MSD Oncology

KEYTRUDA® (pembrolizumab) in combination with chemotherapy for the treatment of locally recurrent unresectable or metastatic triple-negative breast cancer (TNBC) in adults whose tumours express PD-L1 with a CPS ≥10 and who have not received prior chemotherapy for metastatic disease

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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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Job code: GB-PDO-02750 Date of preparation: June 2023

MSD

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TNBC, triple-negative breast cancer.

Prescribing information: GB, NI

Overview of KEYTRUDA plus chemotherapy in metastatic TNBC

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KEYTRUDA plus chemotherapy in advanced TNBC

KEYTRUDA funding and licence

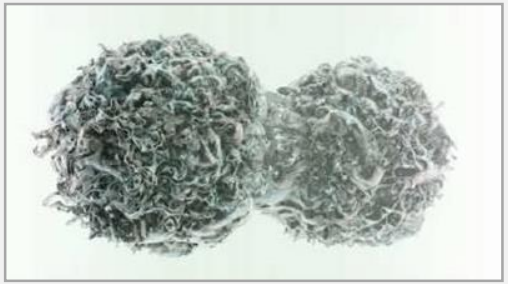
Potential treatment landscape in first-line advanced TNBC

Prescribing information: GB, NI

KEYTRUDA plus chemotherapy in advanced TNBC: Dual mechanisms of action

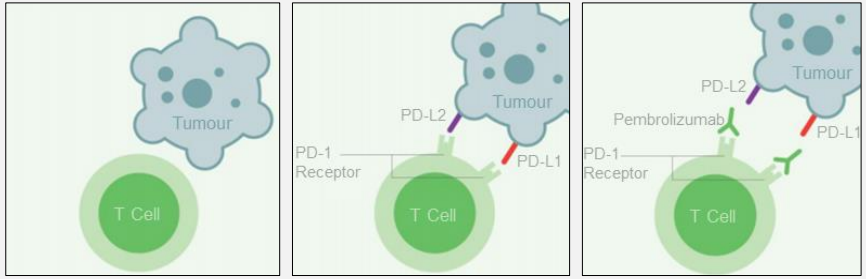
Chemotherapy targets proliferating cells[1,2]

- 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 antitumour 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 plus chemotherapy, click here

Please note that clicking this link will redirect you to the promotional MSD Connect website.

PD-1, programmed cell death protein-1; PD-L1, programmed death ligand-1; PD-L2, programmed death ligand-2; SmPC, Summary of Product Characteristics; TNBC, triple-negative breast cancer.

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

KEYTRUDA funding and licence

NICE guidelines recommends KEYTRUDA plus chemotherapy (paclitaxel or nab-paclitaxel) as an option for treating triple-negative, locally recurrent unresectable or metastatic breast cancer in adults who have not received prior chemotherapy for metastatic disease.[1]

It is only recommended if:[1]

- **The tumours express PD-L1 CPS ≥10 and IC staining <1%**
- **The company provides KEYTRUDA according to the commercial arrangement**

KEYTRUDA, in combination with chemotherapy, is indicated for the treatment of locally recurrent unresectable or metastatic TNBC in adults whose tumours express PD-L1 with a CPS ≥10 and who have not received prior chemotherapy for metastatic disease[2]

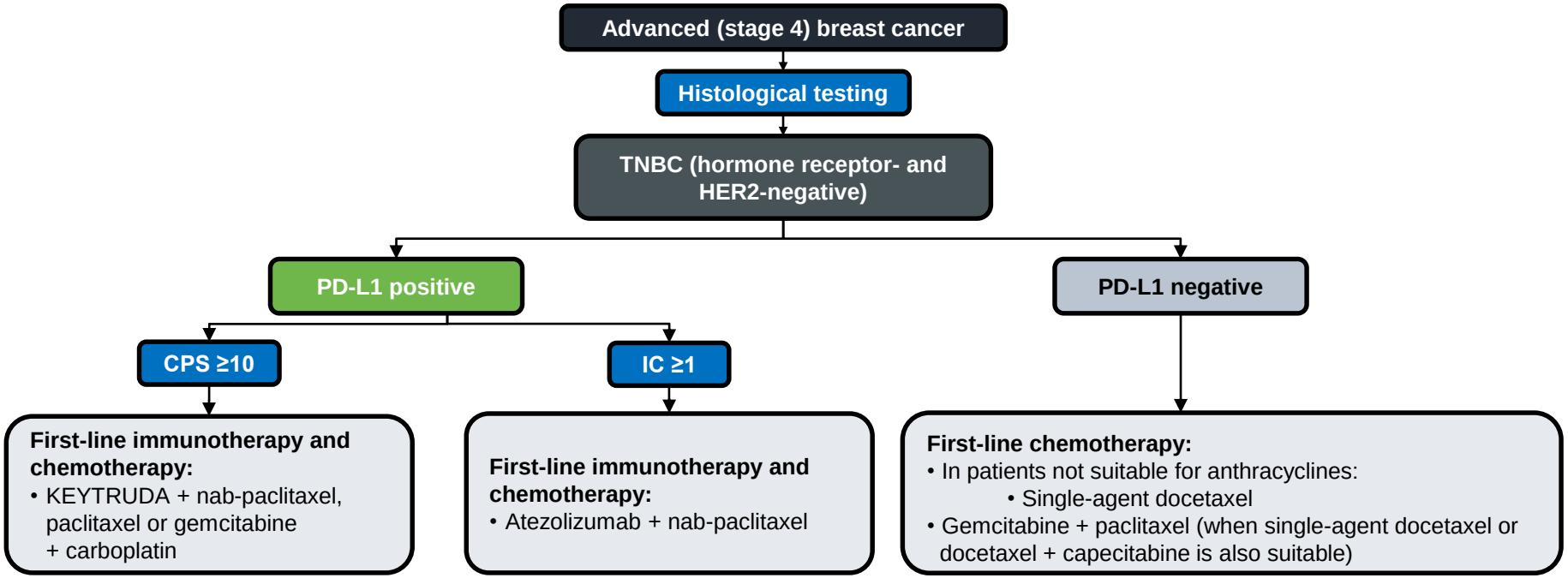
Click here for more information on CPS testing of PD-L1 expression in TNBC

