MSD Oncology

KEYTRUDA® (pembrolizumab) in combination with chemotherapy with or without bevacizumab for the treatment of persistent, recurrent or metastatic cervical cancer in adults whose tumours express PD-L1 CPS ≥1

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Please refer to the full KEYTRUDA Summary of Product Characteristics and Risk Minimisation Materials for patients before prescribing KEYTRUDA.

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ (**please note that the MHRA Yellow Card link will redirect you to an external website, for which MSD does not review or control the content**) or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Merck Sharp & Dohme (UK) Limited (Tel: 020 8154 8000).

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Please click the following links for the KEYTRUDA SmPC and prescribing information: Great Britain; Northern Ireland.
If using a downloaded version of this material, please ensure that you are accessing the most recent version of the 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

Slide deck navigation

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KEYTRUDA + chemotherapy overview

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Overview of KEYTRUDA + chemotherapy in persistent, recurrent or metastatic cervical cancer

Click the links below to navigate to the section of interest

Dual mechanism of action

KEYTRUDA + chemo in persistent, recurrent or metastatic cervical cancer

Current treatment landscape in first-line metastatic cervical cancer

Potential treatment landscape in first-line metastatic cervical cancer

Chemo, chemotherapy.

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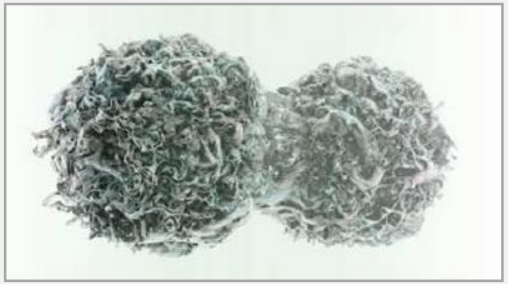
KEYTRUDA + chemotherapy in persistent, recurrent or metastatic cervical cancer: Dual mechanisms of action[1–4]

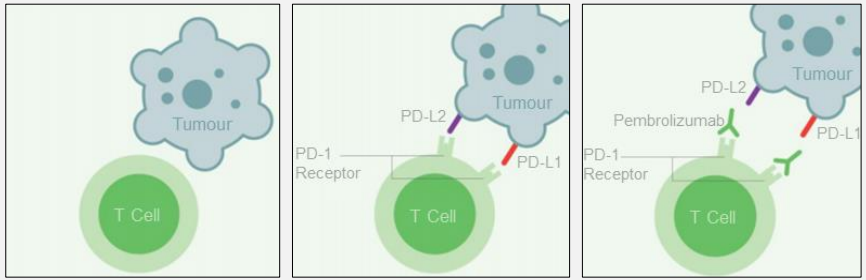
Chemotherapy targets proliferating cells[1,2]

- Chemotherapy targets cells that are actively proliferating, by inhibiting cell division and promoting tumour cell killing through deregulation of DNA replication, cellular metabolism, or microtubule assembly[1]



KEYTRUDA activates the anti-tumour immune response[3,4]

- KEYTRUDA is a selective monoclonal antibody that blocks the PD-1 protein pathway, potentiating T-cell responses, including anti-tumour responses[3]
- Some tumours can evade the immune system through the PD-1 pathway. On the surface of tumour cells, the dual PD-1 ligands, PD-L1 and PD-L2, bind to the PD-1 receptors on T cells to inactivate them, allowing tumour cells to evade detection[3,4]
- By inhibiting this process, KEYTRUDA reactivates tumour-specific cytotoxic T cells and anti-tumour immunity[3]



When combined with immunotherapies, such as KEYTRUDA, chemotherapy may increase tumour immunogenicity and activate immune response by increasing antigen shedding and presentation, and by stimulating T-cell infiltration[1]

For more information on the mechanism of action of KEYTRUDA + chemotherapy, click here
Please note that clicking this link will redirect you to the promotional MSD Connect website.

PD-1, programmed cell death receptor 1; PD-L1, programmed death ligand-1; PD-L2, programmed death ligand-2.

1. Leonetti A et al. *Drug Resist Updat* 2019;46:1–12; 2. American Cancer Society. Chemotherapy side effects. Available at: https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/chemotherapy/chemotherapy-side-effects.html. Accessed June 2023; 3. KEYTRUDA (pembrolizumab) SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/keytruda-epar-product-information_en.pdf. Accessed June 2023; 4. Harvey R et al. *Clin Pharm Therapeutics* 2014:96;214–223.

Prescribing Information: GB; NI

Key considerations for the treatment of persistent, recurrent or metastatic cervical cancer[1,2]

Radical treatments

- Exenteration surgery + chemoradiotherapy

Systemic anticancer therapy (palliative treatments)

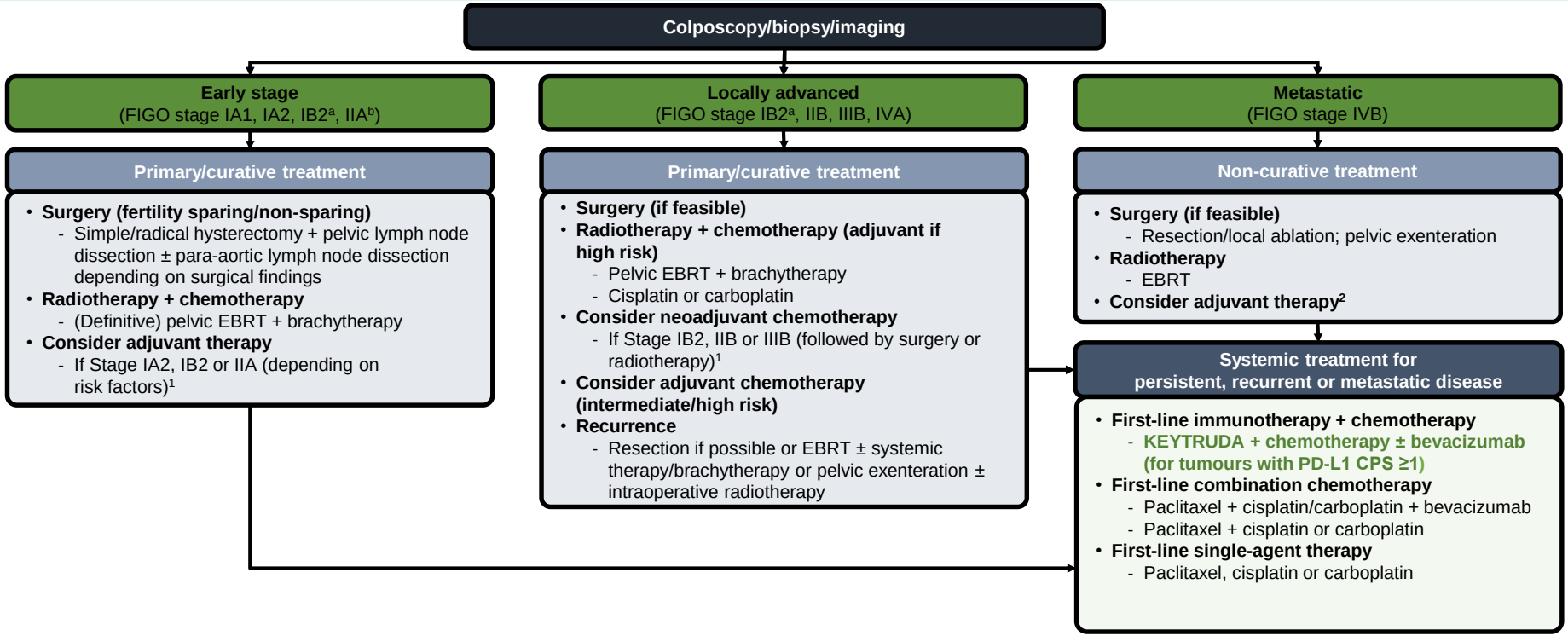
- Paclitaxel + cisplatin (or carboplatin) + bevacizumab
- Paclitaxel + cisplatin or carboplatin
- Topotecan + paclitaxel ± bevacizumab

ECOG PS, Eastern Cooperative Oncology Group performance status; FIGO, International Federation of Gynecology and Obstetrics.

1. Reed N et al. *Eur J Obstet Gynecol Reprod Biol* 2021;256:433–465; 2. Marth C et al. *Ann Oncol* 2017;28:iv72–iv83.

Prescribing Information: GB; NI

Current treatment pathway by FIGO staging in cervical cancer[1–4]



[a]FIGO stage IB2 appears in both early-stage and locally advanced treatment arms in ESMO guidelines; [b]For patients with FIGO stage IIA1 disease, NCCN does not recommend a fertility-sparing option.
CPS, combined positive score; EBRT, external beam radiation therapy; ESMO, European Society for Medical Oncology; FIGO, International Federation of Gynecology and Obstetrics; NCCN, National Comprehensive Cancer Network; NICE, National Institute for Health and Care Excellence; PD-L1, programmed death ligand-1.

