Lenvima

# KEYNOTE-775: AEs with ≥25% incidence in either arm

| AE, n (%) | KEYTRUDA + Lenvima (n=406) | | Chemotherapy (n=388) | |
|---|---|---|---|---|
| | Any grade | Grade ≥3[a] | Any grade | Grade ≥3[a] |
| Hypertension[b] | 260 (64.0) | 154 (37.9) | 20 (5.2) | 9 (2.3) |
| Hypothyroidism[c] | 233 (57.4) | 5 (1.2) | 3 (0.8) | 0 |
| Diarrhoea | 220 (54.2) | 31 (7.6) | 78 (20.1) | 8 (2.1) |
| Nausea | 201 (49.5) | 14 (3.4) | 179 (46.1) | 5 (1.3) |
| Decreased appetite | 182 (44.8) | 32 (7.9) | 82 (21.1) | 2 (0.5) |
| Vomiting | 149 (36.7) | 11 (2.7) | 81 (20.9) | 9 (2.3) |
| Decreased weight | 138 (34.0) | 42 (10.3) | 22 (5.7) | 1 (0.3) |
| Fatigue | 134 (33.0) | 21 (5.2) | 107 (27.6) | 12 (3.1) |
| Arthralgia | 124 (30.5) | 7 (1.7) | 31 (8.0) | 0 |
| Proteinuria[b] | 117 (28.8) | 22 (5.4) | 11 (2.8) | 1 (0.3) |
| Anaemia | 106 (26.1) | 25 (6.2) | 189 (48.7) | 57 (14.7) |
| Constipation | 105 (25.9) | 3 (0.7) | 96 (24.7) | 2 (0.5) |
| Urinary tract infection | 104 (25.6) | 16 (3.9) | 39 (10.1) | 4 (1.0) |
| Neutropenia | 30 (7.4) | 7 (1.7) | 131 (33.8) | 100 (25.8) |
| Alopecia | 22 (5.4) | 0 | 120 (30.9) | 2 (0.5) |

For further information on the safety of KEYTRUDA + Lenvima, please refer to the SmPC: Great Britain, Northern Ireland.

[a]Among patients who received KEYTRUDA + Lenvima, 5.7% died due to Grade 5 AEs (GI disorder in 1.2% of patients, cardiac disorder in 0.5%, general disorder in 1.5%, infection in 0.7%, decreased appetite in 0.2%, and neoplasms, nervous system disorder, psychiatric disorder, renal disorder, reproductive disorder or respiratory disorder in 0.2% each). Among patients who received chemotherapy, 4.9% died due to Grade 5 AEs (cardiac disorder in 1.0%, general disorder in 1.3%, infection in 1.5%, subdural haematoma in 0.3% and respiratory disorder in 0.8%); [b]Clinically significant AE with Lenvima; [c]AE of interest with KEYTRUDA. Table adapted from Makker V et al. *N Engl J Med* 2022.

AE, adverse event; GI, gastrointestinal; SmPC, Summary of Product Characteristics.

Makker V et al. *N Engl J Med* 2022;386:437–448.

**Prescribing Information: KEYTRUDA GB; KEYTRUDA NI; Lenvima**

# KEYNOTE-775: Treatment-emergent adverse events with ≥10% incidence in either arm (1)

| AE, n (%) | KEYTRUDA + Lenvima (n=406) | | Chemotherapy (n=388) | |
|---|---|---|---|---|
| | Any grade | Grade ≥3[a] | Any grade | Grade ≥3[a] |
| Any TEAE | 395 (97.3) | 316 (77.8) | 364 (93.8) | 229 (59.0) |
| Hypertension[b] | 248 (61.1) | 146 (35.9) | 4 (1.0) | 1 (0.3) |
| Hypothyroidism[b,c] | 221 (54.4) | 4 (1.0) | 0 | 0 |
| Diarrhoea | 171 (42.1) | 25 (6.2) | 42 (10.8) | 3 (0.8) |
| Nausea | 158 (38.9) | 12 (3.0) | 157 (40.5) | 4 (1.0) |
| Decreased appetite | 149 (36.7) | 24 (5.9) | 64 (16.5) | 0 |
| Fatigue | 113 (27.8) | 15 (3.7) | 92 (23.7) | 12 (3.1) |
| Proteinuria[b] | 102 (25.1) | 18 (4.4) | 4 (1.0) | 0 |
| Vomiting | 99 (24.4) | 10 (2.5) | 59 (15.2) | 6 (1.5) |
| Decreased weight | 90 (22.2) | 24 (5.9) | 7 (1.8) | 0 |
| PPE syndrome[b] | 84 (20.7) | 11 (2.7) | 3 (0.8) | 0 |
| Arthralgia | 84 (20.7) | 4 (1.0) | 17 (4.4) | 0 |
| Dysphonia | 76 (18.7) | 0 | 2 (0.5) | 0 |
| Asthenia | 75 (18.5) | 17 (4.2) | 76 (19.6) | 9 (2.3) |
| Stomatitis | 70 (17.2) | 8 (2.0) | 46 (11.9) | 2 (0.5) |

