A key to more possibilities for treating your appropriate patients with resectable NSCLC

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 MSD (Tel: 020 8154 8000).
By clicking the above link, you will leave the MSD website and be taken to the MHRA website.

UK prescribing information can be found here

If using a downloaded version of this material, please ensure that you are accessing the most recent version of the prescribing information.

GB-LAM-00061 | Date of preparation: May 2026

MSD Oncology

KEYNOTE-091:

KEYTRUDA® (pembrolizumab) versus placebo as adjuvant therapy for completely resected Stage IB–IIIA non-small cell lung carcinoma (NSCLC)*

KEYTRUDA as monotherapy is indicated for the adjuvant treatment of adults with non-small cell lung carcinoma who are at high risk of recurrence following complete resection and platinum-based chemotherapy.[1]

These slides are provided to UK healthcare professionals as a resource for data for your personal education. To ensure compliance with all relevant codes and regulations these slides must not be amended.

*As defined per American Joint Committee on Cancer (AJCC) 7th edition. Staging throughout this material is based on AJCC 7th edition.[1]

NSCLC, non-small cell lung cancer.

1. KEYTRUDA® (pembrolizumab) Summary of Product Characteristics. United Kingdom. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026.

KEYTRUDA® (pembrolizumab)

MSD

Links to external sites

The links in this slide deck will redirect you to third-party websites. Please note that:

- MSD does not review or control the content of any third-party website
- MSD neither endorses nor is responsible for the accuracy, content, practices or standards of any third-party sources

KEYTRUDA early-stage and advanced NSCLC indications[1]

- **KEYTRUDA as monotherapy is indicated for the adjuvant treatment of adults with NSCLC who are at high risk of recurrence following complete resection and platinum-based chemotherapy**
- KEYTRUDA, in combination with platinum-containing chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment, is indicated for the treatment of resectable non-small cell lung carcinoma (NSCLC) at high risk of recurrence in adults
- KEYTRUDA as monotherapy is indicated for the first-line treatment of metastatic NSCLC in adults whose tumours express PD-L1 with a ≥50% TPS with no *EGFR*- or *ALK*-positive tumour mutations
- KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of metastatic non-squamous NSCLC in adults whose tumours have no *EGFR*- or *ALK*-positive mutations
- KEYTRUDA, in combination with carboplatin and either paclitaxel or nab-paclitaxel, is indicated for the first-line treatment of metastatic squamous NSCLC in adults
- KEYTRUDA as monotherapy is indicated for the treatment of locally advanced or metastatic NSCLC in adults whose tumours express PD-L1 with a ≥1% TPS and who have received at least one prior chemotherapy regimen. Patients with *EGFR*- or *ALK*-positive tumour mutations should also have received targeted therapy before receiving KEYTRUDA
- The recommended dose of KEYTRUDA in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes. For the use of KEYTRUDA as part of combination therapy, see the Summary of Product Characteristics (SmPC) for the concomitant therapies[1]

Please refer to the Summary of Product Characteristics and Risk Minimisation Materials available on the EMC website before prescribing.

ALK, anaplastic lymphoma kinase; *EGFR*, epidermal growth factor receptor; EMC, Electronic Medicines Compendium; NSCLC, non-small cell lung carcinoma; PD-L1, programmed death-ligand 1; TPS, tumour proportion score.

1. KEYTRUDA® (pembrolizumab) Summary of Product Characteristics. United Kingdom. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026.

NSCLC DFS rates by stage[1]

In a retrospective observational study of patients with early-stage NSCLC (Stage IB-IIIA, AJCC 7th edition), two-thirds experienced disease recurrence during 4.5 years of follow-up, even after curative resection.*[1]

Real-world disease-free survival (rwDFS) by stage:[1]