1. Marth C et al. *Ann Oncol* 2017;28:iv72–iv83; 2. Reed N et al. *Eur J Obstet Gynecol Reprod Biol* 2021;256:433–465; 3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Cervical Cancer V1.2022. Available at: https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1426. Accessed June 2023; 4. NICE. Available at: https://www.nice.org.uk/guidance/gid-ta10669/documents/final-scope. Accessed June 2023.

Prescribing Information: GB; NI

KEYNOTE-826: Overview and study design

Click the links below to navigate to the section of interest

Study design

Key characteristics of patients treated with KEYTRUDA + chemo ± bev

Baseline characteristics in the ITT population

Bev, bevacizumab; Chemo, chemotherapy; ITT, intention to treat.

Patient eligibility

RECIST v1.1

- Measurable disease according to RECIST v1.1

Diagnosis

- Persistent, recurrent or metastatic adenocarcinoma, adenosquamous carcinoma, or squamous cell carcinoma of the cervix

PD-L1 status

- Provided a newly obtained biopsy (preferred) or archival tumour tissue sample collected from a nonirradiated lesion for determination of PD-L1 status

Female ≥18 years old

Previous treatment

- No previous treatment with systemic chemotherapy and not amenable to curative treatment
- Previous radiotherapy, including chemoradiotherapy, was permitted if it was completed at least 2 weeks before randomisation and all associated toxic effects had resolved with a 1-week washout period

Organ function

- Adequate organ function as indicated by set laboratory values within 14 days prior to randomisation

ECOG PS

- ECOG PS of 0 or 1

Please refer to Colombo N et al. 2021 for the full patient eligibility criteria.
ECOG PS, Eastern Cooperative Oncology Group performance status; PD-L1, programmed death ligand-1; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1,
Colombo N et al. *N Engl J Med* 2021;385:1856–1867 (plus supplementary materials).

Prescribing Information: GB; NI

KEYNOTE-826: Study design

Randomised, double-blind, placebo-controlled Phase 3 study — published in the New England journal of medicine

Key eligibility criteria
- Age ≥18 years
- Persistent, recurrent or metastatic cervical cancer not amenable to curative treatment
- No prior systemic chemotherapy **(prior radiotherapy and chemoradiotherapy permitted)**
- ECOG PS 0 or 1

Stratification factors
- Metastatic disease at diagnosis (yes vs no)
- PD-L1 CPS (<1 vs 1 to <10 vs ≥10)
- Planned bevacizumab use (yes vs no)

Endpoints
- Dual primary: OS and PFS per RECIST v1.1 by investigator review
- Secondary: ORR, DOR, 12-month PFS, safety
- Exploratory: PROs assessed by EuroQoL EQ-5D-5L VAS

R
1:1
(N=617)

(n=308)

KEYTRUDA 200 mg IV Q3W (up to 35 cycles)
+
Paclitaxel + cisplatin or carboplatin IV Q3W[a]
(up to 6 cycles)
±
Bevacizumab 15 mg/kg IV Q3W

(n=309)

Placebo IV Q3W (up to 35 cycles)
+
Paclitaxel + cisplatin or carboplatin IV Q3W[a]
(up to 6 cycles)
±
Bevacizumab 15 mg/kg IV Q3W

Disease progression or unacceptable toxicity

[a]Paclitaxel: 175 mg/m^2; cisplatin: 50 mg m^2; carboplatin: AUC 5 mg/mL/min. The 6-cycle limit was introduced by protocol amendment 2, although participants with ongoing clinical benefit who were tolerating chemotherapy could continue beyond 6 cycles after sponsor consultation.

AUC, area under the curve; CPS, combined positive score; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; ORR, objective response rate; OS, overall survival; PD-L1, programmed death ligand-1; PFS, progression-free survival; PRO, patient reported outcome; R, randomisation; RECIST, Response Evaluation Criteria in Solid Tumors; Q3W, every 3 weeks; VAS, visual analogue scale.

Colombo N et al. *N Engl J Med* 2021;385:1856–1867 (plus supplementary materials).

Prescribing Information: GB; NI

KEYNOTE-826: Key characteristics of patients treated with KEYTRUDA + chemotherapy ± bevacizumab

Total population: 617 patients (KEYTRUDA + chemotherapy ± bevacizumab [n=308] and placebo + chemotherapy ± bevacizumab [n=309])

Median age

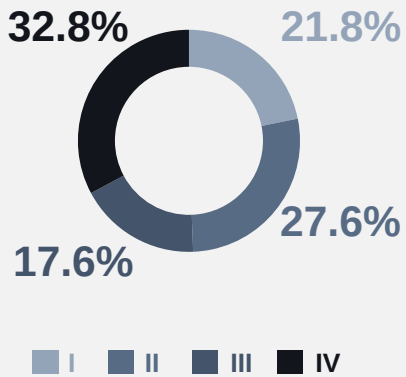
Range

25–82

years

Median 51 years

Stage



PD-L1 CPS

<1
11.4%

1 to <10
37.3%

≥10
51.3%

CPS, combined positive score; PD-L1, programmed death ligand-1.
Colombo N et al. *N Engl J Med* 2021;385:1856–1867 (plus supplementary materials).

Prescribing Information: GB; NI

KEYNOTE-826: Baseline characteristics in the ITT population (1)

Characteristic[a]	KEYTRUDA + chemo ± bev (n=308)[b]	Placebo + chemo ± bev (n=309)[b]
Age		
Range (median), years	25–82 (51)	22–79 (50)
≥65 years, n (%)	48 (15.6)	52 (16.8)
Race, no. (%)[c]		
White	170 (55.2)	190 (61.5)
Non-white	138 (44.8)	119 (38.5)
ECOG PS, n (%)		
0	178 (57.8)	170 (55.0)
1	128 (41.6)	139 (45.0)

Characteristic[a]	KEYTRUDA + chemo ± bev (n=308)[b]	Placebo + chemo ± bev (n=309)[b]
Stage at initial diagnosis (FIGO 2009/NCCN 2017 criteria), n (%)		
I	67 (21.8)	58 (18.8)
II	85 (27.6)	93 (30.1)
III	5 (1.6)	8 (2.6)
IIIA	4 (1.3)	8 (2.6)
IIIB	46 (14.9)	42 (13.6)
IVA	7 (2.3)	4 (1.3)
IVB	94 (30.5)	9 (31.1)

[a]The ITT population included all patients who underwent randomisation. Percentages may not total 100 because of rounding; [b]The assigned regimen in both groups also included paclitaxel, the investigator's choice of cisplatin or carboplatin, and per investigator discretion, bevacizumab; [c]Race was reported by the patient or the investigator according to local practice and where permitted by law; [d]In the KEYTRUDA group, one patient (0.3%) had an ECOG PS score of 2, and one patient (0.3%) had an unknown score.
Bev, bevacizumab; Chemo, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; FIGO, International Federation of Obstetrics and Gynecology; ITT, intention to treat; NCCN, National Comprehensive Cancer Network; PD-L1, programmed cell death ligand-1.
Colombo N et al. *N Engl J Med* 2021;385:1856–1867 (plus supplementary materials).

Prescribing Information: GB; NI

KEYNOTE-826: Baseline characteristics in the ITT population (2)

Characteristic[a]	KEYTRUDA + chemo ± bev (n=308)[b]	Placebo + chemo ± bev (n=309)[b]
Disease status at study entry, n (%)		
Metastatic[c]	58 (18.8)	64 (20.7)
Persistent or recurrent with distant metastases	199 (64.6)	179 (57.9)
Persistent or recurrent without distant metastases	51 (16.6)	66 (21.4)
Histologic type, n (%)[d]		
Adenocarcinoma	56 (18.2)	84 (27.2)
Adenosquamous carcinoma	15 (4.9)	14 (4.5)
Squamous cell carcinoma	235 (76.3)	211 (68.3)
PD-L1 CPS, n (%)[e]		
<1	35 (11.4)	34 (11.0)
≥ 1	273 (88.6)	275 (89)

Characteristic[a]	KEYTRUDA + chemo ± bev (n=308)[b]	Placebo + chemo ± bev (n=309)[b]
Prior therapy, n (%)		
Chemoradiation or radiation with surgery	71 (23.0)	79 (25.5)
Chemoradiation or radiation only	156 (50.7)	142 (46.0)
Surgery only	23 (7.5)	24 (7.8)
None	58 (18.8)	64 (20.7)
Bevacizumab use during the trial, n (%)		
Yes	196 (63.6)	193 (62.5)
No	112 (36.4)	116 (37.5)

[a]The ITT population included all patients who underwent randomisation. Percentages may not total 100 because of rounding; [b]The assigned regimen in both groups also included paclitaxel, the investigator's choice of cisplatin or carboplatin, and per investigator discretion, bevacizumab; [c]Includes patients with para-aortic lymph node involvement. These patients were diagnosed with Stage IVB disease and entered the study with no prior treatment for cervical cancer; [d]In the KEYTRUDA group, histologic type was recorded as epidermoid carcinoma for one patient (0.3%) and undifferentiated carcinoma for one patient (0.3%); [e]The PD-L1 CPS was defined as the number of PD-L1-staining cells (tumour cells, lymphocytes, and macrophages) divided by the total number of viable tumour cells, multiplied by 100.