1L, First-line; CPS, combined positive score; EMA, European Medicines Agency; IC, immune cell; MHRA, Medicines and Healthcare products Regulatory Agency; NICE, National Institute for Health and Care Excellence; PD-L1, programmed death ligand-1; TNBC, triple-negative breast cancer.

1. NICE Pembrolizumab plus chemotherapy for untreated, triple-negative, locally recurrent unresectable or metastatic breast cancer. Available at: https://www.nice.org.uk/guidance/gid-ta10417/documents/final-appraisal-determination-document. Accessed June 2023; 2. KEYTRUDA (pembrolizumab) SmPC. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed June 2023;

Prescribing information: GB, NI

Current treatment landscape in first-line advanced TNBC[1–3]



Scottish Medicines Consortium (SMC): positive decision on KEYTRUDA (pembrolizumab) in combination with chemotherapy as an option in patients with locally recurrent unresectable or metastatic TNBC that express PD-L1 with a CPS≥10.[a,4]

[a]Only paclitaxel and nab-paclitaxel are currently reimbursed by SMC.

CPS, combined positive score; HER2, human epidermal growth factor receptor 2; IC, tumour-infiltrating immune cells; PD-L1, programmed death ligand-1; TNBC, triple-negative breast cancer.

1. NICE Guidelines (TA801). Available at: https://www.nice.org.uk/guidance/ta801. Accessed June 2023; 2. NICE Guidelines (CG81). Available at https://www.nice.org.uk/guidance/cg81. Accessed June 2023;
3. NICE Guidelines (TA639). Available at https://www.nice.org.uk/guidance/ta639. Accessed June 2023; 4. SMC: KEYTRUDA guidance. Available at https://www.scottishmedicines.org.uk/medicines-advice/pembrolizumab-keytruda-tnbc-full-smc2460/.Accessed June 2023.

Prescribing information: GB, NI

KEYNOTE-355: Overview and study design

Click the links below to navigate to the section of interest

KEYNOTE-355: Study design

KEYNOTE-355: Baseline characteristics in the ITT population

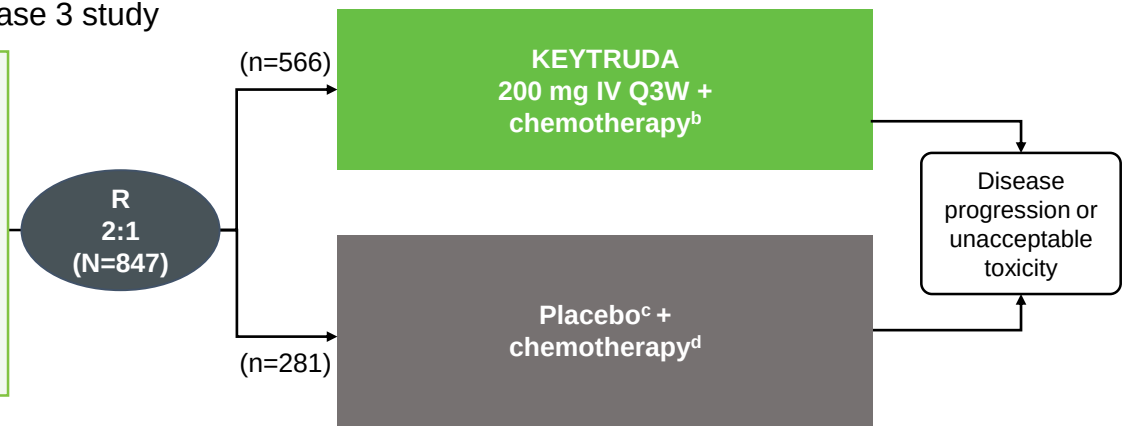
Prescribing information: GB, NI

KEYNOTE-355: Study design

Randomised, double-blind, placebo-controlled Phase 3 study

Key eligibility criteria

- Age ≥18 years
- Central determination of TNBC and PD-L1 expression[a]
- Previously untreated locally recurrent inoperable or metastatic TNBC
- De novo metastasis or completion of treatment with curative intent ≥6 months prior to first disease recurrence
- ECOG PS 0 or 1
- Life expectancy ≥12 weeks from randomisation
- No systemic steroids
- No CNS metastasis or active autoimmune disease



Stratification factors

- Chemotherapy on study (taxane or gemcitabine/carboplatin)
- PD-L1 tumour expression (CPS ≥1 or CPS <1)
- Prior treatment with same class chemotherapy in the neoadjuvant or adjuvant setting (yes or no)

- Dual primary endpoints: OS in patients with PD-L1-positive tumours[f] (CPS ≥10 or CPS ≥1) and in the ITT population: PFS[e] in patients with PD-L1-positive tumours[f] (CPS ≥10 or CPS ≥1) and in the ITT population
- Secondary endpoints: ORR, DOR, DCR, safety in all treated patients