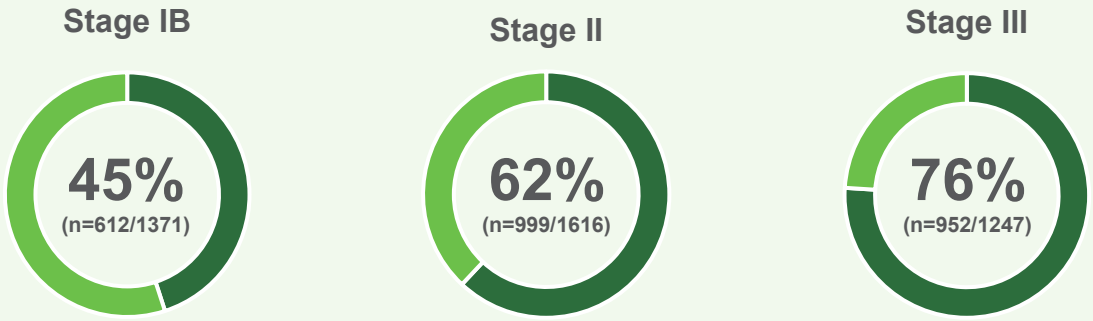
Stage	Median rwDFS	5-year rwDFS
IB	40.9 months	38.9%
II	24.4 months	29.1%
IIIA	13.8 months	21.5%

*Based on 1761 patients from the SEER-Medicare database (2007–2019) with early-stage resected NSCLC.
AJCC, American Joint Committee on Cancer; DFS, disease-free survival; NSCLC, non-small cell lung carcinoma; rwDFS, real-world disease-free survival; SEER, Surveillance, Epidemiology, and End Results; TNM, tumour, node, metastasis.
1. West H, *et al*. *Clin Lung Cancer* 2023;24:260–268.

Despite surgical intervention, there remains a risk of recurrence for NSCLC patients, with or without adjuvant chemotherapy[1]

- Surgery for early-stage NSCLC may not be curative[1]
- Risk of recurrence is associated with disease factors (e.g. stage and N status) and surgical factors (e.g. positive margins)[2]
- Rates of recurrence are higher in patients with a higher stage of NSCLC. Within 5 years, recurrence or death is experienced by:[1]
  - 45% of Stage IB patients
  - 62% of Stage II patients
  - 76% of Stage III patients
- Recurrence often occurs early – most cases within 14 months of surgery[2]

Rate of recurrence or death within 5 years by stage[1]



The rate of recurrence or death is based on a 2008 pooled analysis of 4584 patients across 5 randomised trials, after complete resection, with or without adjuvant chemotherapy. The trials included in this pooled analysis occurred from 1994–2001.*[1]

***Lung Adjuvant Cisplatin Evaluation: a pooled analysis by the LACE collaborative group:** The Lung Adjuvant Cisplatin Evaluation (LACE) study was a pooled analysis of 5 randomised trials conducted by the LACE Collaborative Group. The study evaluated the use of cisplatin-based chemotherapy as an adjuvant treatment for patients with NSCLC. The primary endpoint was overall survival (OS) and a secondary endpoint was disease-free survival (DFS).[1]

Study population: Individual patient data were collected and pooled from 5 trials, including 4584 patients who underwent complete resection. Of these patients, 2281 received adjuvant chemotherapy. The interactions between patient subgroups or treatment types and chemotherapy effect on OS were analysed using hazard ratios and log-rank tests stratified by trial.[1]

Inclusion criteria: Trials eligible for inclusion were those that either randomly assigned more than 300 patients with completely resected NSCLC to receive postoperative cisplatin-based chemotherapy vs no chemotherapy, or cisplatin-based chemotherapy plus postoperative radiotherapy (administered sequentially) vs postoperative radiotherapy alone.[1]

DFS, disease-free survival; LACE, Lung Adjuvant Cisplatin Evaluation; N, nodes; NSCLC, non–small cell lung carcinoma; OS, overall survival.

1. Pignon JP, *et al. J Clin Oncol* 2008;26:3552–3559. **2.** Kelsey CR, *et al. Cancer* 2009;115:5218–27.

KEYNOTE-091 indication:

KEYTRUDA as monotherapy is indicated for the adjuvant treatment of adults with non-small cell lung carcinoma who are at high risk of recurrence following complete resection and platinum-based chemotherapy.[1]

1. KEYTRUDA® (pembrolizumab) Summary of Product Characteristics. United Kingdom. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026.