Bev, bevacizumab; Chemo, chemotherapy; CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; FIGO, International Federation of Obstetrics and Gynecology; ITT, intention to treat; NCCN, National Comprehensive Cancer Network; PD-L1, programmed cell death ligand-1.

Colombo N et al. *N Engl J Med* 2021;385:1856–1867 (plus supplementary materials).

Prescribing Information: GB; NI

KEYNOTE-826: Results

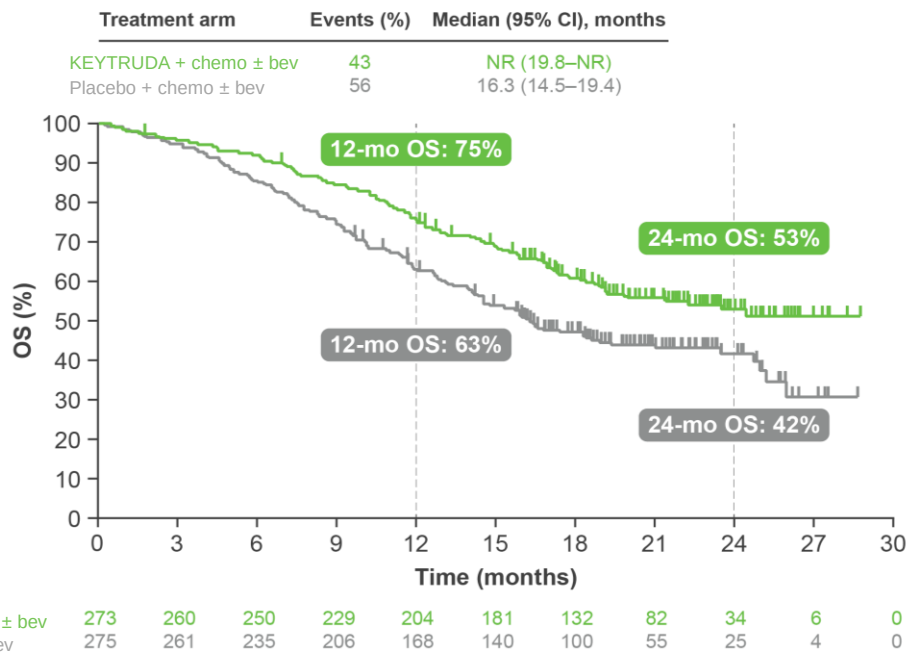
Click the links below to navigate to the section of interest

- Interim analysis: OS in the PD-L1 CPS ≥1 population
- Final analysis: OS in the PD-L1 CPS ≥1 population
- Final analysis: OS in the PD-L1 CPS ≥10 population
- Interim analysis: PFS in the PD-L1 CPS ≥1 population
- Final analysis: PFS in the PD-L1 CPS ≥1 population
- Final analysis: PFS in the PD-L1 CPS ≥10 population
- Response rates in the PD-L1 CPS ≥1 population
- Summary of AEs in the ITT population
- AEs with ≥20% incidence in either arm
- Immune-mediated AEs with ≥2% incidence in either arm

AE, adverse event; CPS, combined positive score; ITT, intention to treat; OS, overall survival; PD-L1, programmed death ligand-1; PFS, progression-free survival.

Prescribing Information: GB; NI

KEYNOTE-826: KEYTRUDA + chemotherapy ± bevacizumab presented superior OS vs placebo + chemotherapy ± bevacizumab in patients whose tumours express PD-L1 CPS ≥1 (interim analysis 1)[1,2]



A 36% reduction in the risk of death was presented with KEYTRUDA + chemotherapy ± bevacizumab vs placebo + chemotherapy ± bevacizumab in the PD-L1 CPS ≥1 population

HR: 0.64; 95% CI: 0.50–0.81; p<0.001

The forest plot for OS in key subgroups is shown in the appendix. Click here to view.

Analysis cut-off date: 3 May 2021.

Figure adapted from Colombo N et al. *N Engl J Med* 2021 and Colombo N et al. ESMO 2021.

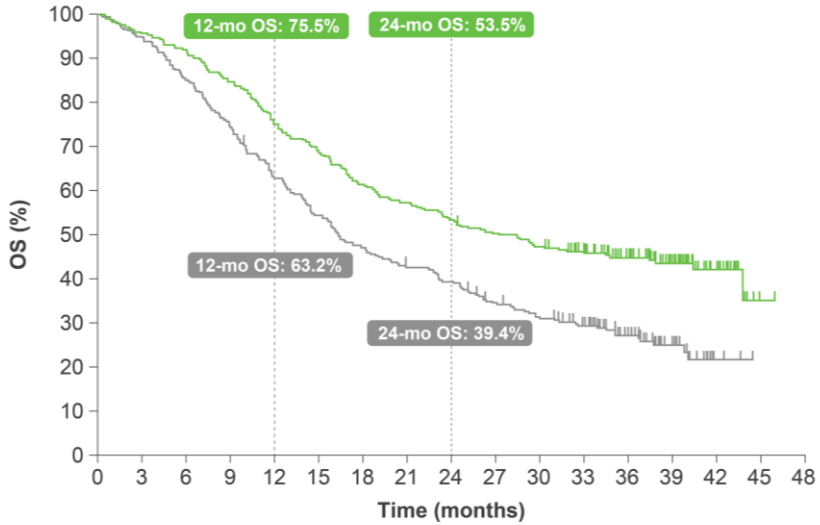
Bev, bevacizumab; Chemo, chemotherapy; CI, confidence interval; CPS, combined positive score; ESMO, European Society of Medical Oncology; HR, hazard ratio; mo, month; NR, not reached; OS, overall survival; PD-L1, programmed cell death ligand-1.

1. Colombo N et al. *N Engl J Med* 2021;385:1856–1867 (plus supplementary materials);
2. Colombo N et al. Presented at the ESMO Virtual Congress 2021, 16–21 September 2021.

Prescribing Information: GB; NI

KEYNOTE-826: OS – PD-L1 CPS ≥1 population (final analysis)

Treatment arm	Events (%)	Median (95% CI), months
KEYTRUDA + chemo ± bev	56.0%	28.6 (22.1–38.0)
Placebo + chemo ± bev	73.1%	16.5 (14.5–20.0)



No. at risk

KEYTRUDA + chemo ± bev	273	261	251	231	206	189	168	157	146	136	128	116	90	52	22	2	0
Placebo + chemo ± bev	275	261	235	207	173	149	129	117	107	91	81	68	45	24	3	0	0

A 40% reduction in the risk of death was presented with KEYTRUDA + chemotherapy ± bevacizumab vs placebo + chemotherapy ± bevacizumab in the PD-L1 CPS ≥1 population

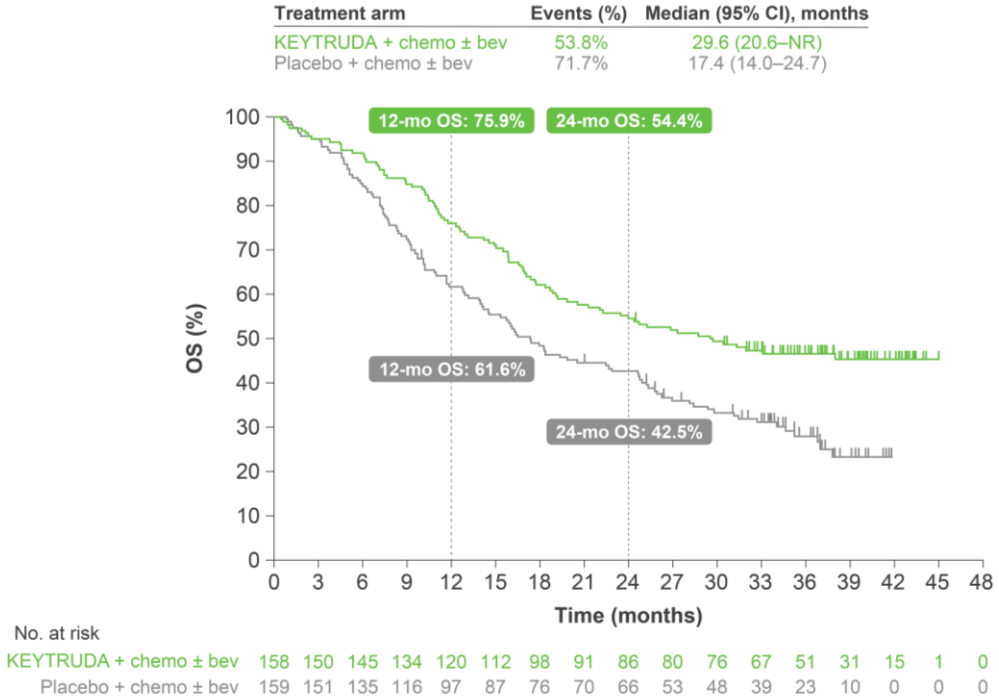
HR: 0.60; 95% CI: 0.49–0.74; nominal p<0.0001

No formal hypothesis testing was performed for the final analysis and all p-values are nominal as statistical significance was met for the primary endpoints in interim analysis 1

Analysis cut-off date: 3 October 2022.
Figure adapted from Monk B. ASCO 2023.
ASCO, American Society of Clinical Oncology; Bev, bevacizumab; Chemo, chemotherapy; CI, confidence interval; CPS, combined positive score; HR, hazard ratio; OS, overall survival; PD-L1, programmed death ligand-1.
Monk BJ et al. Presented at the ASCO Annual Meeting 2023, 2–6 June 2023, Chicago, USA.