[a]Based on a newly obtained tumour sample from a locally recurrent inoperable or metastatic site (an archival tumour sample was used with permission from the study sponsor if a new tumour biopsy was not obtainable); [b]Chemotherapy dosing regimens: nab-paclitaxel 100 mg/m² IV on Days 1, 8 and 15 every 28 days; paclitaxel 90 mg/m² IV on Days 1, 8 and 15 every 28 days; gemcitabine 1000 mg/m²/carboplatin AUC 2 on Days 1 and 8 every 21 days; [c]Normal saline; [d]Treatment may be continued until confirmation of progressive disease; [e]Based on RECIST v1.1 assessed by a central imaging vendor; [f]PD-L1 assessed at a central laboratory using PD-L1 IHC 22C3 pharmDx assay and measured using the CPS (number of PD-L1-positive tumour cells, lymphocytes and macrophages divided by total number of tumours cell ×100).

AUC, area under the curve; CNS, central nervous system; CPS, combined positive score; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ESMO, European Society of Medical Oncology; IHC, immunohistochemistry; ITT, intention to treat; IV, intravenous; ORR, objective response rate; OS, overall survival; PD-L1, programmed death ligand-1; PFS, progression-free survival; Q3W, every 3 weeks; R, randomisation; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1; TNBC, triple-negative breast cancer.

Cortes J et al. *Lancet* 2020;396:1817–1828.

Prescribing information: GB, NI

KEYNOTE-355: Baseline characteristics in the ITT population

Characteristic, n (%)[a]	KEYTRUDA + chemotherapy (n=566)	Placebo + chemotherapy (n=281)
Median age (range), years	53 (25–85)	53 (22–77)
ECOG PS 1	232 (41.0)	108 (38.4)
PD-L1 CPS ≥1	425 (75.1)	211 (75.1)
PD-L1 CPS ≥10	220 (38.9)	103 (36.7)
Chemotherapy on study		
Taxane	255 (45.1)	127 (45.2)
Gemcitabine/carboplatin	311 (54.9)	154 (54.8)
Prior same-class chemotherapy		
Yes	124 (21.9)	62 (22.1)
No	442 (78.1)	219 (77.9)
Disease-free interval		
De novo metastasis	168 (29.7)	84 (29.9)
<12 months	125 (22.1)	50 (17.8)
≥12 months	270 (47.7)	147 (52.3)

38%

of patients had PD-L1 CPS ≥10

These data comprise the full ITT population. Please note that the licensed indication for KEYTRUDA is in locally recurrent unresectable or metastatic TNBC in adults whose tumours express **PD-L1 CPS ≥10** and who have not received prior chemotherapy for metastatic disease

Data cut off: 15 June 2021.

[a]Unless otherwise stated.

Table adapted from Cortes J et al. *NEJM* 2022 (plus supplementary materials).

CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; ITT, intention to treat; PD-L1, programmed death ligand-1; TNBC, triple-negative breast cancer.

Cortes J et al. *NEJM* 2022;387:217–226 (plus supplementary materials).

Prescribing information: GB, NI

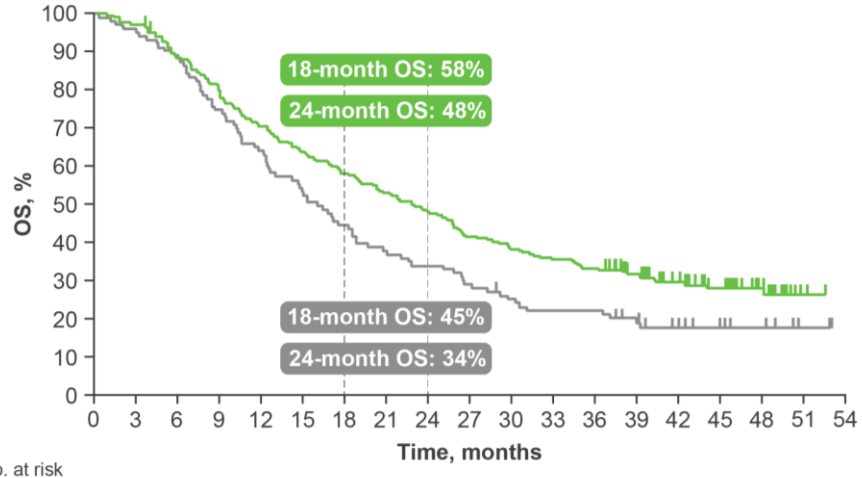
KEYNOTE-355: Results

Click the links below to navigate to the section of interest

- KEYNOTE-355: OS in the PD-L1 CPS ≥10 population
- KEYNOTE-355: PFS in the PD-L1 CPS ≥10 population
- KEYNOTE-355: Response rates in the PD-L1 CPS ≥10 population
- KEYNOTE-355: Summary of TRAEs in all treated patients
- KEYNOTE-355: TRAEs with incidence ≥20% in either arm
- KEYNOTE-355: Immune-mediated AEs with incidence ≥10% in either arm
- KEYTRUDA dosing
- PD-L1 testing in metastatic TNBC

KEYNOTE-355: OS in the PD-L1 CPS ≥10 population[1–3]

Treatment arm	Events (%)	Median (95% CI), months	HR (95% CI)	p value
KEYTRUDA + chemotherapy	70%	23.0 (19.0–26.3)	0.73 (0.55–0.95)	0.0093
Placebo + chemotherapy	82%	16.1 (12.6–18.8)	–	–



No. at risk

KEYTRUDA + chemotherapy	220	214	193	171	154	139	127	116	105	91	84	78	73	59	43	31	17	2	0
Placebo + chemotherapy	103	98	91	77	66	55	46	39	35	30	25	22	22	17	12	8	6	2	0

KEYTRUDA plus chemotherapy is the first anti-PD-1 combination treatment to show a statistically significant survival benefit vs placebo plus chemotherapy in patients with TNBC (PD-L1 CPS ≥10)

- Median OS was 23.0 months (95% CI: 19.0–26.3) with KEYTRUDA plus chemotherapy (n=220) vs 16.1 months (95% CI: 12.6–18.8) with placebo plus chemotherapy (n=103)

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

Data cut off: 15 June 2021.