KEYNOTE-091: Study design[1,2]

KEYNOTE-091 was a randomised, triple-blind, Phase III trial in patients with Stage IB (T2a ≥4 cm), II or IIIA NSCLC*

Patients:

- High risk of recurrence,† completely resected Stage IB (T2a ≥4 cm), II or IIIA NSCLC, regardless of PD-L1 expression (AJCC 7th Edition)
- No prior neoadjuvant radiotherapy and/or neoadjuvant chemotherapy
- No prior or planned adjuvant radiotherapy for current malignancy
- May or may not have received adjuvant chemotherapy (up to 4 cycles)
- No active autoimmune disease requiring systemic therapy
- No medical condition requiring immunosuppression
- Not received >4 cycles of adjuvant chemotherapy

1–4 cycles of adjuvant chemo

Considered for Stage IB (T≥4cm) Strongly recommended for Stage II and IIIA†‡

R 1:1 (N=1177)

Pembrolizumab 200 mg IV Q3W ≤18 cycles

Placebo IV Q3W ≤18 cycles

Survival follow-up

KEYTRUDA is licensed for use as a monotherapy for the adjuvant treatment of adults with NSCLC who are at high risk of recurrence following complete resection and platinum-based chemotherapy.[2] The results of the ITT population are presented as this is the primary endpoint of the study. It allows the results in the licensed population (a subgroup if the ITT population) to be viewed in context of the primary endpoint.[1,2]

Stratification factors:[1]

- Stage (IB vs II vs IIIA)
- Use of adjuvant chemotherapy (No vs Yes)
- PD-L1 status: TPS <1% vs 1 to 49% vs ≥50%
- Regions (Western vs Eastern Europe vs Asia vs RoW)

Dual primary endpoints:

- DFS (all patients)
- DFS (PD-L1 TPS ≥50%)

Secondary endpoints:[1]

- DFS (PD-L1 TPS ≥1%)
- OS (all patients, PD-L1 TPS ≥50%, PD-L1 TPS ≥1%)
- Lung cancer-specific survival (LCSS; all patients)
- Safety

Adapted from O'Brien M, *et al*. *Lancet Oncol* 2022 (and supplementary appendix).[1]

*As defined per AJCC 7th edition.[1] †The following selection criteria define patients with high risk of recurrence who are included in the therapeutic indication and are reflective of the patient population with Stage IB (T2a ≥4 cm), II or IIIA according to the 7th edition staging system: Tumour size ≥4 cm; or tumours of any size that are either accompanied by N1 or N2 status; or tumours that are invasive of thoracic structures (directly invade the parietal pleura, chest wall, diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium, mediastinum, heart, great vessels,trachea, recurrent laryngeal nerve, oesophagus, vertebral body, carina); or tumours that involve the main bronchus <2 cm distal to the carina but without involvement of the carina; or tumours that are associated with atelectasis or obstructive pneumonitis of the entire lung; or tumours with separate nodule(s) in the same lobe or different ipsilateral lobe as the primary. The study did not include patients who had N2 status with tumours also invading the mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, oesophagus, vertebral body, carina, or with separate tumour nodule(s) in a different ipsilateral lobe.[2] ‡Adjuvant chemotherapy was considered for Stage IB (T ≥4 cm in diameter) disease and strongly recommended for Stage II and IIIA disease, limited to ≤4 cycles.[1]

DFS, disease-free survival; IV, intravenous; NSCLC, non-small cell lung cancer; OS, overall survival; PD-L1, programmed death ligand-1; Q3W, once every 3 weeks; R, randomisation; RoW, rest of world; TPS, tumour proportion score.

1. O'Brien M, *et al. Lancet Oncol* 2022;23:1274–1286 (and supplementary appendix). **2.** KEYTRUDA® (pembrolizumab) Summary of Product Characteristics. United Kingdom. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026.

KEYNOTE-091: Patient baseline characteristics[1]

86% (1010/1177) of patients randomised received adjuvant platinum-based chemotherapy following complete resection

	ITT population		PD-L1 TPS ≥50%	
Characteristic, n (%)	KEYTRUDA (n=590)	Placebo (n=587)	KEYTRUDA (n=168)	Placebo (n=165)
Age, median (range), years	65.0 (31–87)	65.0 (37–85)	64.5 (38–82)	65.0 (37–85)
Male	401 (68.0)	403 (68.7)	121 (72.0)	116 (70.3)
ECOG PS 1	210 (35.6)	244 (41.6)	52 (31.0)	64 (38.8)
Former/current smoker	503 (85.3)	521 (88.8)	154 (91.7)	152 (92.1)
EGFR mutation*	39 (6.6)	34 (5.8)	6 (3.6)	5 (3.0)
ALK translocation†	7 (1.2)	7 (1.2)	3 (1.8)	0
Nonsquamous histology	398 (67.5)	363 (61.8)	103 (61.3)	105 (63.6)
Pathologic stage‡				
IB	85 (14.4)	87 (14.8)	22 (13.1)	22 (13.3)
II	330 (55.9)	338 (57.6)	94 (56.0)	94 (57.0)
IIIA	175 (29.7)	160 (27.3)	52 (31.0)	49 (29.7)
Received adjuvant chemotherapy	506 (85.8)	504 (85.9)	143 (85.1)	141 (85.5)
PD-L1 TPS				
<1%	233 (39.5)	232 (39.5)	–	–
1%–49%	189 (32.0)	190 (32.4)	–	–
≥50%	168 (28.5)	165 (28.1)	168 (100.0)	165 (100.0)