Prescribing Information: GB; NI

KEYNOTE-826: OS – PD-L1 CPS ≥10 population (final analysis)



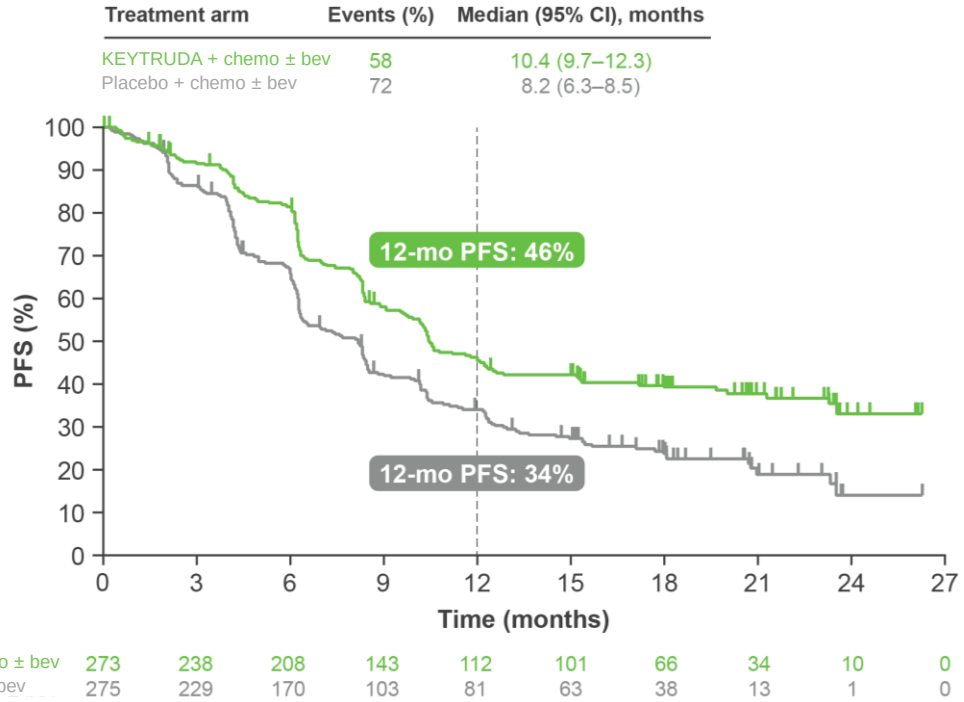
A 42% reduction in the risk of death was presented with KEYTRUDA + chemotherapy ± bevacizumab vs placebo + chemotherapy ± bevacizumab in the PD-L1 CPS ≥10 population

HR: 0.58; 95% CI: 0.44–0.78; nominal p<0.0001

No formal hypothesis testing was performed for the final analysis and all p-values are nominal as statistical significance was met for the primary endpoints in interim analysis 1

Analysis cut-off date: 3 October 2022.
Figure adapted from Monk B. ASCO 2023.
ASCO, American Society of Clinical Oncology; Bev, bevacizumab; Chemo, chemotherapy; CI, confidence interval; CPS, combined positive score; HR, hazard ratio; OS, overall survival; PD-L1, programmed death ligand-1.
Monk BJ et al. Presented at the ASCO Annual Meeting 2023, 2–6 June 2023, Chicago, USA.

KEYTRUDA + chemotherapy ± bevacizumab presented superior PFS vs placebo + chemotherapy ± bevacizumab in patients whose tumours express PD-L1 CPS ≥1 (interim analysis 1)[a,1,2]



A 38% reduction in the risk of disease progression or death was presented with KEYTRUDA + chemotherapy ± bevacizumab vs placebo + chemotherapy ± bevacizumab in the PD-L1 CPS ≥1 population

HR: 0.62; 95% CI: 0.50–0.77; p<0.001

The forest plot for PFS in key subgroups is shown in the appendix. Click here to view.

Analysis cut-off date: 3 May 2021.

Figure adapted from Colombo N et al. *N Engl J Med* 2021 (and supplementary appendix) and Colombo N et al. ESMO 2021.

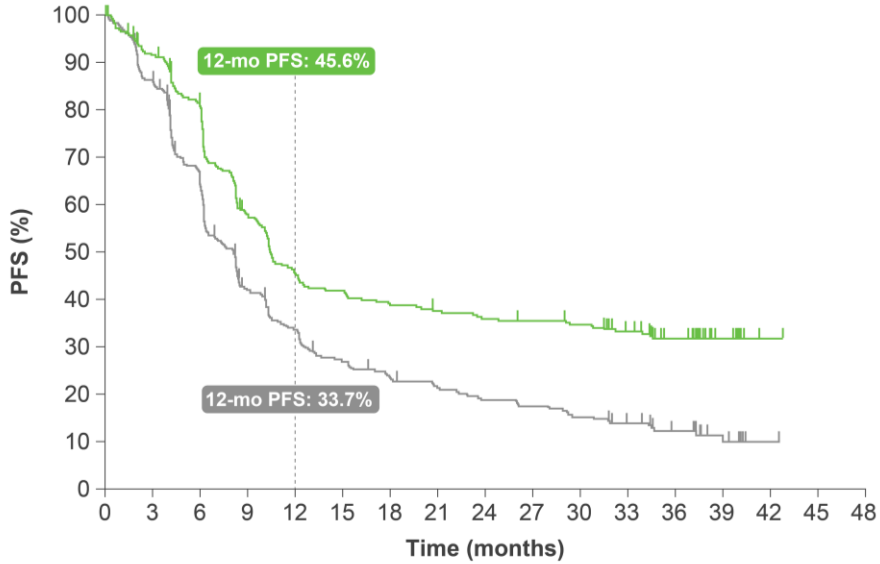
[a]Per RECIST v1.1 and investigator review. Bev, bevacizumab; Chemo, chemotherapy; CI, confidence interval; CPS, combined positive score; ESMO, European Society of Medical Oncology; HR, hazard ratio; mo, month; PD-L1, programmed cell death ligand-1; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors.

1. Colombo N et al. *N Engl J Med* 2021;385:1856–1867 (plus supplementary materials);
2. Colombo N et al. Presented at the ESMO Virtual Congress 2021, 16–21 September 2021.

Prescribing Information: GB; NI

KEYNOTE-826: PFS – PD-L1 CPS ≥1 population (final analysis)

Treatment arm	Events (%)	Median (95% CI), months
KEYTRUDA + chemo ± bev	62.6%	10.5 (9.7–12.3)
Placebo + chemo ± bev	80.0%	8.2 (6.3–8.5)



No. at risk																
KEYTRUDA + chemo ± bev	273	238	208	144	113	104	97	92	88	86	83	70	46	25	6	0	0
Placebo + chemo ± bev	275	229	170	103	81	64	55	49	43	40	35	28	18	7	2	0	0

A 42% reduction in the risk of disease progression or death was presented with KEYTRUDA + chemotherapy ± bevacizumab vs placebo + chemotherapy ± bevacizumab in the PD-L1 CPS ≥1 population

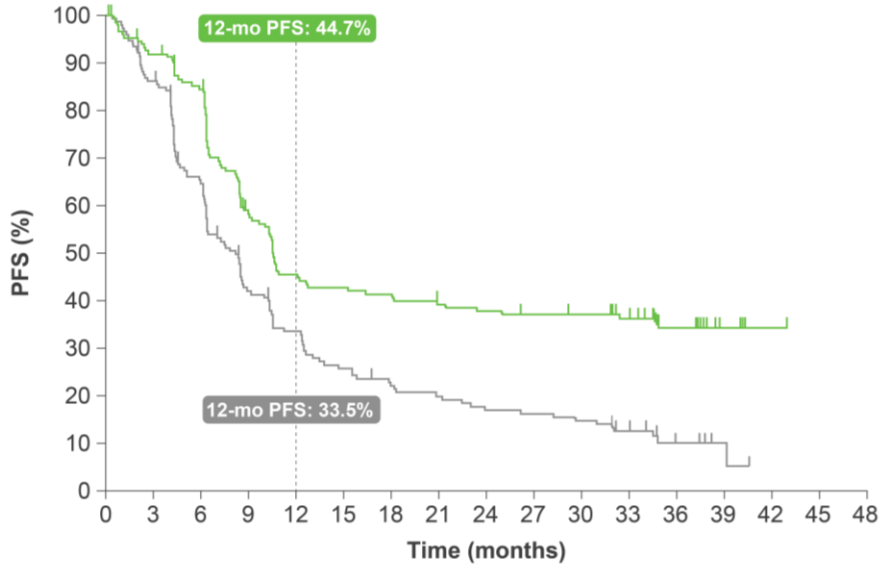
HR: 0.58; 95% CI: 0.47–0.71; nominal p<0.0001

No formal hypothesis testing was performed for the final analysis and all p-values are nominal as statistical significance was met for the primary endpoints in interim analysis 1

Analysis cut-off date: 3 October 2022.
Figure adapted from Monk B. ASCO 2023.
ASCO, American Society of Clinical Oncology; bev, bevacizumab; chemo, chemotherapy; CI, confidence interval; CPS, combined positive score; HR, hazard ratio; mo, months; PD-L1, programmed death ligand-1; PFS, progression-free survival.
Monk BJ et al. Presented at the ASCO Annual Meeting 2023, 2–6 June 2023, Chicago, USA.

