MSD Oncology

KEYNOTE-A18 (ENGOT-cx11/GOG-3047): KEYTRUDA® (pembrolizumab), in combination with chemoradiotherapy, for the treatment of newly diagnosed, high-risk, locally advanced cervical cancer

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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

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

KEYTRUDA (pembrolizumab) is only licensed for use in FIGO 2014 Stage III–IVA, high-risk, locally advanced cervical cancer

- KEYTRUDA, in combination with chemoradiotherapy (external beam radiation therapy followed by brachytherapy), is indicated for the treatment of FIGO 2014 Stage III–IVA locally advanced cervical cancer in adults who have not received prior definitive therapy
- The results for the ITT population are presented as this is the primary endpoint of the study. It allows the results in the licensed population (a subgroup of the ITT population) to be viewed in context of the primary endpoint

BT, brachytherapy; CRT, chemoradiotherapy; FIGO, International Federation of Gynecology and Obstetrics; ITT, intention-to-treat; PI, prescribing information.

KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed April 2026.

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PI, prescribing information.

Slide deck navigation

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PI, prescribing information.

Epidemiology and unmet need

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In females, cervical cancer is the 14th most common cancer and the 19th most common cause of cancer-related death in the UK[a,b]

Overview in the UK

3,300
estimated **new cases** each year[a]

890
estimated **deaths** each year[b]

~9/10
females with cervical cancer aged 15–44 years survive for ≥10 years[c]

~1/5
females with cervical cancer aged 75–99 years survive for ≥10 years[c]

[a]Data from 2017–2019; [b]Data from 2021–2023; [c]Data from 2018.
PI, prescribing information.
Cancer Research UK. Cervical cancer statistics. Available at: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/cervical-cancer#Cervicalcs2. Accessed April 2026.

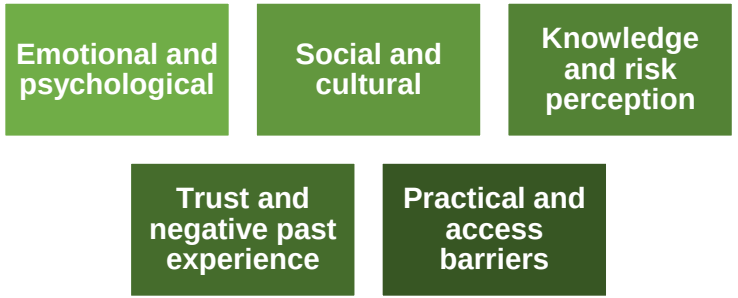
Incidence rates for cervical cancer vary across demographic groups, with screening uptake declining among younger women[1,2]

- Incidence rates for cervical cancer in the UK **are highest in females aged 30–34 years**[a,1]
- In England, cervical cancer incidence rates are **65% higher in the most deprived quintile** compared with the least, and around 520 cases of cervical cancer each year are linked with deprivation[b,1]
- Incidence rates for cervical cancer in females in England are lower in the Asian and Black ethnic groups compared with the White ethnic group[b,1]
- In the UK, uptake of **cervical cancer screening continues to decline**, particularly **in younger age groups**[2]

Cervical cancer screening coverage in the UK, 2023–2024[c,3]

England	Northern Ireland	Scotland	Wales
68.8%	67.7%	63.3%	68.7%

Barriers to screening participation in the UK[4]



[a]Data from 2017–2019; [b]Data from 2013–2017; [c]Coverage is the percentage of people in the population who are eligible for screening at a particular point in time and who have had a test with a recorded result at least once within the screening round (i.e. within the last 3.5 years for people aged 25-49 years and within the last 5.5 years for people aged 50-64 years).[3]

PI, prescribing information.

1. Cancer Research UK. Cervical cancer statistics. Available at: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/cervical-cancer. Accessed April 2026;
2. Ellis LB et al. *BJOG* 2025;132:e185–e193; 3. Cancer Research UK. Early Cancer Diagnosis Data Hub. Available at: https://crukcancerintelligence.shinyapps.io/EarlyDiagnosis/_w_edb77ba25730452cb4cce447fa102d25/_w_61bddbb73be04c5ca8bcd0e5006904fb/_w_8f2c82738d4042f08eb23f1f3c086b1c/#shiny-tab-hometab. Accessed April 2026;
4. Cancer Research UK. Encouraging informed participation in cervical screening. Available at: https://www.cancerresearchuk.org/health-professional/cancer-screening/cervical-screening/encouraging-informed-participation#understanding-the-barriers-to-screening-participation. Accessed April 2026.

Risk factors for cervical cancer in the UK are multifactorial[1,2]

- In the UK, 99.8% of cervical cancer cases are preventable[a,1]
- Risk factors for cervical cancer include:[1,2]

HPV infection

Sexual history
- Becoming sexually active at a young age (especially ≤14 years old)
- Having six or more sexual partners

HIV infection

Long-term use of oral contraceptives

Family history of cervical cancer

Reproductive factors
- Multiple full-term pregnancies
- Aged <17 years at their first full-term pregnancy

Tobacco smoking

Low socioeconomic status

Decreasing trends in incidence observed worldwide and in the UK since the early 1990s are attributed to effective precautionary procedures combined with sociocultural factors, including access to healthcare, changes in family planning behaviour and increasing coverage of vaccination against HPV[1,3]

[a]Data from 2015.[1]

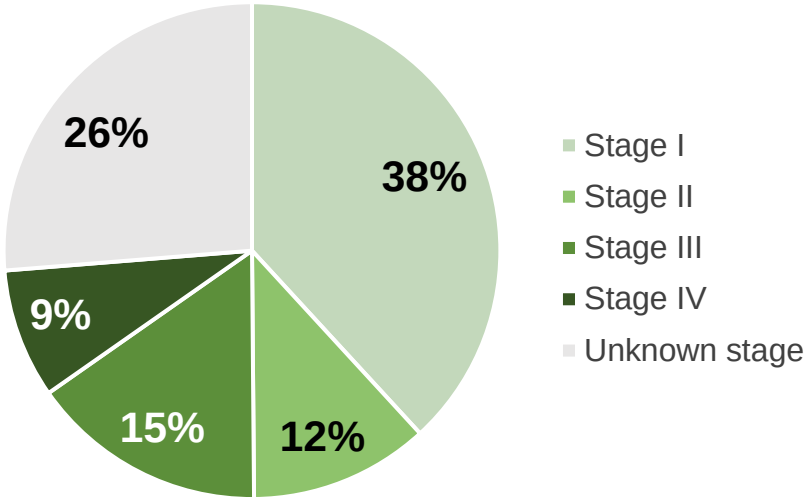
HIV, human immunodeficiency virus; HPV, human papillomavirus; PI, prescribing information.

1. Cancer Research UK. Cervical cancer statistics. Available at: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/cervical-cancer#Cervicalcs2. Accessed April 2026;
2. Cancer Research UK. Cervical cancer risk. Available at: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/cervical-cancer/risk-factors#heading-One. Accessed April 2026;
3. Zhang X et al. *BMC Public Health* 2021;21:894.

High 5-year disease recurrence rates underscore the need for alternative treatment options in locally advanced cervical cancer[1]

- In England, ~35% of patients with cervical cancer are diagnosed with Stage II, III or IV[2]
- According to the 2017 ESMO guidelines for cervical cancer, CRT has been the standard of care for patients with bulky IB2–IVA disease for almost two decades[3]
- A prospective, observational, cohort study of 1341 patients conducted at 24 centres in Europe, Asia and North America from 2008 to 2015 reported that 24–53% of patients with Stage III–IVA[a] (n=237) treated with CRT alone experienced a disease recurrence, metastasis or death within 5 years[1]
- In a 3-year follow-up of the RTOG 90-01 trial[b] involving 403 women with Stage IIB–IVA[a] disease, the risk of recurrence was 29% among those with Stage III–IVA disease (n=194) compared with 13% among those with Stage IB2–IIB disease[4]

Proportion of patients by stage at diagnosis (England, 2022)[2]



[a]FIGO stage; [b]Dates from 1990–1997.
CRT, chemoradiotherapy; ESMO, European Society for Medical Oncology; FIGO, International Federation of Gynecology and Obstetrics; PI, prescribing information.
1. Pötter R et al. *Lancet Oncol* 2021;22:538–547; 2. Cancer Research UK. Early Cancer Diagnosis Data Hub. Available at: https://crukcancerintelligence.shinyapps.io/EarlyDiagnosis/_w_edb77ba25730452cb4cce447fa102d25/_w_61bddbb73be04c5ca8bcd0e5006904fb/_w_8f2c82738d4042f08eb23f1f3c086b1c/#shiny-tab-hometab. Accessed April 2026; 3. Marth C et al. *Ann Oncol* 2017;28:iv72–iv83; 4. Eifel PJ et al. *J Clin Oncol* 2004;22:872–880.

Mechanisms of action

PI, prescribing information.

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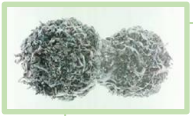
KEYTRUDA is the **first** IO + CRT combination therapy indicated for patients with FIGO 2014 Stage III–IV locally advanced cervical cancer[1]

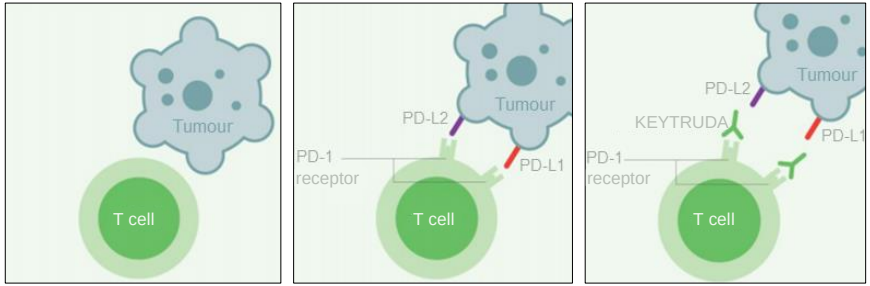
CRT synergistically combines the effects of chemotherapy and radiotherapy



- **Chemotherapy** administration can result in the immunogenic death of tumour cells, leading to the release of tumour antigens that are recognised by the immune system[2]
- Radiosensitising agents (e.g. some cytotoxic chemotherapies) enhance the effects of radiation on cancer cells[3]

- **Radiotherapy** works by damaging tumour cell DNA[4]
  - Directly by ionising radiation
  - Indirectly by promoting the absorption of high-energy wavelengths by other molecules surrounding DNA, resulting in the production of DNA-damaging free radicals

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[2,5,6]
- KEYTRUDA is a humanised monoclonal antibody that binds to PD-1, blocking its interaction with PD-L1/-L2 and potentiating T-cell responses, including the anti-tumour response[1]

Radiotherapy can increase tumour antigen release and presentation, potentially enhancing tumour-specific T-cell responses and immune cell infiltration, thus providing a rationale for combining it with PD-1 inhibitors such as KEYTRUDA[7]

Radiotherapy photo by unknown author is licensed under CC BY-SA-NC.