Figure adapted from KEYTRUDA (pembrolizumab) SmPC.

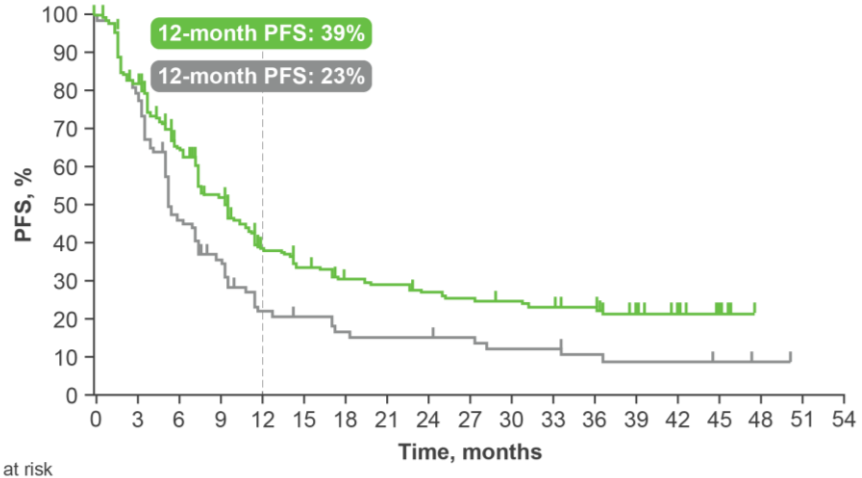
CI, confidence interval; CPS, combined positive score; HR, hazard ratio; OS, overall survival; PD-1, programmed cell death protein-1; PD-L1, programmed cell death ligand-1; SmPC, Summary of Product Characteristics; TNBC, triple-negative breast cancer.

1. Rugo HS et al. Presented at the European Society for Medical Oncology congress, September 16–21 2021; 2. KEYTRUDA (pembrolizumab) SmPC. Available at: https://www.medicines.org.uk/emc/product/2498/smpc/. Accessed June 2023; 3. Cortes J et al. *NEJM* 2022;387:217–226 (plus supplementary materials).

Prescribing information: GB, NI

KEYNOTE-355: PFS in the PD-L1 CPS ≥10 population[1–3]

Treatment arm	Events (%)	Median (95% CI), months	HR (95% CI)	p value
KEYTRUDA + chemotherapy	66%	9.7 (7.6–11.3)	0.66 (0.50–0.88)	0.0018
Placebo + chemotherapy	79%	5.6 (5.3–7.5)	–	–



No. at risk

KEYTRUDA + chemotherapy	220	173	122	95	63	52	44	42	38	36	34	32	27	19	13	6	0	0	0
Placebo + chemotherapy	103	80	41	30	18	15	12	11	11	10	8	8	6	4	4	3	1	0	0

Median PFS was 9.7 months (95% CI: 7.6–11.3) with KEYTRUDA plus paclitaxel, nab-paclitaxel, or gemcitabine/carboplatin and 5.6 months (95% CI: 5.3–7.5) with placebo plus chemotherapy

- 34% reduction in risk of disease progression with KEYTRUDA plus chemotherapy (n=220) vs placebo plus chemotherapy (n=103) (HR=0.66; 95% CI: 0.49–0.86; p=0.0012)
- The number of patients with an event was 144 (65%) with KEYTRUDA plus chemotherapy vs 81 (79%) with placebo plus chemotherapy

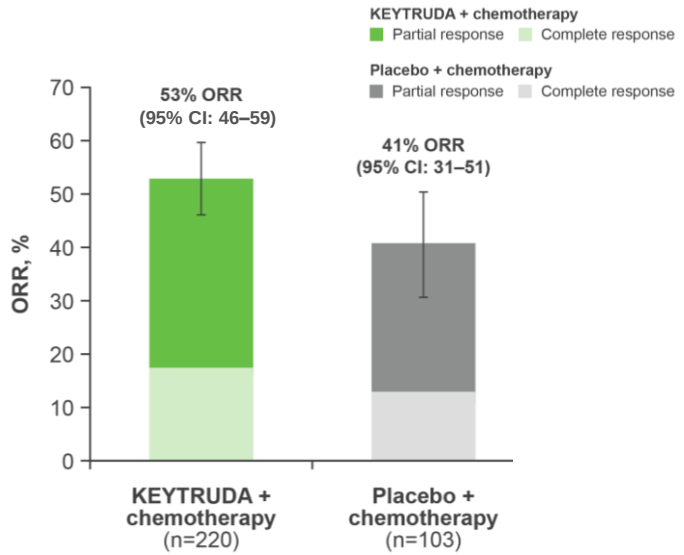
The forest plot for PFS in key subgroups is shown in the appendix. Click here to view.