KEYNOTE-826: PFS – PD-L1 CPS ≥10 population (final analysis)

Treatment arm	Events (%)	Median (95% CI), months
KEYTRUDA + chemo ± bev	59.5%	10.4 (8.9–15.1)
Placebo + chemo ± bev	81.8%	8.1 (6.2–8.8)



No. at risk																
KEYTRUDA + chemo ± bev	158	138	124	81	63	60	57	54	52	50	49	42	26	14	5	0	0
Placebo + chemo ± bev	159	131	95	60	47	36	30	27	23	22	20	13	6	1	0	0	0

A 48% reduction in the risk of disease progression or death was presented with KEYTRUDA + chemotherapy ± bevacizumab vs placebo + chemotherapy ± bevacizumab in the PD-L1 CPS ≥10 population

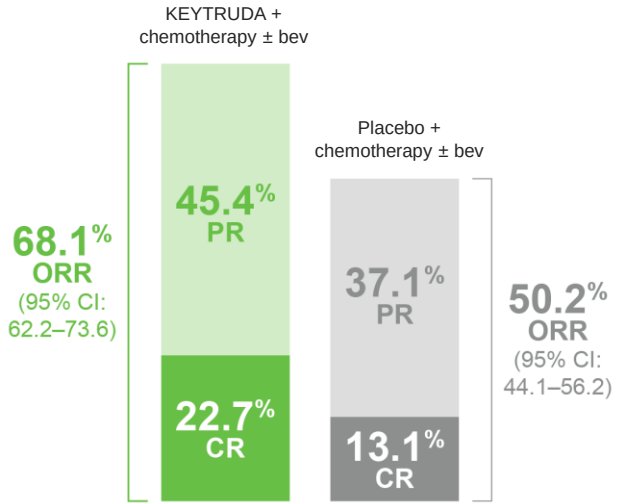
HR: 0.52; 95% CI: 0.40–0.68; nominal p<0.0001

No formal hypothesis testing was performed for the final analysis and all p-values are nominal as statistical significance was met for the primary endpoints in interim analysis 1

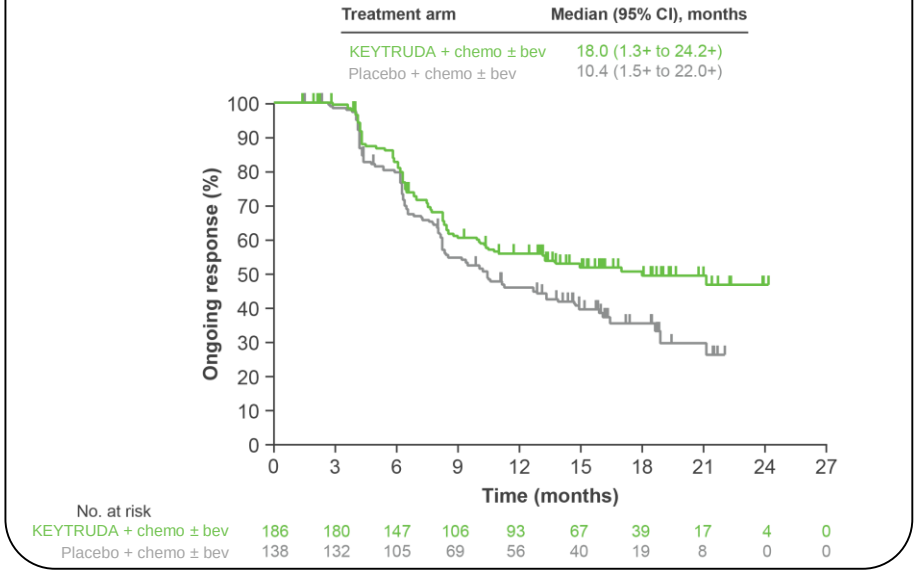
Analysis cut-off date: 3 October 2022.
Figure adapted from Monk B. ASCO 2023.
ASCO, American Society of Clinical Oncology; bev, bevacizumab; chemo, chemotherapy; CI, confidence interval; CPS, combined positive score; HR, hazard ratio; mo, months; PD-L1, programmed death ligand-1; PFS, progression-free survival.
Monk BJ et al. Presented at the ASCO Annual Meeting 2023, 2–6 June 2023, Chicago, USA.

KEYNOTE-826: ORR and DOR in the PD-L1 CPS≥1 population (interim analysis 1)

68% of patients whose tumours expressed PD-L1 CPS ≥1 achieved an objective response with KEYTRUDA + chemotherapy ± bevacizumab vs 50% of patients receiving placebo + chemotherapy ± bevacizumab



Median DOR was 18.0 months (95% CI: 1.3+ to 24.2+) with KEYTRUDA + chemotherapy ± bevacizumab vs 10.4 months (95% CI: 1.5+ to 22.0+) with placebo + chemotherapy ± bevacizumab



Analysis cut-off date: 3 May 2021.

Figure adapted from Colombo N et al. *N Engl J Med* 2021 (and supplementary appendix).

Bev, bevacizumab; Chemo, chemotherapy; CI, confidence interval; CPS, combined positive score; CR, complete response; DOR, duration of response; ORR, objective response rate; PD-L1, programmed cell death ligand-1; PR, partial response.

Colombo N et al. *N Engl J Med* 2021;385:1856–1867 (plus supplementary materials).

Prescribing Information: GB; NI

KEYNOTE-826: Summary of AEs in the ITT population (interim analysis 1)

AE, n (%)	All-cause AEs		TRAEs[a]		Immune-mediated AEs[b]	
	KEYTRUDA + chemo ± bev (n=307)	Placebo + chemo ± bev (n=309)	KEYTRUDA + chemo ± bev (n=307)	Placebo + chemo ± bev (n=309)	KEYTRUDA + chemo ± bev (n=307)	Placebo + chemo ± bev (n=309)
Any grade	305 (99.3)	307 (99.4)	298 (97.1)	300 (97.1)	104 (33.9)	47 (15.2)
Grade ≥3	251 (81.8)	232 (75.1)	210 (68.4)	198 (64.1)	35 (11.4)	9 (2.9)
Serious	153 (49.8)	131 (42.4)	93 (30.3)	71 (23.0)	22 (7.2)	7 (2.3)
Led to death	14 (4.6)	14 (4.5)	2 (0.7)[c]	4 (1.3)[c]	1 (0.3)[c]	0
Led to discontinuation						
Any treatment	115 (37.5)	82 (26.5)	96 (31.3)	69 (22.3)	16 (5.2)	1 (0.3)
All treatment	18 (5.9)	15 (4.9)	10 (3.3)	6 (1.9)	3 (1.0)	0

These data comprise the full ITT population. Please note that the licensed indication for KEYTRUDA is in combination with chemotherapy with or without bevacizumab for the treatment of persistent, recurrent or metastatic cervical cancer in adults whose tumours express **PD-L1 CPS ≥1.**

Click here to access the irAE slide deck for adverse event management of KEYTRUDA + chemotherapy combinations.
Further information on the safety of KEYTRUDA + chemotherapy combinations can be found in the GB SmPC here or NI SmPC here.

Analysis cut-off date: 3 May 2021.