CRT, chemoradiotherapy; FIGO, International Federation of Gynecology and Obstetrics; IO, immuno-oncology; PD-1, programmed death receptor-1; PD-L1, programmed death ligand-1; PD-L2, programmed death ligand-2;PI, prescribing information.

1. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed April 2026; 2. Emens LA, Middleton G. *Cancer Immunol Res* 2015;3:436–443;
3. Rallis KS et al. *Anticancer Res* 2021;41:1–7; 4. Liu YP et al. *MedComm (2020)* 2021;2:315–340; 5. Yi M et al. *J Hematol Oncol* 2021;14:10; 6. Pardoll DM. *Nat Rev Cancer* 2012;12:252–264;
7. Lee L, Matulonis U. *Gynecol Oncol* 2019;154:236–245.

Study design and baseline characteristics

PI, prescribing information.

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KEYNOTE-A18 (ENGOT-cx11/GOG-3047): ITT population – Study design[1]

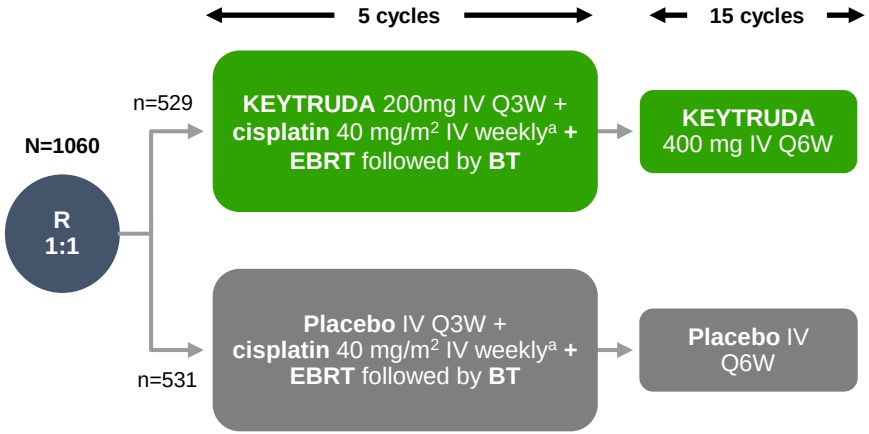
A multicentre, randomised, double-blind, placebo-controlled trial, Phase 3 trial evaluating KEYTRUDA + CRT in high-risk, locally advanced cervical cancer

Key eligibility criteria

- Newly diagnosed, locally advanced, squamous cell carcinoma, adenocarcinoma or adenosquamous carcinoma of the cervix
- High-risk: FIGO 2014 Stage IB2–IIB with node-positive disease or Stage III–IVA regardless of nodal status
- No previous systemic therapy, immunotherapy, definitive surgery or radiation
- ECOG PS of 0 or 1
- Tumour tissue sample collected from a core, incisional or excisional biopsy

Stratification factors

- Planned type of EBRT: IMRT or VMAT vs non-IMRT and non-VMAT
- Stage at screening: FIGO 2014 Stage IB2–IIB with node-positive disease vs FIGO 2014 Stage III–IVA
- Planned total radiotherapy dose: EBRT + BT dose of <70 Gy vs ≥70 Gy as per equivalent dose



Assessment of tumour status was performed at Week 12, then every 12 weeks during years 1 and 2, followed by every 24 weeks in Year 3, and then annually

KEYTRUDA, in combination with chemoradiotherapy (external beam radiation therapy followed by brachytherapy), is indicated for the treatment of FIGO 2014 Stage III–IVA locally advanced cervical cancer in adults who have not received prior definitive therapy.[2]

The results for the ITT population are presented as this is the primary endpoint of the study. It allows the results in the licensed population (a subgroup of the ITT population) to be viewed in context of the primary endpoint.

- **Primary endpoints:** PFS assessed per RECIST v1.1 by investigator review or by histopathological confirmation of suspected progression and OS
- **Key secondary endpoints:**[b] PFS assessed per RECIST v1.1 by BICR, the percentage of patients alive and progression-free at 24 months, PFS and OS by PD-L1 status, PFS2, ORR, the percentage of patients with confirmed CR at 12 weeks, PROs and safety

Analysis cutoff date: 9 January 2023. Subsequent mentions of CRT refer to cisplatin and EBRT followed by BT.

[a]An optional sixth infusion could be administered per local practice; [b]The percentage of patients alive at 36 months is an additional secondary endpoint planned for future reporting following sufficient follow-up.

BICR, blinded independent central review; BT, brachytherapy; CR, complete response; CRT, chemoradiotherapy; EBRT; external beam radiotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; FIGO, International Federation of Gynecology and Obstetrics; Gy, gray; IMRT, intensity-modulated radiation therapy; ITT, intention-to-treat; IV, intravenous; ORR, objective response rate; OS, overall survival; PD-L1, programmed death ligand-1; PFS, progression-free survival; PFS2, the time from randomisation to subsequent disease progression after initiation of new anticancer therapy or death from any cause; PI, prescribing information; PRO, patient-reported outcome; Q3W, every 3 weeks; Q6W, every 6 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1; VMAT, volumetric modulated arc therapy.

1. Lorusso D et al. *Lancet* 2024;403:1341–1350; 2. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed April 2026.

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KEYNOTE-A18 (ENGOT-cx11/GOG-3047): ITT population – Baseline characteristics[1] | Interim analysis 1

IA1

	KEYTRUDA + CRT (n=529)	Placebo + CRT (n=531)
Median age (IQR), years	49 (40–57)	50 (41–59)
Age ≥65 years, n (%)	56 (11)	77 (15)
Race, n (%)		
White	254 (48)	264 (50)
Asian	155 (29)	148 (28)
Black	14 (3)	8 (2)
ECOG PS, n (%)		
0	380 (72)	397 (75)
1	149 (28)	134 (25)
Lymph node status,[a] n (%)		
Positive pelvic only	326 (62)	324 (61)
Positive para-aortic only	14 (3)	10 (2)
Positive pelvic and para-aortic	105 (20)	104 (20)
No positive pelvic or para-aortic	84 (16)	93 (18)
PD-L1 CPS, n (%)		
CPS <1	22 (4)	28 (5)
CPS ≥1	502 (95)	498 (94)

	KEYTRUDA + CRT (n=529)	Placebo + CRT (n=531)
Stage at screening (FIGO 2014), n (%)		
Stage IB2–IIB	235 (44)	227 (43)
Stage III–IVA	294 (56)	304 (57)
Histology, n (%)		
Squamous cell carcinoma	433 (82)	451 (85)
Non-squamous cell carcinoma	96 (18)	80 (15)
Radiotherapy type, n (%)		
IMRT or VMAT EBRT	469 (89)	470 (89)
Other	60 (11)	61 (11)
Planned total radiotherapy dose, n (%)		
<70 Gy (EQD2)	47 (9)	46 (9)
≥70 Gy (EQD2)	482 (91)	485 (91)

Adapted from Lorusso D et al. 2024.[1]

Patients were enrolled in KEYNOTE-A18 regardless of PD-L1 status[1,2]

KEYTRUDA, in combination with chemoradiotherapy (external beam radiation therapy followed by brachytherapy), is indicated for the treatment of FIGO 2014 Stage III–IVA locally advanced cervical cancer in adults who have not received prior definitive therapy.[2]
The results for the ITT population are presented as this is the primary endpoint of the study. It allows the results in the licensed population (a subgroup of the ITT population) to be viewed in context of the primary endpoint.

Analysis cutoff date: 9 January 2023.[1]

[a]Per protocol, a lymph node is defined as ≥1.5 cm shortest dimension by MRI or CT.[1]

CPS, combined positive score; CRT, chemoradiotherapy; EBRT, external beam radiation therapy; ECOG PS, Eastern Cooperative Oncology Group performance status; EQD2, equivalent dose in 2 Gy fractions; FIGO, International Federation of Gynecology and Obstetrics; Gy, gray; IMRT, intensity-modulated radiation therapy; IQR, interquartile range; ITT, intention-to-treat; PI, prescribing information; VMAT, volumetric modulated arc therapy.

1. Lorusso D et al. *Lancet* 2024;403:1341–1350; 2. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed April 2026.

KEYNOTE-A18 (ENGOT-cx11/GOG-3047): ITT population – Baseline characteristics[1] | Interim analysis 2

IA2

	KEYTRUDA + CRT (n=529)	Placebo + CRT (n=531)
Median age (IQR), years	49 (40–57)	50 (41–59)
Age ≥65 years, n (%)	56 (11)	77 (15)
Race, n (%)		
White	254 (48)	264 (50)
Asian	156 (29)	148 (28)
Black	14 (3)	8 (2)
ECOG PS, n (%)		
0	380 (72)	398 (75)
1	149 (28)	133 (25)
Lymph node status,[a] n (%)		
Positive pelvic only	327 (62)	324 (61)
Positive para-aortic only	14 (3)	10 (2)
Positive pelvic and para-aortic	104 (20)	104 (20)
No positive pelvic or para-aortic	84 (16)	93 (18)
PD-L1 CPS, n (%)		
CPS <1	22 (4)	28 (5)
CPS ≥1	502 (95)	498 (94)

	KEYTRUDA + CRT (n=529)	Placebo + CRT (n=531)
Stage at screening (FIGO 2014), n (%)		
Stage IB2–IIB	233 (44)	226 (43)
Stage III–IVA	296 (56)	305 (57)
Histology, n (%)		
Squamous cell carcinoma	434 (82)	451 (85)
Non-squamous cell carcinoma	95 (18)	80 (15)
Radiotherapy type, n (%)		
IMRT or VMAT EBRT	469 (89)	470 (89)
Other	60 (11)	61 (11)
Planned total radiotherapy dose, n (%)		
<70 Gy (EQD2)	47 (9)	46 (9)
≥70 Gy (EQD2)	482 (91)	485 (91)

Adapted from Lorusso D et al. 2024.[1]

Patients were enrolled in KEYNOTE-A18 regardless of PD-L1 status[1,2]

KEYTRUDA, in combination with chemoradiotherapy (external beam radiation therapy followed by brachytherapy), is indicated for the treatment of FIGO 2014 Stage III–IVA locally advanced cervical cancer in adults who have not received prior definitive therapy.[2]
The results for the ITT population are presented as this is the primary endpoint of the study. It allows the results in the licensed population (a subgroup of the ITT population) to be viewed in context of the primary endpoint.