Data cut off: 15 June 2021.
Figure adapted from KEYTRUDA (pembrolizumab) SmPC.
CI, confidence interval; CPS, combined positive score; HR, hazard ratio; PD-L1, programmed death ligand-1; PFS, progression-free survival; SmPC, Summary of Product Characteristics; TNBC, triple-negative breast cancer.
1. Rugo HS et al. Presented at the European Society for Medical Oncology congress, September 16–21 2021; 2. KEYTRUDA (pembrolizumab) SmPC. Available at: https://www.medicines.org.uk/emc/product/2498/smpc/. Accessed June 2023; 3. Cortes J et al. *NEJM* 2022;387:217–226 (plus supplementary materials).

Prescribing information: GB, NI

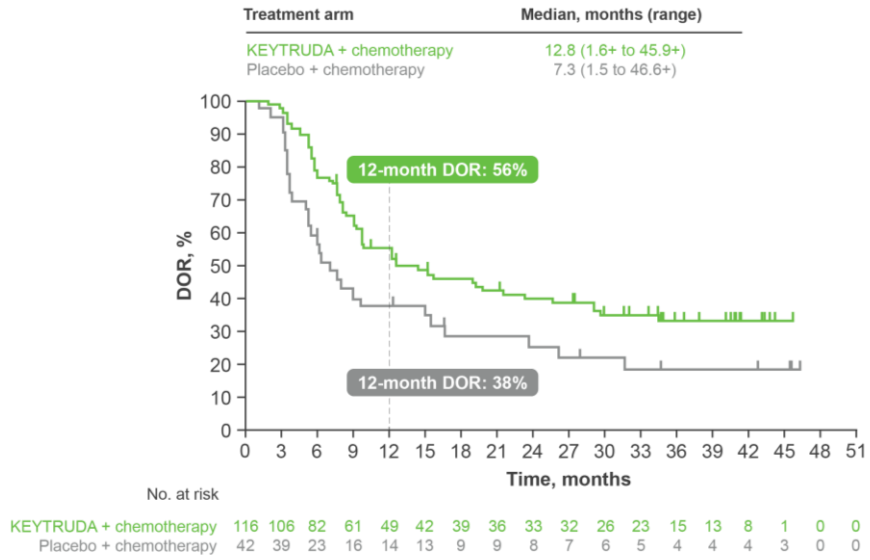
KEYNOTE-355: Response rates in the PD-L1 CPS ≥10 population[1–3]

ORR



53% (95% CI: 46–59) of patients achieved an ORR with KEYTRUDA plus chemotherapy vs 41% (95% CI: 31–51) with placebo plus chemotherapy

DOR[a]



Median DOR was 12.8 months (95% CI: 1.6+ to 45.9+) with KEYTRUDA plus chemotherapy vs 7.3 months (95% CI: 1.5–46.6+) with placebo plus chemotherapy

Data cut off: 15 June 2021.

[a]'+' indicates there is no progressive disease by the time of last disease assessment.

Figures adapted from Cortes J et al. *NEJM* 2022 (plus supplementary materials), KEYTRUDA (pembrolizumab) SmPC and Rugo HS et al. Presented at ESMO 2021.

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; SmPC, Summary of Product Characteristics.

1. Cortes J et al. *NEJM* 2022;387:217–226 (plus supplementary materials); 2. KEYTRUDA (pembrolizumab) SmPC. Available at: https://www.emcmedicines.com/en-gb/northernireland/medicine?id=ce680467-8438-4e60-ab4f-dfab6767ccbe&type=smpc. Accessed June 2023; 3. Rugo HS et al. Presented at the European Society for Medical Oncology congress, September 16–21 2021.

Prescribing information: GB, NI

KEYNOTE-355: Summary of TRAEs in all treated patients[1–3]

TRAEs, %	KEYTRUDA + chemotherapy (n=562)	Placebo + chemotherapy (n=281)
Any grade	96.3	95.0
Grade 3–5	68.1	66.9
Led to death	0.4[a]	0.0
Led to discontinuation	18.3	11.0

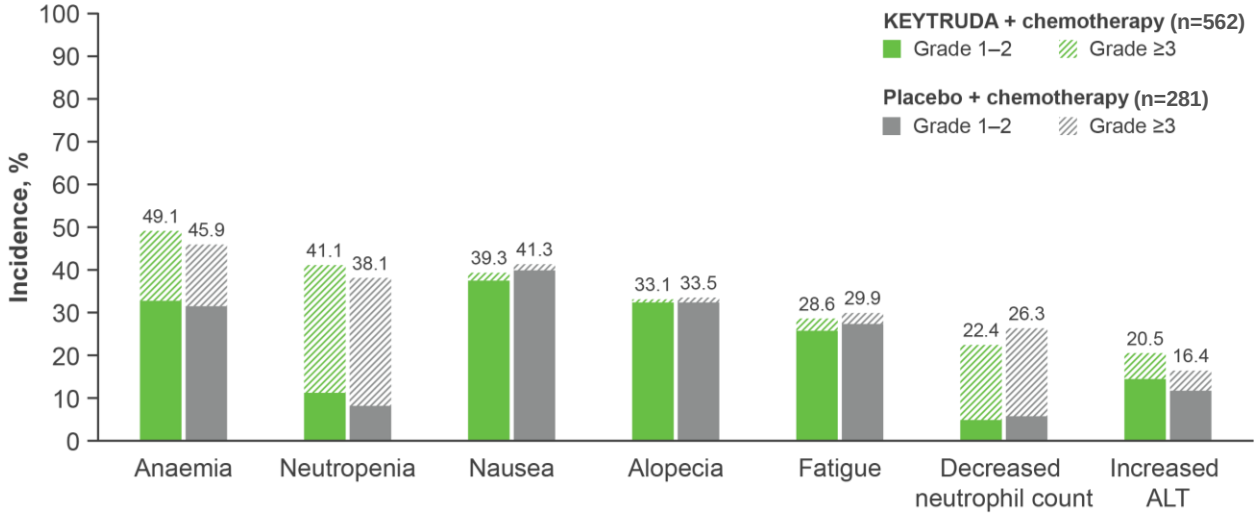
These data comprise the full ITT population. Please note that the licensed indication for KEYTRUDA is in locally recurrent unresectable or metastatic TNBC in adults whose tumours express **PD-L1 CPS ≥10** and who have not received prior chemotherapy for metastatic disease.