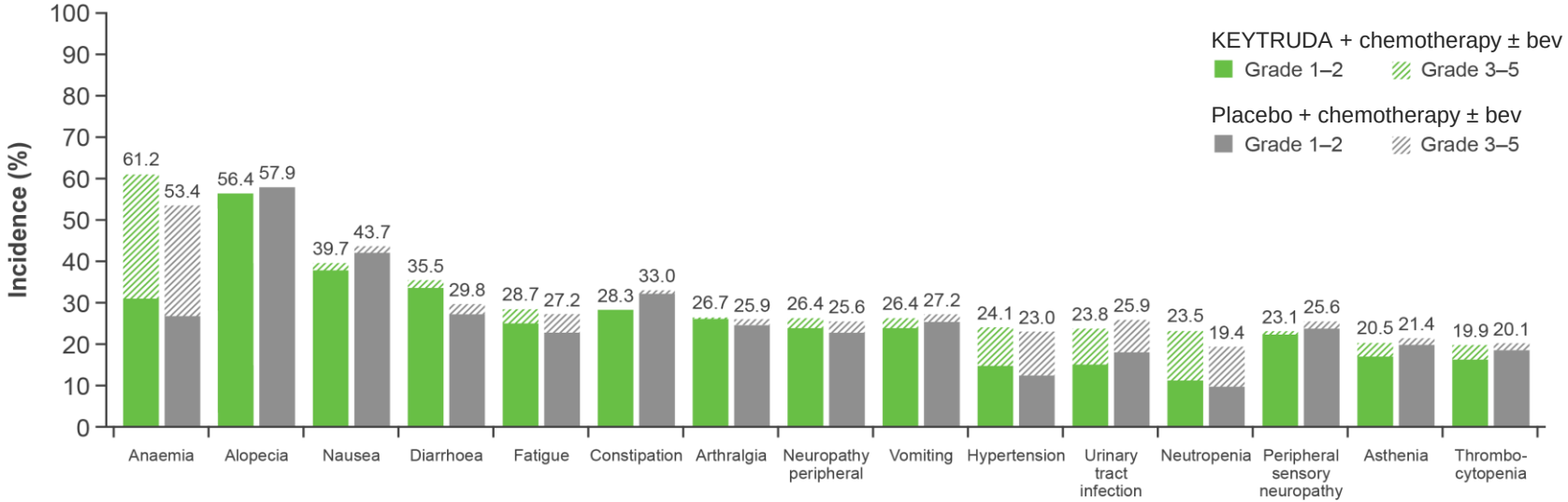
Table adapted from Colombo N et al. *N Engl J Med* 2021 (and supplementary appendix) and Colombo N et al. ESMO 2021.

[a]Per investigator assessment; [b]Events were considered regardless of attribution to treatment; [c]Autoimmune encephalitis (also immune mediated) and intestinal perforation; embolism, female genital tract fistula, large intestine perforation and pulmonary sepsis. AE, adverse event; Bev, bevacizumab; Chemo, chemotherapy; CPS, combined positive score; ESMO, European Society of Medical Oncology; ITT, intention to treat; irAE, immune-related AE; PD-L1, programmed death ligand-1; SmPC, Summary of Product Characteristics; TRAE, treatment-related AE.

Colombo N et al. *N Engl J Med* 2021;385:1856–1867 (plus supplementary materials).

Prescribing Information: GB; NI

KEYNOTE-826: AEs with ≥20% incidence in either arm (interim analysis 1)



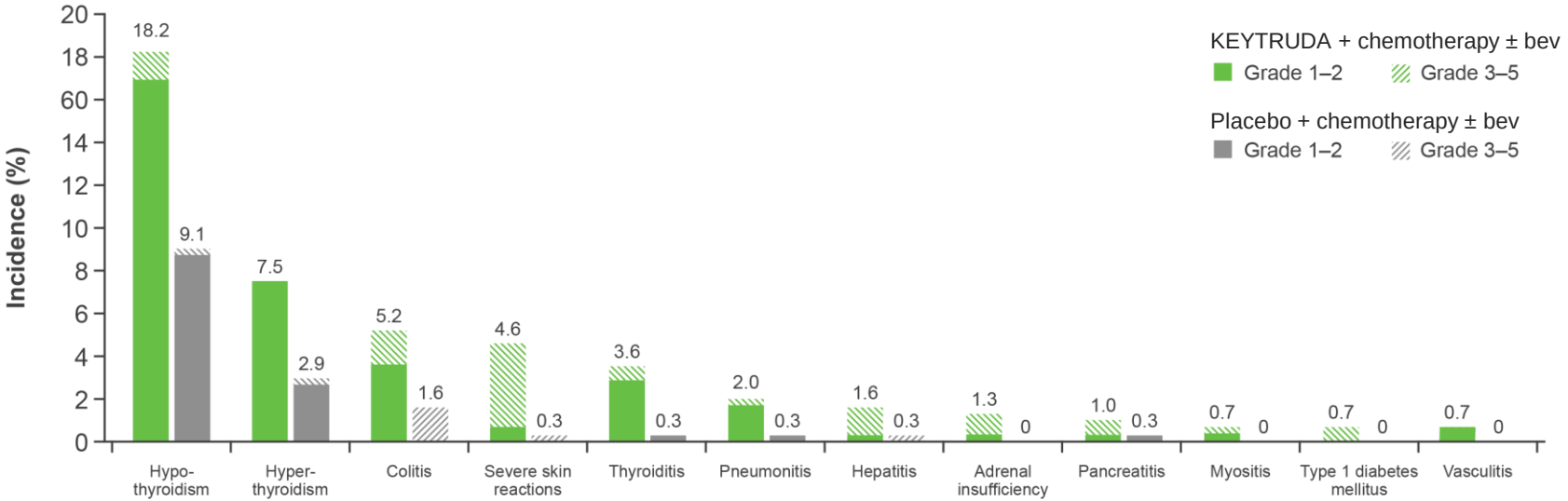
These data comprise the full ITT population. Please note that the licensed indication for KEYTRUDA is in combination with chemotherapy with or without bevacizumab for the treatment of persistent, recurrent or metastatic cervical cancer in adults whose tumours express **PD-L1 CPS ≥1.**

Click here to access the irAE slide deck for adverse event management of KEYTRUDA + chemotherapy combinations.
Further information on the safety of KEYTRUDA + chemotherapy combinations can be found in the GB SmPC here or NI SmPC here.

Analysis cut-off date: 3 May 2021.
Figure adapted from Colombo N et al. *N Engl J Med* 2021.
AE, adverse event; Bev, bevacizumab; CPS, combined positive score; Chemo, chemotherapy; irAE, immune-related AE; ITT, intention to treat; PD-L1, programmed death ligand-1; SmPC, Summary of Product Characteristics.
Colombo N et al. *N Engl J Med* 2021;385:1856–1867 (plus supplementary materials).

Prescribing Information: GB; NI

KEYNOTE-826: Immune-mediated AEs with ≥1% incidence in either arm (interim analysis 1)[a]



These data comprise the full ITT population. Please note that the licensed indication for KEYTRUDA is in combination with chemotherapy with or without bevacizumab for the treatment of persistent, recurrent or metastatic cervical cancer in adults whose tumours express **PD-L1 CPS ≥1.**

Click here to access the irAE slide deck for adverse event management of KEYTRUDA + chemotherapy combinations.
Further information on the safety of KEYTRUDA + chemotherapy combinations can be found in the GB SmPC here or NI SmPC here.

Analysis cut-off date: 3 May 2021.

Figure adapted from Colombo N et al. *N Engl J Med* 2021 (and supplementary appendix).

[a]Events were considered regardless of attribution to treatment by the investigator. Related terms were included in additional to the specific terms listed.

AE, adverse event; Bev, bevacizumab; CPS, combined positive score; Chemo, chemotherapy; irAE, immune-related AE; ITT, intention to treat; PD-L1, programmed death ligand-1; SmPC, Summary of Product Characteristics.

Colombo N et al. *N Engl J Med* 2021;385:1856–1867 (plus supplementary materials).

Prescribing Information: GB; NI

KEYNOTE-826: Implementing KEYTRUDA + chemotherapy +/- bevacizumab for the treatment of persistent, recurrent or metastatic cervical

Click the links below to navigate to the section of interest

KEYTRUDA dosing

PD-L1 testing in metastatic cervical cancer

PD-L1, programmed death ligand-1.

KEYTRUDA dosing

Administered as an IV infusion

Over 30 minutes

Adults: 200 mg

Adults: 400 mg

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

For further information on KEYTRUDA dosing, please refer to the SmPC: Great Britain, Northern Ireland

AE, adverse event; IV, intravenous; SmPC, Summary of Product Characteristics.
KEYTRUDA (pembrolizumab) SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/keytruda-epar-product-information_en.pdf. Accessed June 2023.

Prescribing Information: GB; NI

KEYTRUDA license requires CPS ≥1[1,2]

CPS: A snapshot of the tumour microenvironment

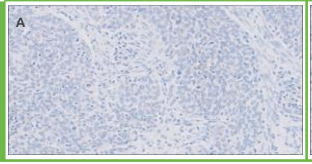
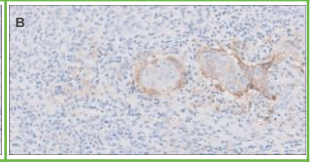
- CPS is used to evaluate PD-L1 expression in tumour cells and certain immune cells in cervical cancer[1]
- This helps to identify the most appropriate treatment for patients[1]
- In KEYNOTE-826, PD-L1 expression was assessed by CPS using the PD-L1 22C3 IHC pharmDx assay[2]
- The PD-L1 22C3 IHC pharmDx assay, scored using the CPS algorithm, is used to define eligibility for treatment with KEYTRUDA + chemotherapy ± bevacizumab with the eligibility for KEYTRUDA use being CPS ≥1[1]

Calculating CPS[1]

$$\text{CPS} = \frac{\text{\#PD-L1 staining cells (tumour cells, lymphocytes, macrophages)}}{\text{Total \#viable tumour cells}} \times 100$$

Although the result of the calculation can exceed 100, the maximum score is defined as CPS 100

CPS for cervical cancer[1]

PD-L1 expression level	CPS <1	CPS ≥1
Stained with PD-L1 22C3 pharmDx primary antibody (×20)		

Cervical cancer specimen stained with PD-L1 22C3 pharmDx primary antibody exhibiting CPS <1 (A) and CPS ≥1 (B). Both images were taken at ×20 magnification.