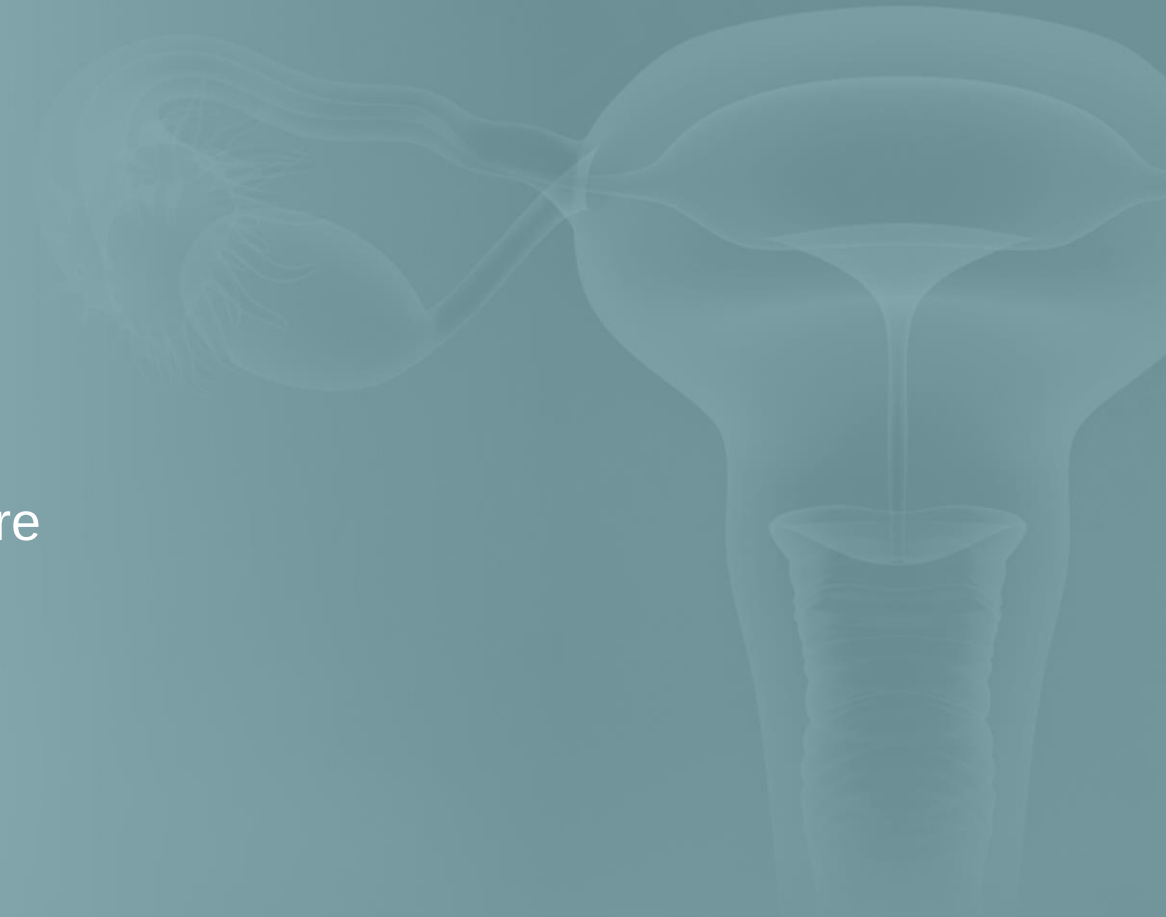
Analysis cutoff date: 8 January 2024.[1]
[a]Per protocol, a lymph node is defined as ≥1.5 cm shortest dimension by MRI or CT.[1]
CPS, combined positive score; CRT, chemoradiotherapy; EBRT, external beam radiation therapy; ECOG PS, Eastern Cooperative Oncology Group performance status; EQD2, equivalent dose in 2 Gy fractions; FIGO, International Federation of Gynecology and Obstetrics; Gy, gray; IMRT, intensity-modulated radiation therapy; IQR, interquartile range; ITT, intention-to-treat; PI, prescribing information; VMAT, volumetric modulated arc therapy.
1. Lorusso D et al. *Lancet* 2024;404:1321–1332; 2. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed April 2026.

KEYNOTE-A18 (ENGOT-cx11/GOG-3047): Overview of study analyses

Analysis name	DCO	Median duration of follow-up (range), months[a]	Key milestones
Interim analysis 1[1]	9 January 2023[1]	17.9 (0.9–31.0)[3]	Assessing whether the addition of KEYTRUDA to CRT significantly improves PFS and OS[1,3]
Interim analysis 2[2]	8 January 2024[2]	29.9 (12.8–43.0)[3]	Assessing whether the addition of KEYTRUDA to CRT significantly improves OS[2,3]
Final analysis[3]	7 January 2025[3]	41.9 (24.8–55.0)[3]	Final OS analysis without hypothesis testing for PFS and OS[3]

[a]Defined as the time from randomisation to the DCO date.[3]
ASCO, American Society for Clinical Oncology; CRT, chemoradiotherapy; DCO, data cutoff; OS, overall survival, PFS, progression-free survival; PI, prescribing information.
1. Lorusso D et al. *Lancet* 2024;403:1341–1350; 2. Lorusso D et al. *Lancet* 2024;404:1321–1332;
3. Duska LR et al. Presented at the American Society of Clinical Oncology (ASCO) Congress 2025, 30 May–3 June. Abstract LBA5504.

Treatment exposure



PI, prescribing information.

UK KEYTRUDA PI

CRT-treated population[a] – Summary of treatment exposure[1] | Interim analysis 2

IA2

	KEYTRUDA + CRT (n=527)	Placebo + CRT (n=530)
Total number of cycles, median (range)		
KEYTRUDA or placebo	17 (1–20)	16 (1–20)
Cisplatin	5 (1–7)	5 (1–7)
Radiation therapy		
Overall treatment time, median (range), days	52 (12–139)	52 (2–166)
Within 50 days,[b] n (%)	187 (35.5)	195 (36.8)
Within 56 days, n (%)	391 (74.2)	396 (74.7)
Duration of EBRT, median (range), days	37 (12–139)	37 (2–143)
Duration of brachytherapy, median (range),[c] days	12 (1–74)	12 (1–59)

KEYTRUDA, in combination with chemoradiotherapy (external beam radiation therapy followed by brachytherapy), is indicated for the treatment of FIGO 2014 Stage III–IVA locally advanced cervical cancer in adults who have not received prior definitive therapy.[2] The results for the ITT population are presented as this is the primary endpoint of the study. It allows the results in the licensed population (a subgroup of the ITT population) to be viewed in context of the primary endpoint.

Adapted from Lorusso D et al. 2024.[1]

For further information on the safety of KEYTRUDA, please refer to the UK SmPC

Analysis cutoff date: 8 January 2024; median (range) months of follow-up: 29.9 (12.8–43.0).[1]

[a]The CRT-treated population is the number of patients who completed CRT at this interim analysis and had final data review by the vendor;[1] [b]Total radiation therapy (EBRT and brachytherapy) should not exceed 50 days, with extension to a maximum of 56 days for unforeseen delays, per the study protocol;[1] [c]Includes patients who started brachytherapy and completed CRT at this interim analysis and had final data review by the vendor (KEYTRUDA arm, n=513; placebo arm, n=504).[1]

CRT, chemoradiotherapy; EBRT, external beam radiotherapy; FIGO, International Federation of Gynecology and Obstetrics; ITT, intention-to-treat; PI, prescribing information; SmPC, Summary of Product Characteristics.

1. Lorusso D et al. Presented at the European Society for Medical Oncology (ESMO) Congress 2024, 13–17 September. Abstract 709O;
2. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed April 2026.

CRT-treated population[a] – Summary of radiation treatment exposure[1] | Interim analysis 2

IA2

	KEYTRUDA + CRT (n=527)	Placebo + CRT (n=530)
HR-CTV D90% total dose (Gy), median (range)		
Total physical dose[b]	76 (73–79)	76 (73–78)
Total EQD2 dose[b]	87 (83–92)	87 (83–92)
EBRT technique, n (%)		
IMRT or VMAT	471 (89.4)	464 (87.5)
Non-IMRT and non-VMAT	56 (10.6)	66 (12.5)
EBRT to elective target volume		
Total physical dose[b]	45 (45–50)	45 (45–50)
Total EQD2 dose[b]	44 (44–50)	44 (44–50)
EBRT to lymph nodes, n	444	440
Total physical dose[b]	56 (55–58)	56 (55–58)
Total EQD2 dose[b]	56 (56–59)	56 (56–59)
No. of EBRT fractions[c] (cervix and lymph nodes)	25 (7–35)	25 (2–35)

	KEYTRUDA + CRT (n=527)	Placebo + CRT (n=530)
Type of BT, n (%)		
3D HR-CTV D90%	465 (88.2)	460 (86.8)
3D Point A	48 (9.1)	44 (8.3)
Not started	14 (2.7)	26 (4.9)
BT technique, n (%)		
HDR	496 (94.1)	500 (94.3)
Total EQD2 dose[b]	41 (37–45)	41 (38–45)[d]
PDR/LDR	17 (3.2)	4 (0.8)
Total physical dose[b]	35 (31–39)	37 (33–40)
No. of BT fractions[c]	4 (1–7)[e]	4 (1–6)[f]
Technique, n (%)		
Intracavitary	389 (73.8)	381 (71.9)
Intracavitary + interstitial	124 (23.5)	123 (23.2)

Please note that KEYTRUDA, in combination with chemoradiotherapy (external beam radiation therapy followed by brachytherapy), is indicated for the treatment of FIGO 2014 Stage III–IVA locally advanced cervical cancer in adults who have not received prior definitive therapy.[2]
The results for the ITT population are presented as this is the primary endpoint of the study. It allows the results in the licensed population (a subgroup of the ITT population) to be viewed in context of the primary endpoint.