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

Data cut off: 15 June 2021.
Figure adapted from Cortes J et al. *NEJM* 2022, KEYTRUDA (pembrolizumab) SmPC and Rugo H et al. ESMO 2021.
[a]One patient died from acute kidney injury and one died patient from pneumonia.
CPS, combined positive score; irAE, immune-related adverse event; ITT, intention to treat; PD-L1, programmed death ligand-1; SmPC, Summary of Product Characteristics; TNBC, triple-negative breast cancer; TRAE, treatment-related adverse event.
1. Cortes J et al. *NEJM* 2022;387:217–226; 2. KEYTRUDA (pembrolizumab) SmPC. Available at: https://www.medicines.org.uk/emc/product/2498/smpc/. Accessed June 2023;
3. Rugo H et al. Presented at ESMO Virtual Congress, 16–21 September 2021.

Prescribing information: GB, NI

KEYNOTE-355: TRAEs with incidence ≥20% in either arm



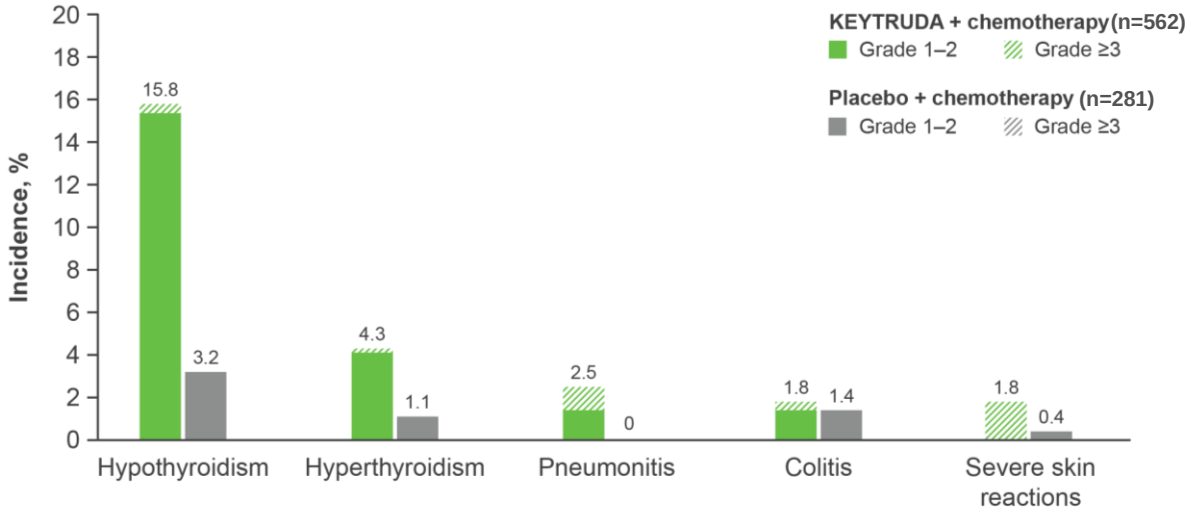
These data comprise the full ITT population. Please note that the licensed indication for KEYTRUDA is in locally recurrent unresectable or metastatic TNBC in adults whose tumours express PD-L1 CPS ≥10 and who have not received prior chemotherapy for metastatic disease.

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

Data cut off: 15 June 2021.
Figure adapted from Cortes J et al. *NEJM* 2022.
ALT, alanine transaminase; CPS, combined positive score; irAE, immune-related adverse event; ITT, intention to treat; PD-L1, programmed death ligand-1; SmPC, Summary of Product Characteristics; TNBC, triple-negative breast cancer; TRAE, treatment-related adverse event.
Cortes J et al. *NEJM* 2022;387:217–226

Prescribing information: GB, NI

KEYNOTE-355: Immune-mediated AEs with incidence ≥10% in either arm[a]



These data comprise the full ITT population. Please note that the licensed indication for KEYTRUDA is in locally recurrent unresectable or metastatic TNBC in adults whose tumours express PD-L1 CPS ≥10 and who have not received prior chemotherapy for metastatic disease.

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Further information on the safety of KEYTRUDA plus chemotherapy combinations can be found in the GB SmPC here or NI SmPC here.

Data cut off: 15 June 2021.

Figure adapted from Cortes J et al. *NEJM* 2022.

[a]Based on a list of terms prespecified by the sponsor and included regardless of attribution to study treatment or immune relatedness by the investigator; related terms included.

AE, adverse event; CPS, combined positive score; irAE, immune-related adverse event; ITT, intention to treat; PD-L1, programmed death ligand-1; SmPC, Summary of Product Characteristics; TNBC, triple-negative breast cancer; TRAE, treatment-related adverse event.

Cortes J et al. *NEJM* 2022;387:217–226

Prescribing information: GB, NI

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.medicines.org.uk/emc/product/2498/smpc/. Accessed June 2023.