For further information on CPS testing, click here

CPS, combined positive score; IHC, immunohistochemistry; PD-L1, programmed death ligand-1.

1. PD-L1 IHC 22C3 pharmDx interpretation manual – Cervical cancer. Agilent Dako. Available at: https://www.agilent.com/cs/library/usermanuals/public/29257_22c3_pharmDx_cervical_interpretation_manual_us.pdf. Accessed June 2023; 2. Colombo N et al. *N Engl J Med* 2021;385:1856–1867 (plus supplementary materials).

Prescribing Information: GB; NI

KEYNOTE-826: Summary

KEYNOTE-826: Summary of efficacy and safety outcomes in the PD-L1 CPS ≥1 population[1,2]

KEYTRUDA + chemotherapy ± bevacizumab showed statistically significant and clinically meaningful improvements in OS and PFS vs placebo + chemotherapy ± bevacizumab in patients with persistent, recurrent or metastatic cervical cancer with PD-L1 CPS ≥1[1,2]

89% of patients with persistent, recurrent or metastatic cervical cancer had a PD-L1 CPS ≥1 in KEYNOTE-826

KEYTRUDA + chemotherapy ± bevacizumab presented superior OS vs placebo + chemotherapy ± bevacizumab in patients with PD-L1 CPS ≥1 (HR: 0.60; 95% CI: 0.49–0.74; nominal p<0.0001)[2]

Statistical significance was met for the primary endpoints in interim analysis 1 (2021)

KEYTRUDA + chemotherapy ± bevacizumab presented superior PFS vs placebo + chemotherapy ± bevacizumab in patients with PD-L1 CPS ≥1 (HR: 0.58; 95% CI: 0.47–0.71; nominal p<0.0001)[2]

Statistical significance was met for the primary endpoints in interim analysis 1 (2021)

Grade ≥3 AEs occurred in 81.8% of patients in the KEYTRUDA + chemotherapy ± bevacizumab arm and 75.1% of patients in the placebo + chemotherapy ± bevacizumab arm[1]

Of those treated, patients in the KEYTRUDA + chemotherapy ± bevacizumab arm had a higher proportion of discontinuations of any trial agent (37.5%) compared with the placebo + chemotherapy ± bevacizumab arm (26.5%)

Immune-mediated AEs occurred more frequently in patients who received KEYTRUDA + chemotherapy ± bevacizumab (33.9%) compared with those receiving placebo + chemotherapy ± bevacizumab (15.2%)

AE, adverse event; CI, confidence interval; CPS, combined positive score; HR, hazard ratio; OS, overall survival; PD-L1, programmed death ligand-1; PFS, progression-free survival.

1. Colombo N et al. *N Engl J Med* 2021;385:1856–1867 (plus supplementary materials);
2. Monk BJ et al. Presented at the ASCO Annual Meeting 2023, 2–6 June 2023, Chicago, USA.

Prescribing Information: GB; NI

KEYNOTE-826: Appendix

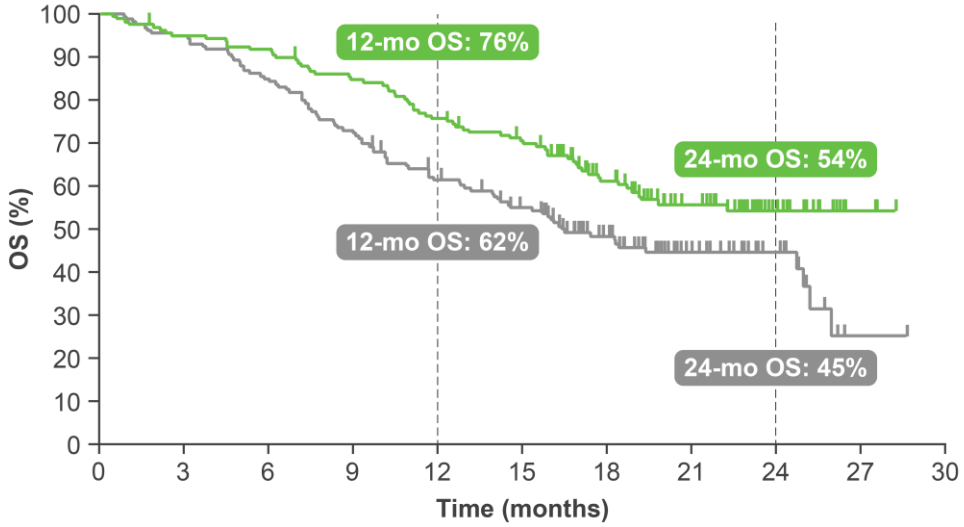
Click the links below to navigate to the section of interest

- OS in the ITT population
- OS in the PD-L1 CPS ≥10 population
- OS in key subgroups of the ITT population
- PFS in the ITT population
- PFS in the PD-L1 CPS ≥10 population
- PFS in key subgroups of the ITT population

CPS, combined positive score; ITT, intention to treat; OS, overall survival; PD-L1, programmed death ligand-1; PFS, progression-free survival.

KEYNOTE-826: KEYTRUDA + chemotherapy ± bevacizumab demonstrated superior OS vs placebo + chemotherapy ± bevacizumab in patients whose tumours express PD-L1 CPS ≥10 (interim analysis 1)[1,2]

Treatment arm	Events (%)	Median (95% CI), months
KEYTRUDA + chemo ± bev	42	NR (19.1–NR)
Placebo + chemo ± bev	55	16.5 (14.0–25.0)



No. at risk											
KEYTRUDA + chemo ± bev	158	149	144	132	118	106	76	46	21	3	0
Placebo + chemo ± bev	159	151	135	116	95	81	56	31	15	1	0

A 39% reduction in the risk of death was observed with KEYTRUDA + chemotherapy ± bevacizumab vs placebo + chemotherapy ± bevacizumab in the PD-L1 CPS ≥10 population

HR: 0.61; 95% CI: 0.44–0.84; p=0.001

Analysis cut-off date: 3 May 2021.

Figure adapted from Colombo N et al. *N Engl J Med* 2021 and Colombo N et al. ESMO 2021.

Bev, bevacizumab; Chemo, chemotherapy; CI, confidence interval; CPS, combined positive score; ESMO, European Society of Medical Oncology; HR, hazard ratio; mo, month; NR, not reached; OS, overall survival; PD-L1, programmed death ligand-1.

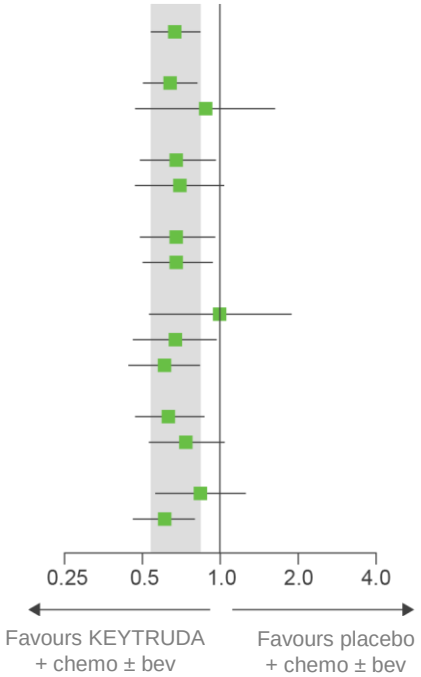
1. Colombo N et al. *N Engl J Med* 2021;385:1856–1867 (plus supplementary materials);
2. Colombo N et al. Presented at the ESMO Virtual Congress 2021, 16–21 September 2021.

Prescribing Information: GB; NI

KEYNOTE-826: OS in key subgroups (interim analysis 1)

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

Subgroup	No. of events/No. of patients	Hazard ratio (95% CI)
Overall	312/617	0.67 (0.54–0.84)
Age, yr		
<65	265/517	0.64 (0.50–0.82)
≥65	47/100	0.88 (0.47–1.64)
Race		
White	189/360	0.68 (0.50–0.91)
All others	107/221	0.70 (0.47–1.04)
ECOG PS		
0	141/348	0.68 (0.49–0.96)
1	169/267	0.68 (0.50–0.94)
PD-L1 CPS		
<1	40/69	1.00 (0.53–1.89)
1 to <10	118/231	0.67 (0.46–0.97)
≥10	154/317	0.61 (0.44–0.84)
Concomitant bevacizumab		
Yes	166/389	0.63 (0.47–0.87)
No	146/228	0.74 (0.53–1.04)
Metastatic disease at diagnosis		
Yes	104/190	0.84 (0.56–1.26)
No	208/427	0.61 (0.46–0.80)



Analysis cut-off date: 3 May 2021.