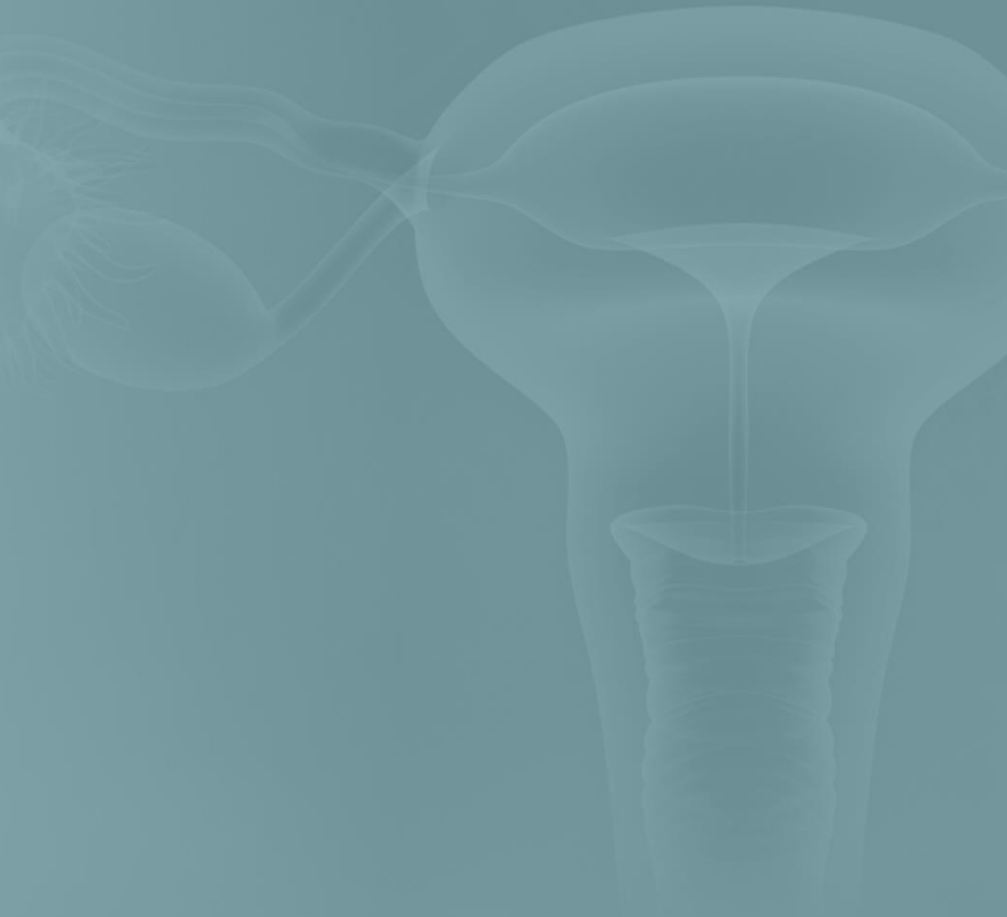
Adapted from Lorusso D et al. 2024.[1]

For further information on the safety of KEYTRUDA, please refer to the UK SmPC

Analysis cutoff date: 8 January 2024; median (range) months of follow-up: 29.9 (12.8–43.0).[1]
[a]The CRT-treated population is the number of patients who completed CRT at this interim analysis and had final data review by the vendor;[1] [b]Total physical dose and total EQD2 dose shown are median (interquartile range) Gy;[1] [c]Number of fractions shown are median (range);[1] [d]n=498;[1] [e]n=513;[1] [f]n=501.[1]
BT, brachytherapy; CRT, chemoradiotherapy; EBRT, external beam radiotherapy; EQD2, equivalent dose in 2 Gy fractions; Gy, gray; HDR, high-dose-rate; HR-CTV, high-risk clinical target volume; FIGO, International Federation of Gynecology and Obstetrics; IMRT, intensity-modulated radiation therapy; ITT; intention-to-treat; LDR, low-dose-rate; PDR, pulsed-dose-rate; PI, prescribing information; SmPC, Summary of Product Characteristics; VMAT, volumetric modulated arc therapy.

1. Lorusso D et al. Presented at the European Society for Medical Oncology (ESMO) Congress 2024, 13–17 September. Abstract 709O;
2. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed April 2026.

Efficacy results

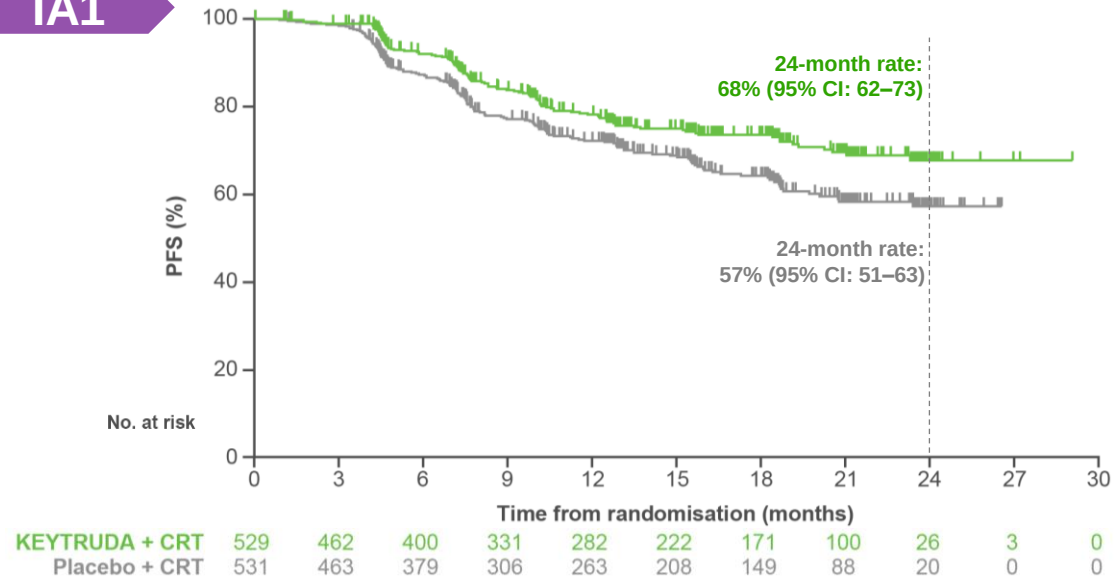


PI, prescribing information.

UK KEYTRUDA PI

Primary endpoint: ITT population – PFS[a]

IA1



PFS[a]	Patients with event, n	Median PFS (95% CI), months	HR[b] (95% CI)	p-value[c]
KEYTRUDA + CRT (n=529)	115	NR (NR–NR)	0.70 (0.55–0.89)	0.0020
Placebo + CRT (n=531)	154	NR (NR–NR)		

KEYTRUDA, in combination with chemoradiotherapy (external beam radiation therapy followed by brachytherapy), is indicated for the treatment of FIGO 2014 Stage III–IVA locally advanced cervical cancer in adults who have not received prior definitive therapy.[3]

The results for the ITT population are presented as this is the primary endpoint of the study. It allows the results in the licensed population (a subgroup of the ITT population) to be viewed in context of the primary endpoint.

Adapted from Lorusso D et al. 2024.[1]

IA2

At **interim analysis 2**, 29% and 40% of patients had a PFS event in the KEYTRUDA + CRT and the placebo + CRT arm, respectively (median PFS was NR in either arm; HR: 0.68; 95% CI: 0.56–0.84).[d,2]

Analysis cutoff date interim analysis 1: 9 January 2023; median (IQR) months of follow-up: 17.9 (11.3–22.3).[1] Tick marks indicate censored data.[1]

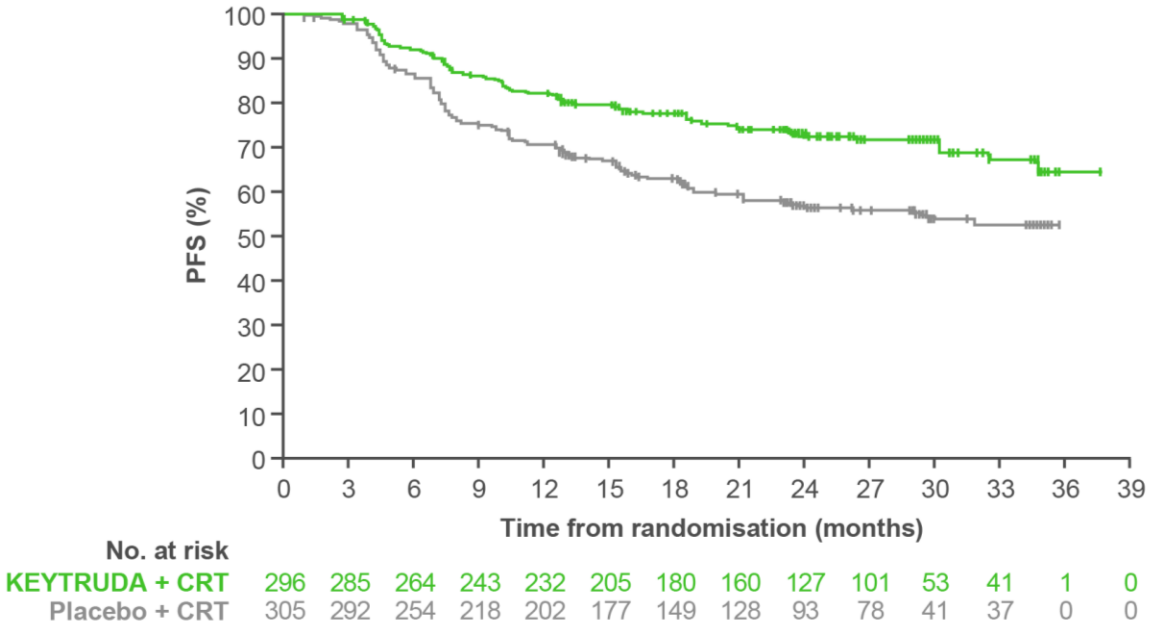
[a]Assessed per RECIST v1.1 by investigator review or by histopathological confirmation of suspected progression;[1] [b]Magnitude of the difference assessed using the stratified Cox proportional hazards model and Efron's method of tie handling;[1] [c]Assessed using the stratified log-rank test (based on the prespecified statistical boundary of 0.0172; one-sided);[1] [d]Because there was a statistically significant improvement in PFS in the KEYTRUDA + CRT group as compared with the placebo + CRT group at interim analysis 1, no formal testing of PFS was performed at this analysis.[2]

CI, confidence interval; CRT, chemoradiotherapy; FIGO, International Federation of Gynecology and Obstetrics; HR, hazard ratio; IA, interim analysis; IQR, interquartile range; ITT, intention-to-treat; NR, not reached; PFS, progression-free survival; PI, prescribing information; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1.