For further information on the safety of KEYTRUDA + Lenvima, please refer to the SmPC: Great Britain, Northern Ireland.

[a]TEAEs led to death in 1.5% of patients in the KEYTRUDA + Lenvima group (cardiac disorder [n=1]; gastrointestinal disorder [n=1]; general disorders and administration site conditions [n=2]; benign, malignant and unspecified neoplasms [n=1]; nervous system disorders [n=1]), and 2.1% of patients in the chemotherapy group (cardiac disorders [n=3]; infections and infestations [n=3]; respiratory, thoracic, mediastinal disorders [n=2]); [b]Clinically significant AEs for Lenvima in all patients; [c]AE of interest for KEYTRUDA in all patients. Table adapted from Makker V et al. *N Engl J Med* 2022 (supplementary appendix).

AE, adverse event; PPE, palmar–plantar erythrodysesthesia; SmPC, Summary of Product Characteristics; TEAE, treatment-emergent adverse event.

Makker V et al. *N Engl J Med* 2022;386:437–448 (supplementary appendix).

**Prescribing Information:** KEYTRUDA GB; KEYTRUDA NI; Lenvima

# KEYNOTE-775: Treatment-emergent adverse events with ≥10% incidence in either arm (2)

| AE, n (%) | KEYTRUDA + Lenvima (n=406) | | Chemotherapy (n=388) | |
|---|---|---|---|---|
| | Any grade | Grade ≥3[a] | Any grade | Grade ≥3[a] |
| Increased ALT | 63 (15.5) | 13 (3.2) | 14 (3.6) | 2 (0.5) |
| Increased AST | 58 (14.3) | 13 (3.2) | 12 (3.1) | 2 (0.5) |
| Anaemia | 58 (14.3) | 8 (2.0) | 150 (38.7) | 43 (11.1) |
| Myalgia | 54 (13.3) | 3 (0.7) | 13 (3.4) | 0 |
| Headache | 53 (13.1) | 1 (0.2) | 14 (3.6) | 0 |
| Rash | 47 (11.6) | 2 (0.5) | 6 (1.5) | 0 |
| Mucosal inflammation | 45 (11.1) | 6 (1.5) | 35 (9.0) | 3 (0.8) |
| Decreased platelet count | 43 (10.6) | 7 (1.7) | 20 (5.2) | 3 (0.8) |
| Increased blood TSH | 40 (9.9) | 0 | 1 (0.3) | 0 |
| Constipation | 36 (8.9) | 0 | 51 (13.1) | 0 |
| Neutropenia | 22 (5.4) | 4 (1.0) | 127 (32.7) | 95 (24.5) |
| Leukopenia | 20 (4.9) | 0 | 47 (12.1) | 27 (7.0) |
| Alopecia | 17 (4.2) | 0 | 117 (30.2) | 2 (0.5) |
| Decreased neutrophil count | 17 (4.2) | 7 (1.7) | 93 (24.0) | 82 (21.2) |
| Decreased white blood cell count | 15 (3.7) | 4 (1.0) | 58 (14.9) | 40 (10.3) |

For further information on the safety of KEYTRUDA + Lenvima, please refer to the SmPC: Great Britain, Northern Ireland.