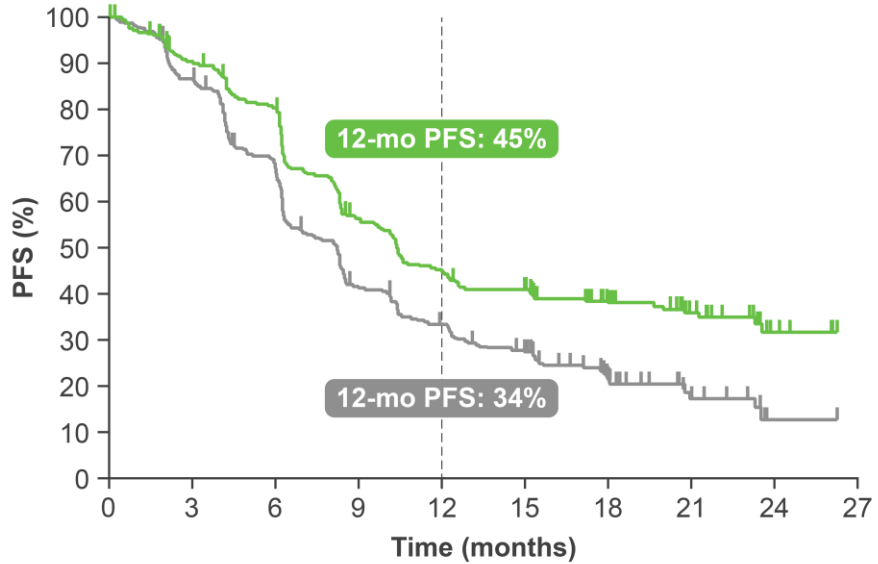
Bev, bevacizumab; Chemo, chemotherapy; CI, confidence interval; CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; ITT, intention to treat; OS, overall survival; PD-L1, programmed death ligand-1; yr, years.

Colombo N et al. *N Engl J Med* 2021;385:1856–1867 (plus supplementary materials).

Prescribing Information: GB; NI

KEYNOTE-826: KEYTRUDA + chemotherapy ± bevacizumab demonstrated superior PFS vs placebo + chemotherapy ± bevacizumab (interim analysis 1)[1,2]

Treatment arm	Events (%)	Median (95% CI), months
KEYTRUDA + chemo ± bev	58	10.4 (9.1–12.1)
Placebo + chemo ± bev	73	8.2 (6.4–8.4)



No. at risk										
KEYTRUDA + chemo ± bev	308	263	229	155	123	110	70	35	10	0
Placebo + chemo ± bev	309	259	195	113	89	71	39	13	1	0

A 35% reduction in the risk of disease progression or death was observed with KEYTRUDA + chemotherapy ± bevacizumab vs placebo + chemotherapy ± bevacizumab

HR: 0.65; 95% CI: 0.53–0.79; p<0.001

Analysis cut-off date: 3 May 2021.

Figure adapted from Colombo N et al. *N Engl J Med* and Colombo N et al. ESMO 2021.

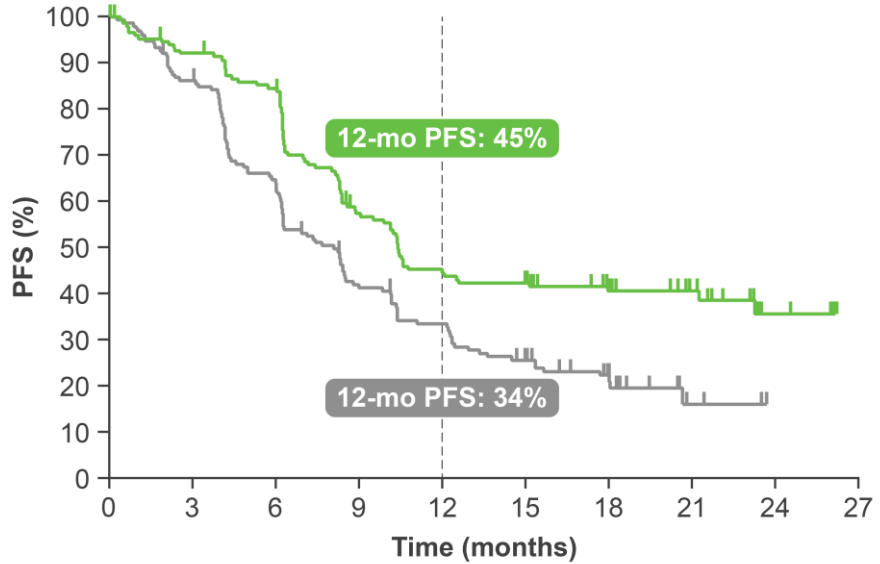
Bev, bevacizumab; Chemo, chemotherapy; CI, confidence interval; ESMO, European Society of Medical Oncology; HR, hazard ratio; ITT, intention to treat; mo, month; PFS, progression-free survival.

1. Colombo N et al. *N Engl J Med* 2021;385:1856–1867 (plus supplementary materials);
2. Colombo N et al. Presented at the ESMO Virtual Congress 2021, 16–21 September 2021.

Prescribing Information: GB; NI

KEYNOTE-826: KEYTRUDA + chemotherapy ± bevacizumab demonstrated superior PFS vs placebo + chemotherapy ± bevacizumab in patients whose tumours express PD-L1 CPS ≥10 (interim analysis 1)[1,2]

Treatment arm	Events (%)	Median (95% CI), months
KEYTRUDA + chemo ± bev	55	10.4 (8.9–15.1)
Placebo + chemo ± bev	73	8.1 (6.2–8.8)



No. at risk										
KEYTRUDA + chemo ± bev	158	138	124	80	62	58	35	21	7	0
Placebo + chemo ± bev	159	131	95	60	47	35	19	3	0	0

A 42% reduction in the risk of disease progression or death was observed with KEYTRUDA + chemotherapy ± bevacizumab vs placebo + chemotherapy ± bevacizumab in the PD-L1 CPS ≥10 population

HR: 0.58; 95% CI: 0.44–0.77; p<0.001

Analysis cut-off date: 3 May 2021.
Figure adapted from Colombo N et al. *N Engl J Med* 2021 and Colombo N et al. ESMO 2021.
Bev, bevacizumab; Chemo, chemotherapy; CI, confidence interval; CPS, combined positive score; ESMO, European Society of Medical Oncology; HR, hazard ratio; ITT, intention to treat; PD-L1, programmed death ligand-1; PFS, progression-free survival.

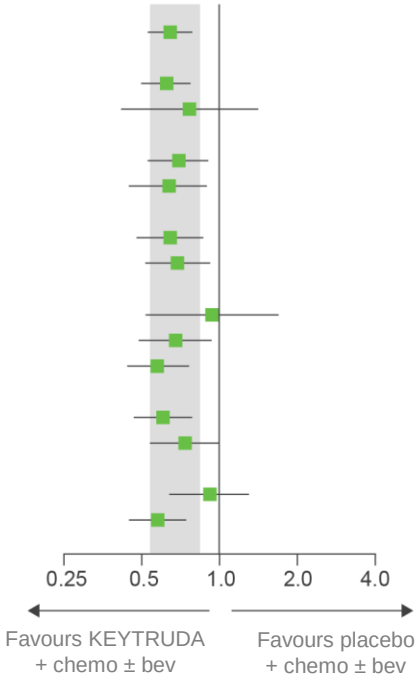
1. Colombo N et al. *N Engl J Med* 2021;385:1856–1867 (plus supplementary materials);
2. Colombo N et al. Presented at the ESMO Virtual Congress 2021, 16–21 September 2021.

Prescribing Information: GB; NI

KEYNOTE-826: PFS in key subgroups (interim analysis 1)

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

Subgroup	No. of events/No. of patients	Hazard ratio (95% CI)
Overall	406/617	0.65 (0.53–0.79)
Age, yr		
<65	345/517	0.63 (0.50–0.78)
≥65	61/100	0.77 (0.42–1.42)
Race		
White	238/360	0.70 (0.53–0.91)
All others	139/221	0.64 (0.45–0.90)
ECOG PS		
0	197/348	0.65 (0.48–0.87)
1	207/267	0.69 (0.52–0.93)
PD-L1 CPS		
<1	51/69	0.94 (0.52–1.70)
1 to <10	152/231	0.68 (0.49–0.94)
≥10	203/317	0.58 (0.44–0.77)
Concomitant bevacizumab		
Yes	234/389	0.61 (0.47–0.79)
No	172/228	0.74 (0.54–1.01)
Metastatic disease at diagnosis		
Yes	137/190	0.92 (0.64–1.30)
No	269/427	0.58 (0.45–0.75)



Analysis cut-off date: 3 May 2021.

Bev, bevacizumab; Chemo, chemotherapy; CI, confidence interval; CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; PD-L1, programmed death ligand-1; PFS, progression-free survival; yr, year.

Colombo N et al. *N Engl J Med* 2021;385:1856–1867 (plus supplementary materials).

Prescribing Information: GB; NI