1. Lorusso D et al. *Lancet* 2024;403:1341–1350; 2. Lorusso D et al. *Lancet* 2024;404:1321–1332; 3. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed April 2026.

Exploratory endpoint: Patients with FIGO 2014 Stage III–IVA cervical cancer – PFS[a,1] | Interim analysis 2

IA2



PFS[a]	Patients with event, n (%)	Median PFS (95% CI), months	HR[b] (95% CI)
KEYTRUDA + CRT (n=296)	79 (27)	NR (NR–NR)	0.57 (0.43–0.76)
Placebo + CRT (n=305)	125 (41)	NR (26.3–NR)	

LIMITATIONS

- These results are from a subgroup exploratory analysis and should be interpreted with caution
- Significance was not tested; therefore, no statistical conclusions can be drawn from this analysis

Adapted from KEYTRUDA SmPC.[1]

Analysis cutoff date: 8 January 2024; median (range) months of follow-up: 26.6 (0.9–41.7).[1,2]

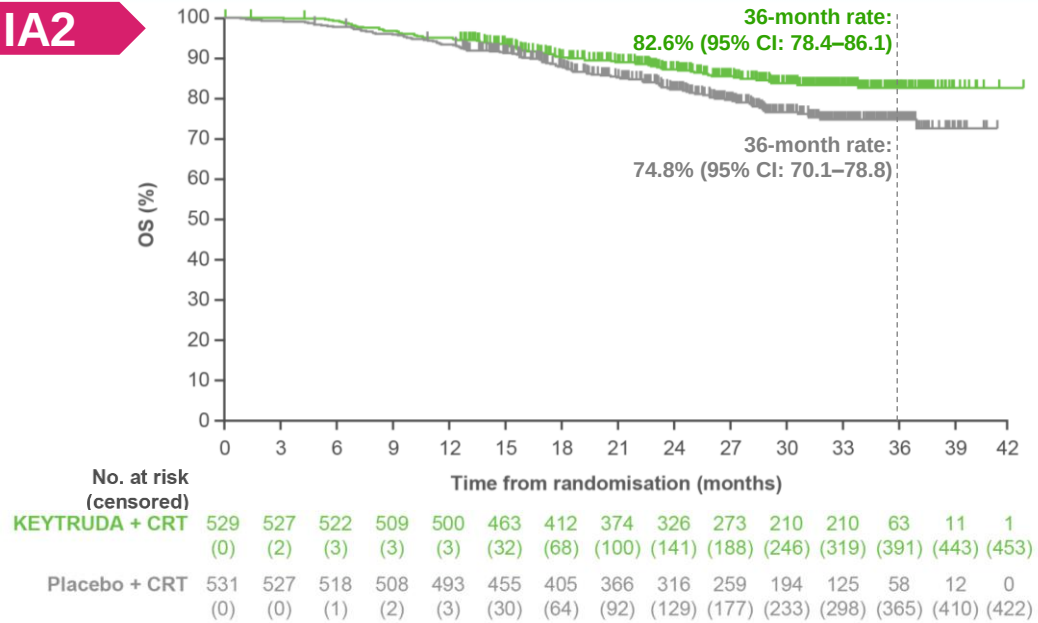
[a]Assessed per RECIST v1.1 by investigator review or by histopathological confirmation of suspected progression;[1] [b]Based on the unstratified proportional hazard model.[1]

CI, confidence interval; CRT, chemoradiotherapy; FIGO, International Federation of Gynecology and Obstetrics; HR, hazard ratio; IA, interim analysis; NR, not reached; PFS, progression-free survival; PI, prescribing information; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SmPC, Summary of Product Characteristics.

1. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed April 2026 ; 2. Lorusso D et al. *Lancet* 2024;404:1321–1332.

Primary endpoint: ITT population – OS[1]

IA2



OS	Patients with event, n	Median OS (95% CI), months	HR[a] (95% CI)	p-value[b]
KEYTRUDA + CRT (n=529)	75	NR (NR–NR)	0.67 (0.50–0.90)	0.0040
Placebo + CRT (n=531)	109	NR (NR–NR)		

KEYTRUDA, in combination with chemoradiotherapy (external beam radiation therapy followed by brachytherapy), is indicated for the treatment of FIGO 2014 Stage III–IVA locally advanced cervical cancer in adults who have not received prior definitive therapy.[3]

The results for the ITT population are presented as this is the primary endpoint of the study. It allows the results in the licensed population (a subgroup of the ITT population) to be viewed in context of the primary endpoint.

Adapted from Lorusso D et al. 2024.[1]

IA1

At **interim analysis 1**, data were immature (42.9% information fraction) and the median OS was NR for either the KEYTRUDA + CRT or the placebo + CRT arm (HR: 0.73; 95% CI: 0.49–1.07; 8% and 11% of patients with event, respectively).[c,2]

Analysis cutoff date interim analysis 2: 8 January 2024; median (IQR) months of follow-up: 29.9 (23.3–34.3).[1] Tick marks indicate censored data.[1]

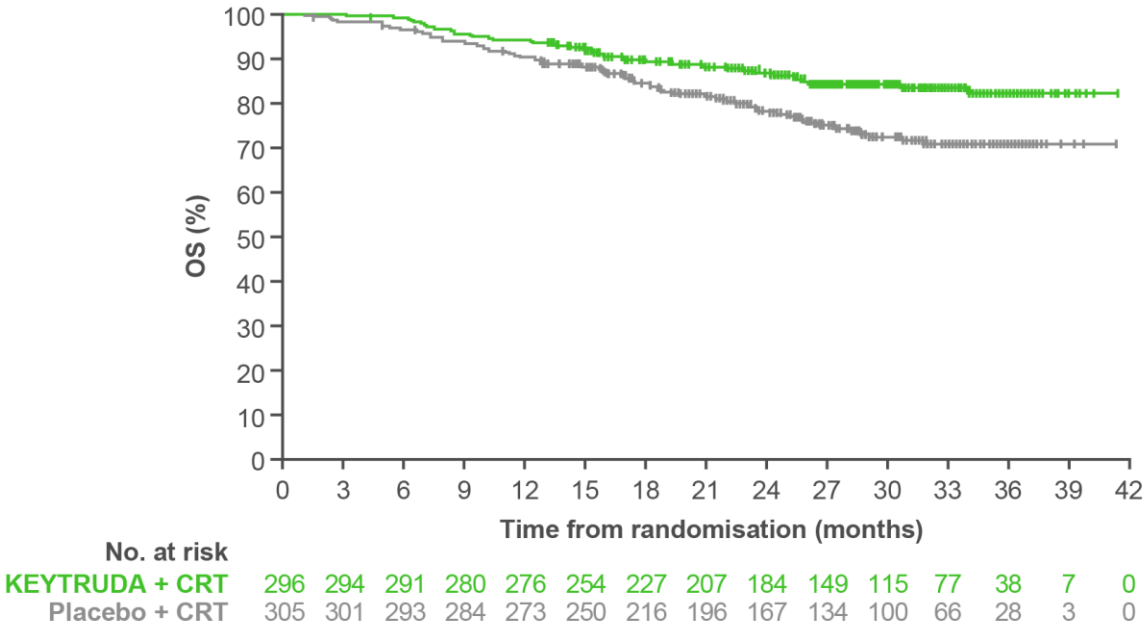
[a]Magnitude of the difference assessed using the stratified Cox proportional hazards model and Efron's method of tie handling;[1] [b]Assessed using the stratified log-rank test (based on the prespecified statistical boundary of 0.01026; one-sided);[1] [c]The observed p-value did not cross the prespecified efficacy boundary at this interim analysis.[2]

CI, confidence interval; CRT, chemoradiotherapy; FIGO, International Federation of Gynaecology and Obstetrics; HR, hazard ratio; IA, interim analysis; ITT, intention-to-treat; NR, not reached; OS, overall survival; PI, prescribing information; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1.

1. Lorusso D et al. *Lancet* 2024;404:1321–1332; 2. Lorusso D et al. *Lancet* 2024;403:1341–13502;
3. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed April 2026.