Prescribing information: GB, NI

PD-L1 testing in metastatic TNBC

Combined positive score: A snapshot of the tumour microenvironment

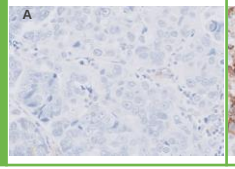
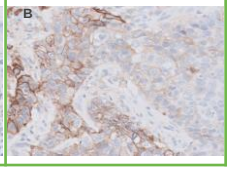
- CPS is used to evaluate PD-L1 expression in tumour cells and certain immune cells in TNBC[1]
- This helps to identify patients the most appropriate treatment for patients[1]
- In KEYNOTE-355, PD-L1 expression was assessed by CPS using the PD-L1 22C3 IHC pharmDx assay[2]
- The PD-L1 22C3 IHC pharmDx assay, scored using the CPS algorithm, is used to define eligibility for treatment with KEYTRUDA plus chemotherapy[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 TNBC[1]

PD-L1 expression level	CPS <10	CPS ≥10
Stained with PD-L1 22C3 pharmDx primary antibody (x20)		

TNBC specimen stained with PD-L1 22C3 pharmDx primary antibody exhibiting a CPS of 0 (A) and a CPS of 60 (B). Both images were taken at 20x magnification.

For further information on CPS testing, click here

CPS, combined positive score; IHC, immunohistochemistry; PD-L1, programmed death ligand-1; TNBC, triple-negative breast cancer.

1. PD-L1 IHC 22C3 pharmDx interpretation manual - NSCLC. Agilent Dako. Available at: https://www.agilent.com/cs/library/usermanuals/public/29389_22c3_pharmdx_tnbc_interpretation_manual_kn355.pdf. Accessed June 2023;
2. Cortes J et al. *Lancet* 2020;396:1817–1828.

Prescribing information: GB, NI

KEYNOTE-355: Summary

KEYNOTE-355: Summary of results in the PD-L1 CPS ≥10 population

- KEYTRUDA plus chemotherapy is the first anti-PD-1 combination treatment to show a statistically significant survival benefit vs placebo plus chemotherapy in patients with TNBC with a PD-L1 CPS ≥10
  - Median OS was 23.0 months (95% CI: 19.0–26.3 months) with KEYTRUDA plus chemotherapy (n=155/220) vs 16.1 months (95% CI: 12.6–18.8 months) with placebo plus chemotherapy (n=84/103) (HR=0.73; 95% CI: 0.55–0.95; p=0.0093)[1]
- Superior PFS was observed with KEYTRUDA plus chemotherapy vs placebo plus chemotherapy in patients with PD-L1 CPS ≥10
  - 34% reduction in risk of disease progression with KEYTRUDA plus chemotherapy vs placebo plus chemotherapy (HR=0.66; 95% CI:0.50–0.88]; p=0.0018)[1]
- 38% of patients with advanced TNBC had a PD-L1 CPS ≥10 in KEYNOTE-355[1]
- Grade ≥3 TRAEs occurred in 68.1% of patients in the KEYTRUDA plus chemotherapy arm and 66.9% of patients in the placebo plus chemotherapy arm.[1] **Click here for an overview of TRAEs**
  - Of those treated, patients in the KEYTRUDA plus chemotherapy arm had a higher proportion of discontinuations of trial drugs and immune-mediated AEs compared with the placebo plus chemotherapy arm (18.3% vs 11.0% and 26.5% vs 6.4%, respectively)[1,2]
  - Treatment-related deaths were 0.4% in the KEYTRUDA plus chemotherapy arm and 0.0% in the placebo plus chemotherapy arm[1]

AE, adverse event; CI, confidence interval; CPS, combined positive score; HR, hazard ratio; IHC, immunohistochemistry; OS, overall survival; PD-1, programmed cell death protein-1; PD-L1, programmed death ligand-1; PFS, progression-free survival; TNBC, triple-negative breast cancer; TRAE, treatment-related adverse event.

1. Cortes J et al. *NEJM* 2022;387:217–226; Rugo H et al. Presented at ESMO Virtual Congress 2021, 16–21 September 2021.

Appendix

Click the links below to navigate to the section of interest

KEYNOTE-355: PFS in key subgroups of the PD-L1 CPS ≥10 population

KEYNOTE-355: OS in key subgroups of the PD-L1 CPS ≥10 population

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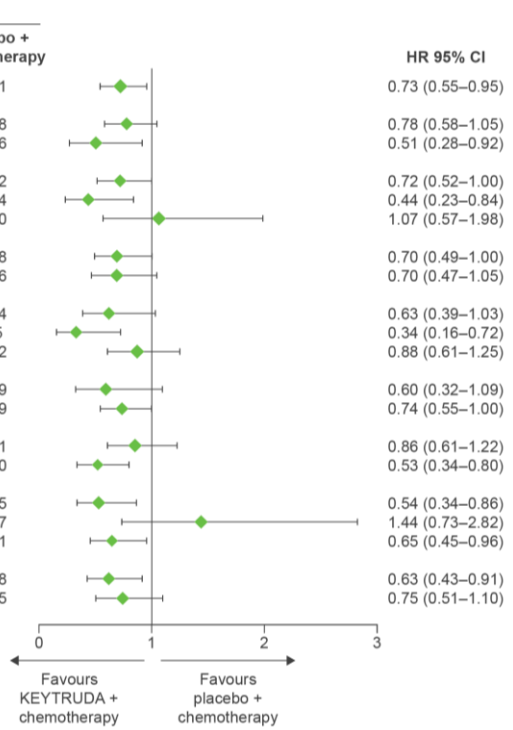
KEYNOTE-355: OS in key subgroups of the PD-L1 CPS ≥10 population