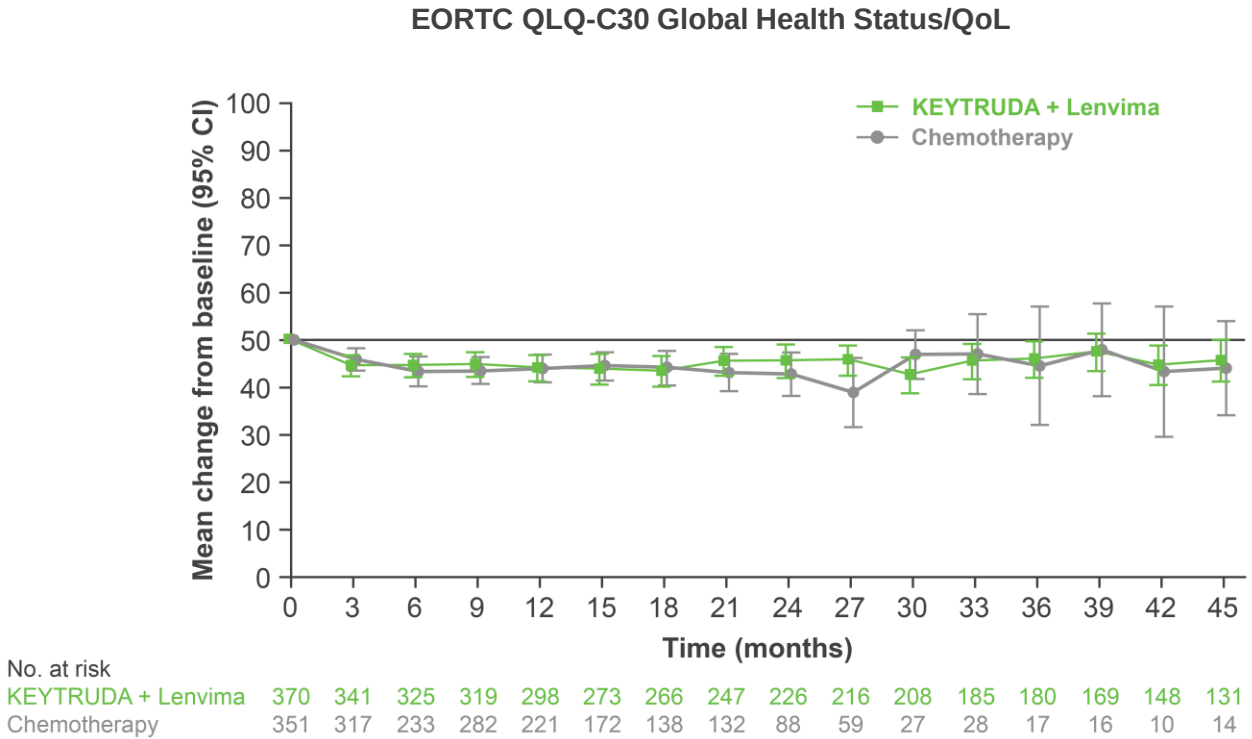
[a]TEAEs led to death in 1.5% of patients in the KEYTRUDA + Lenvima group (cardiac disorder [n=1]; gastrointestinal disorder [n=1]; general disorders and administration site conditions [n=2]; benign, malignant and unspecified neoplasms [n=1]; nervous system disorders [n=1]), and 2.1% of patients in the chemotherapy group (cardiac disorders [n=3]; infections and infestations [n=3]; respiratory, thoracic, mediastinal disorders [n=2]).
Table adapted from Makker V et al. *N Engl J Med* 2022 (supplementary appendix).

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; SmPC, Summary of Product Characteristics; TEAE, treatment-emergent adverse event; TSH, thyroid-stimulating hormone.

Makker V et al. *N Engl J Med* 2022;386:437–448 (supplementary appendix).

**Prescribing Information: KEYTRUDA GB; KEYTRUDA NI; Lenvima**

# KEYNOTE-775: No substantial between-group differences were observed in the QLQ-C30 global health status QoL scores over time




**Analysis cut-off date: 26 October 2020.**

Figure adapted from Makker V et al. *N Engl J Med* 2022 (supplementary appendix).

CI, confidence interval; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; QoL, quality of life.

Makker V et al. *N Engl J Med* 2022;386:437–448 (supplementary appendix).

**Prescribing Information:** KEYTRUDA GB; KEYTRUDA NI; Lenvima