Exploratory endpoint: Patients with FIGO 2014 Stage III–IVA cervical cancer – OS[1] | Interim analysis 2

IA2



OS	Patients with event, n (%)	Median OS (95% CI), months	HR[a] (95% CI)
KEYTRUDA + CRT (n=296)	43 (15)	NR (NR–NR)	0.57 (0.39–0.83)
Placebo + CRT (n=305)	73 (24)	NR (NR–NR)	

LIMITATIONS

- These results are from a subgroup exploratory analysis and should be interpreted with caution
- Significance was not tested; therefore, no statistical conclusions can be drawn from this analysis

Adapted from KEYTRUDA SmPC.[1]

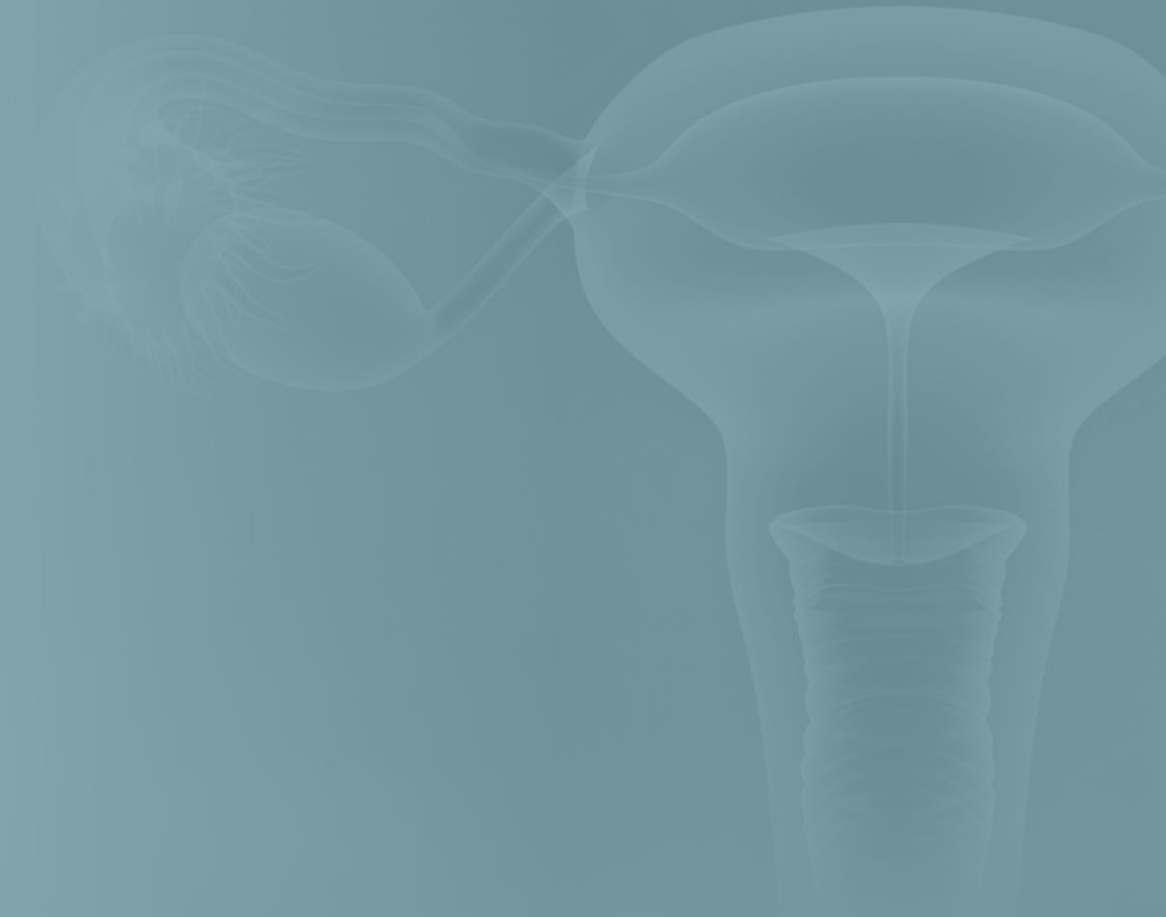
Analysis cutoff date interim analysis 2: 8 January 2024; median (range) months of follow-up: 26.6 (0.9–41.7).[1,2]

[a]Based on the unstratified proportional hazard model.[1]

CI, confidence interval; CRT, chemoradiotherapy; FIGO, International Federation of Gynecology and Obstetrics; HR, hazard ratio; IA, interim analysis; NR, not reached; OS, overall survival; PI, prescribing information; SmPC, Summary of Product Characteristics.

1. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed April 2026; 2. Lorusso D et al. *Lancet* 2024;404:1321–1332.

Safety results



PI, prescribing information.

Treatment disposition: As-treated population[a,1] | Interim analysis 1

IA1

Median follow-up: 17.9 months

	KEYTRUDA + CRT (n[a]=528)	Placebo + CRT (n[a]=530)
Discontinued treatment, n	165	183
Reason for discontinuing treatment, n		
Radiographic progression	84	122
AEs	45	18
Patient withdrew consent	21	24
Clinical progression	5	8
Physician decision	4	4
Progressive disease[b]	2	5
Other	4[c]	2[d]

These data comprise all randomly allocated patients who received at least one dose of study treatment.[1]
Please note that KEYTRUDA, in combination with chemoradiotherapy (external beam radiation therapy followed by brachytherapy), is indicated for the treatment of FIGO 2014 Stage III–IVA locally advanced cervical cancer in adults who have not received prior definitive therapy.[2]

Adapted from Lorusso D et al. 2024.[1]

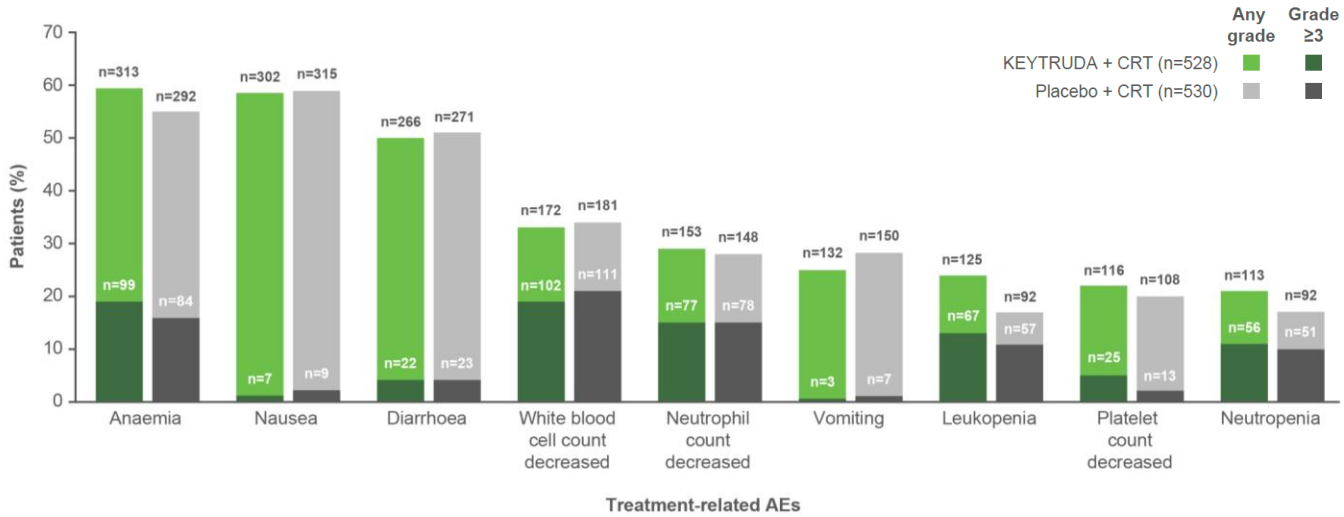
For further information on the safety of KEYTRUDA, please refer to the UK SmPC

Analysis cutoff date: 9 January 2023.[1]
[a]The as-treated population included all patients who received at least one dose of study treatment;[1] [b]Defined as histopathological progression without radiographic progression. Histopathological confirmation of suspected disease progression in the absence of radiographic disease progression per RECIST v1.1 was allowed but not required;[1] [c]Other reasons for discontinuing treatment in the KEYTRUDA + CRT-treated arm included non-compliance,[1] excluded medication and protocol violation; [d]Other reasons for discontinuing treatment in the placebo + CRT-treated arm included being lost to follow-up and non-compliance.
AE, adverse event; CRT, chemoradiotherapy; IA, interim analysis; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1; PI, prescribing information; SmPC, Summary of Product Characteristics.
1. Lorusso D et al. *Lancet* 2024;403:1341–1350; 2. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed April 2026.

Safety data: As-treated population[a,1] – Treatment-related AEs[b] with ≥20% incidence| Interim analysis 1

IA1

Median follow-up: 17.9 months



These data comprise all randomly allocated patients who received at least one dose of study treatment.[1]
Please note that KEYTRUDA, in combination with chemoradiotherapy (external beam radiation therapy followed by brachytherapy), is indicated for the treatment of FIGO 2014 Stage III–IVA locally advanced cervical cancer in adults who have not received prior definitive therapy.[2]

Adapted from Lorusso D et al. 2024.[1]

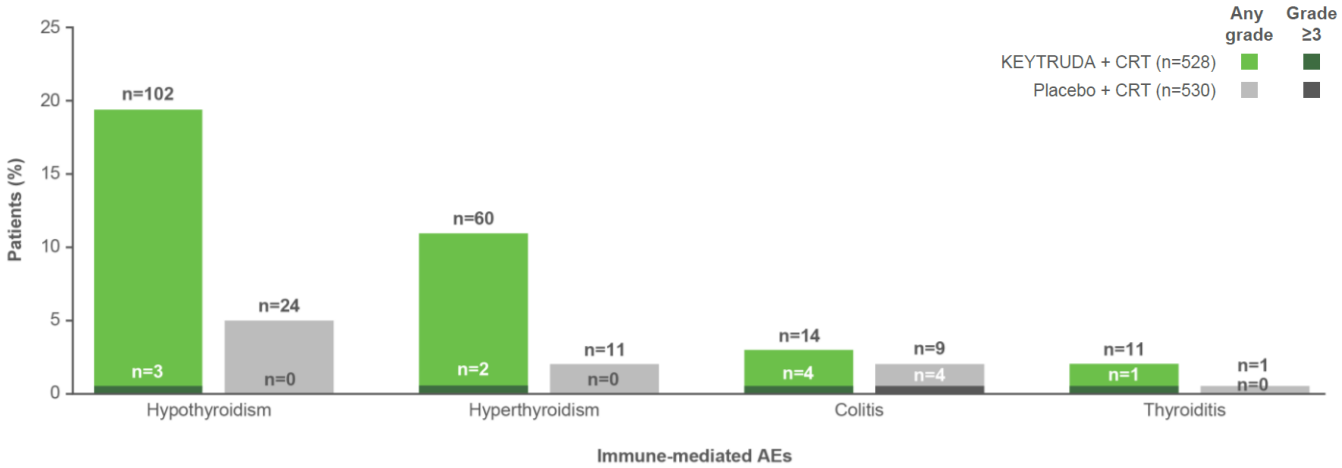
For further information on the safety of KEYTRUDA, please refer to the UK SmPC

Analysis cutoff date: 9 January 2023.[1]
[a]The as-treated population included all the patients who had undergone randomisation and received at least one trial treatment;[1] [b]Listed are AEs that occurred during the treatment period or within 30 days after the treatment period (within 90 days for serious events).[1]
AE, adverse event; CRT, chemoradiotherapy; IA, interim analysis; PI, prescribing information; SmPC, Summary of Product Characteristics.
1. Lorusso D et al. *Lancet* 2024;403:1341–1350; 2. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed April 2026.