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

Subgroup	N	Median OS (mo) KEYTRUDA + chemotherapy	Median OS (mo) Placebo + chemotherapy	HR 95% CI
Overall	323	23.0	16.1	0.73 (0.55–0.95)
Age, years				
<65	257	21.8	16.8	0.78 (0.58–1.05)
≥65	66	28.3	12.6	0.51 (0.28–0.92)
Geographic region				
North America/Europe/ANZ	212	23.5	15.2	0.72 (0.52–1.00)
Asia	56	26.7	17.4	0.44 (0.23–0.84)
Rest of World	55	18.0	22.0	1.07 (0.57–1.98)
ECOG PS				
0	196	26.4	19.8	0.70 (0.49–1.00)
1	127	17.7	10.6	0.70 (0.47–1.05)
On-study chemotherapy				
Nab-paclitaxel	99	29.8	18.4	0.63 (0.39–1.03)
Paclitaxel	44	28.6	8.5	0.34 (0.16–0.72)
Gemcitabine/carboplatin	180	19.1	16.2	0.88 (0.61–1.25)
Prior same-class chemotheraphy				
Yes	65	23.5	14.9	0.60 (0.32–1.09)
No	258	22.8	16.9	0.74 (0.55–1.00)
Prior neoadjuvant/adjuvant chemotherapy				
Yes	193	20.3	17.1	0.86 (0.61–1.22)
No	130	28.3	13.0	0.53 (0.34–0.80)
Disease-free interval				
De novo metastasis	104	26.4	12.5	0.54 (0.34–0.86)
<12 months	65	17.1	19.7	1.44 (0.73–2.82)
≥12 months	153	24.9	17.1	0.65 (0.45–0.96)
Number of metastatic sites				
<3	184	32.1	18.8	0.63 (0.43–0.91)
≥3	138	13.2	10.5	0.75 (0.51–1.10)



Data cut off: 15 June 2021.

Figure adapted from Cortes J et al. *NEJM* 2022 (plus supplementary materials).

ANZ, Australia and New Zealand; CI, confidence interval; CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; mo, months; OS, overall survival; PD-L1, programmed death ligand-1.

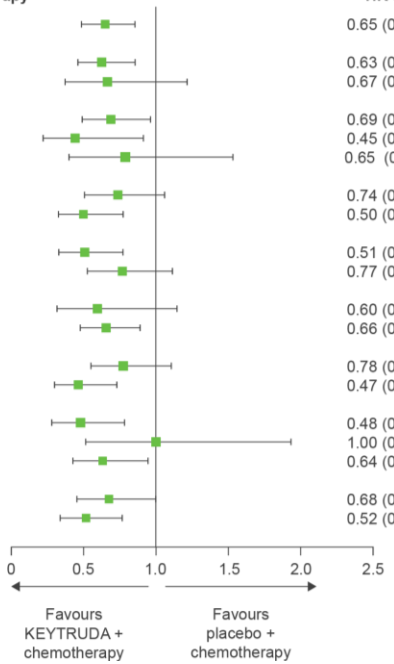
Cortes J et al. *NEJM* 2022;387:217–226.

Prescribing information: GB, NI

KEYNOTE-355: PFS in key subgroups of the PD-L1 CPS ≥10 population

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

Subgroup	N	Median PFS (mo) KEYTRUDA + chemotherapy	Median PFS (mo) Placebo + chemotherapy	HR 95% CI
Overall	323	9.7	5.6	0.65 (0.49–0.86)
Age, years				
<65	257	9.5	5.5	0.63 (0.46–0.87)
≥65	66	10.7	7.6	0.67 (0.37–1.23)
Geographic region				
North America/Europe/ANZ	212	9.6	5.7	0.69 (0.49–0.97)
Asia	56	17.3	5.6	0.45 (0.22–0.91)
Rest of World	55	7.6	6.2	0.65 (0.40–1.55)
ECOG PS				
0	196	9.8	7.5	0.74 (0.51–1.07)
1	127	7.6	3.9	0.50 (0.33–0.78)
On-study chemotherapy				
Taxane	143	9.9	5.4	0.51 (0.33–0.78)
Gemcitabine/carboplatin	180	8.0	7.2	0.77 (0.53–1.11)
Prior same-class chemotherapy				
Yes	65	7.5	5.4	0.60 (0.32–1.15)
No	258	9.9	5.7	0.66 (0.48–0.90)
Prior neoadjuvant/adjuvant chemotherapy				
Yes	193	7.9	5.7	0.78 (0.55–1.12)
No	130	11.0	5.4	0.47 (0.30–0.74)
Disease-free interval				
De novo metastasis	103	9.7	5.3	0.48 (0.29–0.79)
<12 months	66	7.5	7.2	1.00 (0.51–1.95)
≥12 months	153	9.9	6.6	0.64 (0.43–0.95)
Number of metastatic sites				
<3	184	11.8	9.0	0.68 (0.46–1.00)
≥3	138	7.6	4.5	0.52 (0.34–0.78)



Data cut off: 11 December 2019.

Figure adapted from Cortes J et al. ASCO 2020.

ANZ, Australian and New Zealand; ASCO, American Society of Clinical Oncology; CI, confidence interval; CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; mo, months; PD-L1, programmed death ligand-1; PFS, progression-free survival.

Cortes J et al. Presented at the American Society for Clinical Oncology (ASCO) Virtual Congress 2020, 29–31 May 2020.

Prescribing information: GB, NI