Safety data: As-treated population[a] – Immune-mediated AEs with an incidence of ≥15 patients in either arm[1] | Interim analysis 1

IA1

Median follow-up: 17.9 months



These data comprise all randomly allocated patients who received at least one dose of study treatment.[1]
Please note that KEYTRUDA, in combination with chemoradiotherapy (external beam radiation therapy followed by brachytherapy), is indicated for the treatment of FIGO 2014 Stage III–IVA locally advanced cervical cancer in adults who have not received prior definitive therapy.[2]

Adapted from Lorusso D et al. 2024.[1]

For further information on the safety of KEYTRUDA, please refer to the UK SmPC

Analysis cutoff date: 9 January 2023.[1]
[a]The as-treated population included all the patients who had undergone randomisation and received at least one trial treatment.[1]
AE, adverse event; CRT, chemoradiotherapy; IA, interim analysis; PI, prescribing information; SmPC, Summary of Product Characteristics.
1. Lorusso D et al. *Lancet* 2024;403:1341–1350; 2. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed April 2026.

Treatment disposition: As-treated population[a,1] | Interim analysis 2

IA2

Median follow-up: 29.9 months

	KEYTRUDA + CRT (n=528)	Placebo + CRT (n=530)
Discontinued treatment, n	223	236
Reason for discontinuing treatment, n		
Radiographic progression	108	158
AEs	64	24
Patient withdrew consent	30	28
Clinical progression	4	9
Physician decision	8	7
Progressive disease[b]	2	8
Other	7[c]	2[d]

These data comprise all randomly allocated patients who received at least one dose of study treatment.[1]
Please note that KEYTRUDA, in combination with chemoradiotherapy (external beam radiation therapy followed by brachytherapy), is indicated for the treatment of FIGO 2014 Stage III–IVA locally advanced cervical cancer in adults who have not received prior definitive therapy.[2]

Adapted from Lorusso D et al. 2024.[1]

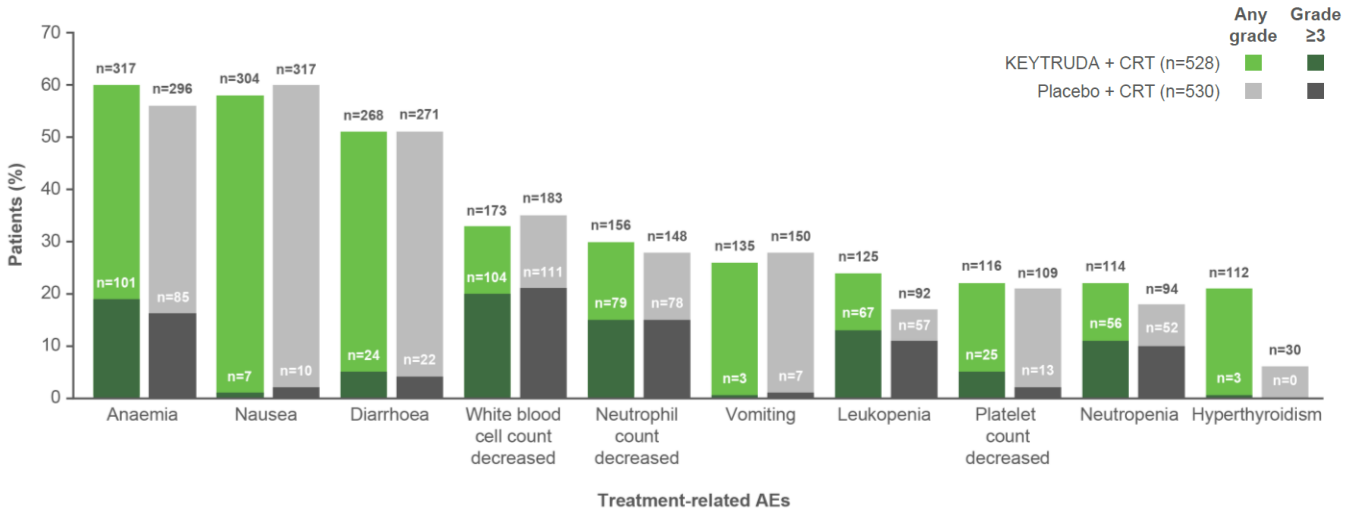
For further information on the safety of KEYTRUDA, please refer to the UK SmPC

Analysis cutoff date: 8 January 2024.[1]
[a]The as-treated population included all patients who received at least one dose of study treatment;[1] [b]Defined as histopathological progression without radiographic progression. Histopathological confirmation of suspected disease progression in the absence of radiographic disease progression per RECIST v1.1 was allowed but not required;[1] [c]Other reasons for discontinuing treatment in the KEYTRUDA + CRT-treated arm included protocol non-compliance and being lost to follow-up;[1] [d]Other reasons for discontinuing treatment in the placebo + CRT-treated arm included being lost to follow-up and protocol non-compliance.[1]
AE, adverse event; CRT, chemoradiotherapy; IA, interim analysis; PI, prescribing information; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1; SmPC, Summary of Product Characteristics.
1. Lorusso D et al. *Lancet* 2024;404:1321–1332; 2. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed April 2026.

Safety data: As-treated population[a] – Treatment-related AEs[b] with ≥20% incidence[1] | Interim analysis 2

IA2

Median follow-up: 29.9 months



These data comprise all randomly allocated patients who received at least one dose of study treatment.[1]
Please note that KEYTRUDA, in combination with chemoradiotherapy (external beam radiation therapy followed by brachytherapy), is indicated for the treatment of FIGO 2014 Stage III–IVA locally advanced cervical cancer in adults who have not received prior definitive therapy.[2]

Adapted from Lorusso D et al. 2024.[1]

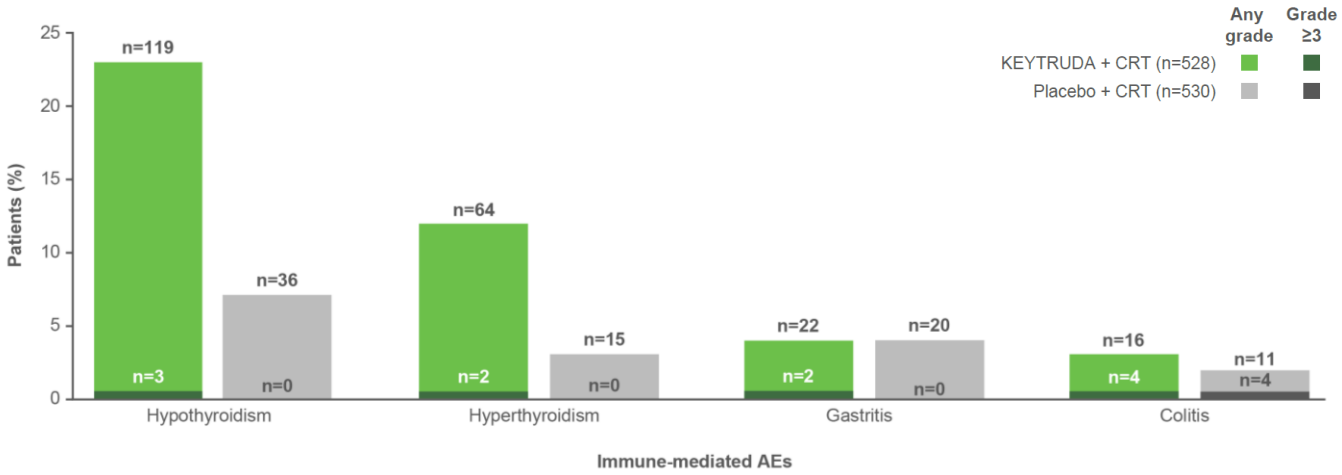
For further information on the safety of KEYTRUDA, please refer to the UK SmPC

Analysis cutoff date: 8 January 2024.[1]
[a]The as-treated population included all the patients who had undergone randomisation and received at least one trial treatment;[1]
[b]Listed are AEs that occurred during the treatment period or within 30 days after the treatment period(within 90 days for serious events).[1]
AE, adverse event; CRT, chemoradiotherapy; IA, interim analysis; PI, prescribing information; SmPC, Summary of Product Characteristics.
1. Lorusso D et al. *Lancet* 2024;404:1321–1332; 2. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed April 2026.

Safety data: As-treated population[a] – Immune-mediated AEs with an incidence of ≥15 patients in either arm[1] | Interim analysis 2

IA2

Median follow-up: 29.9 months



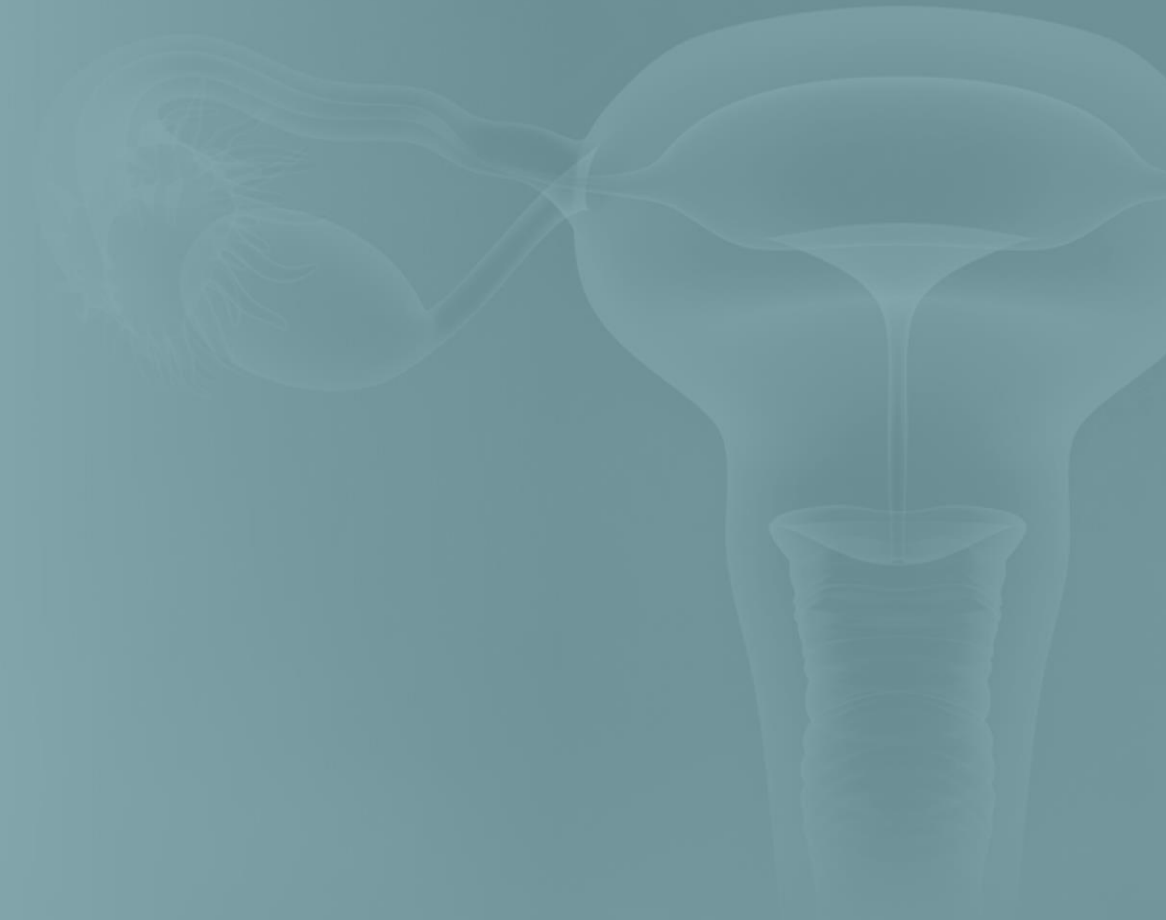
These data comprise all randomly allocated patients who received at least one dose of study treatment.[1]
Please note that KEYTRUDA, in combination with chemoradiotherapy (external beam radiation therapy followed by brachytherapy), is indicated for the treatment of FIGO 2014 Stage III–IVA locally advanced cervical cancer in adults who have not received prior definitive therapy.[2]

Adapted from Lorusso D et al. 2024.[1]

For further information on the safety of KEYTRUDA, please refer to the UK SmPC

Analysis cutoff date: 8 January 2024.[1]
[a]The as-treated population included all the patients who had undergone randomisation and received at least one trial treatment.[1]
AE, adverse event; CRT, chemoradiotherapy; FIGO, International Federation of Gynecology and Obstetrics; IA, interim analysis; PI, prescribing information; SmPC, Summary of Product Characteristics.
1. Lorusso D et al. *Lancet* 2024;404:1321–1332; 2. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed April 2026.

Summary



PI, prescribing information.

UK KEYTRUDA PI

KEYNOTE-A18: Summary (1/2)

PFS results

- At interim analysis 1, first-line treatment with **KEYTRUDA + CRT** demonstrated statistically significant improvement in PFS compared with **placebo + CRT** in patients with newly diagnosed, high-risk, locally advanced cervical cancer (HR: 0.70; 95% CI: 0.55–0.89; p=0.0020)[1]
  - Median PFS was NR in both treatment arms
- At interim analysis 2, 29% of patients in the **KEYTRUDA + CRT** arm and 40% of patients in the **placebo + CRT** arm had a PFS event (HR: 0.68; 95% CI: 0.56–0.84)[a,2]
  - In the FIGO 2014 Stage III–IVA subpopulation, 27% and 41% of patients in the **KEYTRUDA + CRT** and the **placebo + CRT** arms, respectively, presented with a PFS event (HR: 0.57; 95% CI: 0.43–0.76); median PFS was NR in either arm[3]

OS results

- At interim analysis 1, data were immature (42.9% information fraction) and the median OS was NR for either the **KEYTRUDA + CRT** or the **placebo + CRT** arm (HR: 0.73; 95% CI: 0.49–1.07; 8% and 11% of patients with event, respectively).[b,1]
- At interim analysis 2, **KEYTRUDA + CRT** showed a statistically significant improvement in OS compared with **placebo + CRT** (HR: 0.67; 95% CI: 0.50–0.90; p=0.0040); median OS was NR in either arm[2]
  - Within the FIGO Stage III–IVA cervical cancer subpopulation, 15% of patients in the **KEYTRUDA + CRT** arm vs 24% of patients in the **placebo + CRT** arm presented with an event (HR: 0.57; 95% CI: 0.39–0.83); median OS was NR in either arm[3]

[a]Because there was a statistically significant improvement in PFS in the KEYTRUDA + CRT group as compared with the placebo + CRT group at interim analysis 1, no formal testing of PFS was performed at interim analysis 2;[2]
[b]The observed p-value did not cross the prespecified efficacy boundary at this interim analysis.
CI, confidence interval; CRT, chemoradiotherapy; HR, hazard ratio; NR, not reached; OS, overall survival; PFS, progression-free survival; PI, prescribing information.
1. Lorusso D et al. *Lancet* 2024;403:1341–1350; 2. Lorusso D et al. *Lancet* 2024;404:1321–1332;
3. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed April 2026.

KEYNOTE-A18: Summary (2/2)

Safety results

- The safety profiles of **KEYTRUDA + CRT** at interim analysis 1 and interim analysis 2 were consistent with known profiles of individual therapies and no new safety signals were identified[1,2]

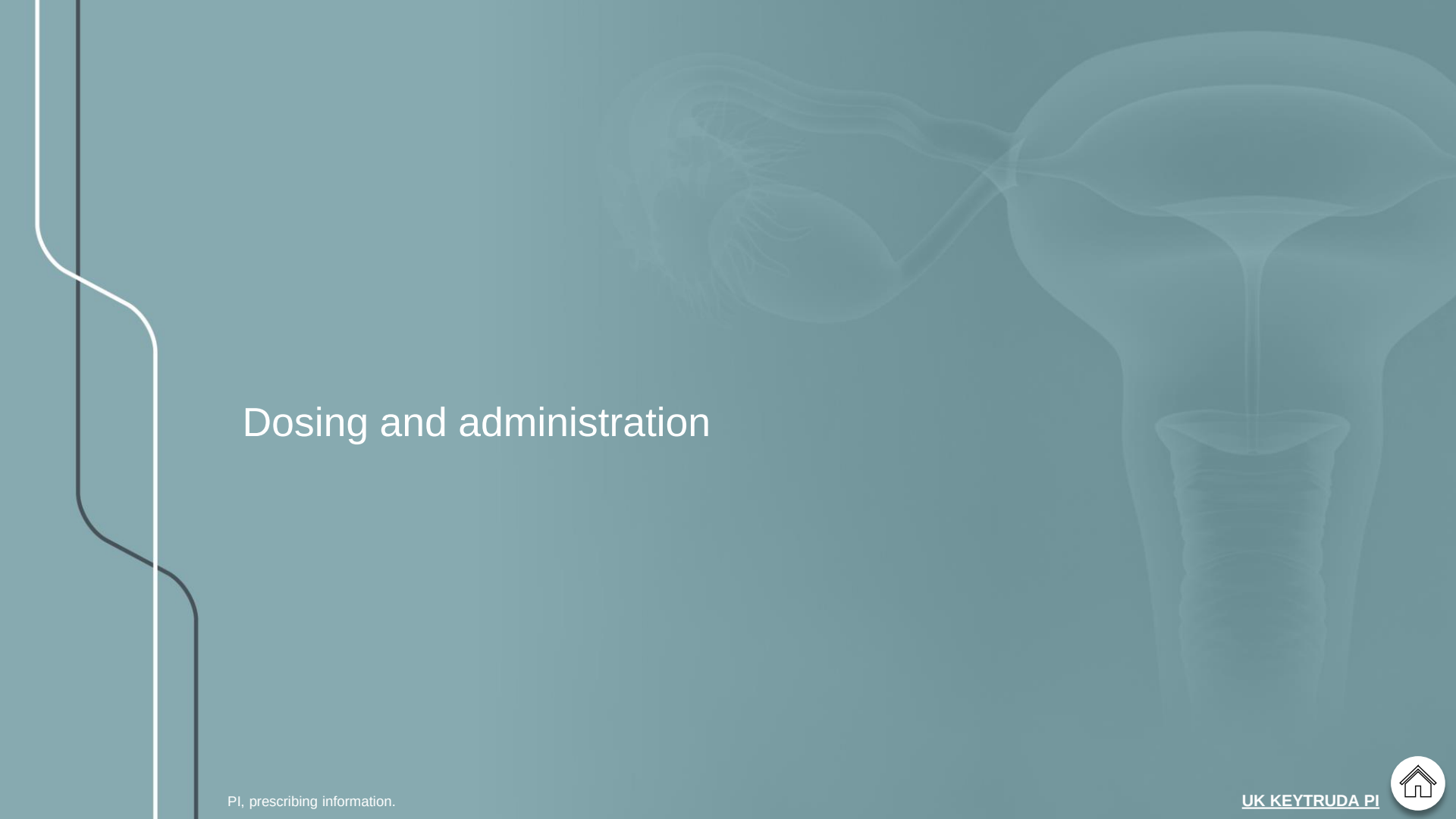
Conclusion

- **KEYTRUDA** is the **first** IO + CRT combination therapy indicated for patients with FIGO 2014 Stage III–IV locally advanced cervical cancer[3]

CRT, chemoradiotherapy; FIGO, International Federation of Gynecology and Obstetrics; IO, immuno-oncology; PI, prescribing information.

1. Lorusso D et al. *Lancet* 2024;403:1341–1350; 2. Lorusso D et al. *Lancet* 2024;404:1321–1332;
3. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed April 2026.

Dosing and administration



PI, prescribing information.

KEYTRUDA dosing: IV

KEYTRUDA offers flexibility of IV dosing

Administered as an IV infusion

Over 30 minutes

200 mg Q3W or 400 mg Q6W

The 200 mg Q3W (once Q3W) IV regimen has been assessed in Phase 2 and 3 registration studies across a multitude of indications of KEYTRUDA. An exposure–response evaluation, using modelling and simulation, led to the approval of the 400 mg Q6W (once Q6W) dosing for monotherapy and combination therapy.

What does the flexibility of dosing mean for you and your patients?

IV, intravenous; PI, prescribing information; Q3W, every 3 weeks; Q6W, every 6 weeks.

KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc#about-medicine. Accessed April 2026.