Adapted from Besse B, *et al*. ESMO 2023.[1]

*EGFR status unknown for 333 (56.4%) in KEYTRUDA group and 337 (57.4%) in placebo group in ITT population.[1] †ALK status unknown for 357 (60.5% in KEYTRUDA group and 390 (66.4%) in placebo group in ITT population.[1] ‡As defined per AJCC 7th edition.[1]
AJCC, American Joint Committee on Cancer; *ALK*, anaplastic lymphoma kinase; ECOG PS, Eastern Cooperative Oncology Group Performance Status; *EGFR*, epidermal growth factor receptor; PD-L1, programmed death-ligand 1; TPS, tumour proportion score.

1. Besse B. Adjuvant pembrolizumab versus placebo for early-stage NSCLC after resection and optional chemotherapy: updated results from PEARLS/KEYNOTE-091. ESMO Immuno-oncology. 6–8 December 2023. Geneva, Switzerland.

IA2

KEYNOTE-091: Summary of initial efficacy data[1,2]

After 32.4 months median follow-up, adjuvant KEYTRUDA following complete resection and adjuvant chemotherapy (where recommended), **significantly extended the dual primary endpoint of DFS in the overall population** compared with placebo[1,2]

Summary of key data from the primary endpoint and secondary efficacy endpoints at IA2[1]

		Population	KEYTRUDA, n	Placebo, n	Median, months	HR (95% CI)*	P-value†	Outcome
Dual primary endpoints	DFS	ITT	590	587	53.6 vs 42.0	0.76 (0.63–0.91)	0.00143	Positive
	DFS	TPS ≥50%	168	165	NR vs NR	0.82 (0.57–1.18)	0.13639	Not positive; to be tested again at next IA
Key secondary endpoints	DFS	TPS ≥1%	357	355	53.6 vs 42.0	0.73 (0.57–0.92)	–	Not tested; to be tested once positive DFS in TPS ≥50%
	OS	ITT	590	587	NR vs NR	0.87 (0.67–1.15)	0.16811	Not positive; to be tested again at next IA
	OS	TPS ≥50%	168	165	NR vs NR	0.92 (0.52–1.62)	0.38517	Not positive; to be tested again at next IA
	OS	TPS ≥1%	357	355	NR vs NR	0.76 (0.52–1.09)	–	Not tested; to be tested once positive OS in TPS ≥50%

DFS was defined as the time between the date of randomisation and the date of first recurrence (local/regional recurrence, distant metastasis), a second malignancy, or death, whichever occurred first. OS was defined as the time from randomisation to death from any cause.[1]
Adapted from KN-091 EPAR report 2023.[1]

IA2: median follow-up: 32.4 months; data-cut off date: 20 September 2021.[1]

*Based on the multivariate Cox regression model with treatment adjusted by the following covariates: Stage (IB vs II vs IIIA), PD-L1 status (≥50% vs 1-49% vs <1%), region (Western Europe vs Eastern Europe vs rest of world vs Asia), histology (squamous vs non-squamous), and smoking status (never vs former/current).[1] †One-sided p-values for DFS endpoints are based on the permutation test with the multivariate Cox regression model; one-sided p-values for OS endpoints are based on the Wald test in the multivariate Cox regression model.[1]

CI, confidence interval; DFS, disease-free survival; EPAR, European public assessment report; HR, hazard ratio; IA, interim analysis; ITT, intention-to-treat; NR, not reached; OS, overall survival; PD-L1, programmed death-ligand 1; TPS, tumour proportion score.

1. European Medicines Agency. European public assessment report: KEYTRUDA. Available at: https://www.ema.europa.eu/en/documents/variation-report/keytruda-h-c-003820-ii-0121-epar-assessment-report-variation_en.pdf. Accessed: May 2026. **2.** KEYTRUDA® (pembrolizumab) Summary of Product Characteristics. United Kingdom. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026.

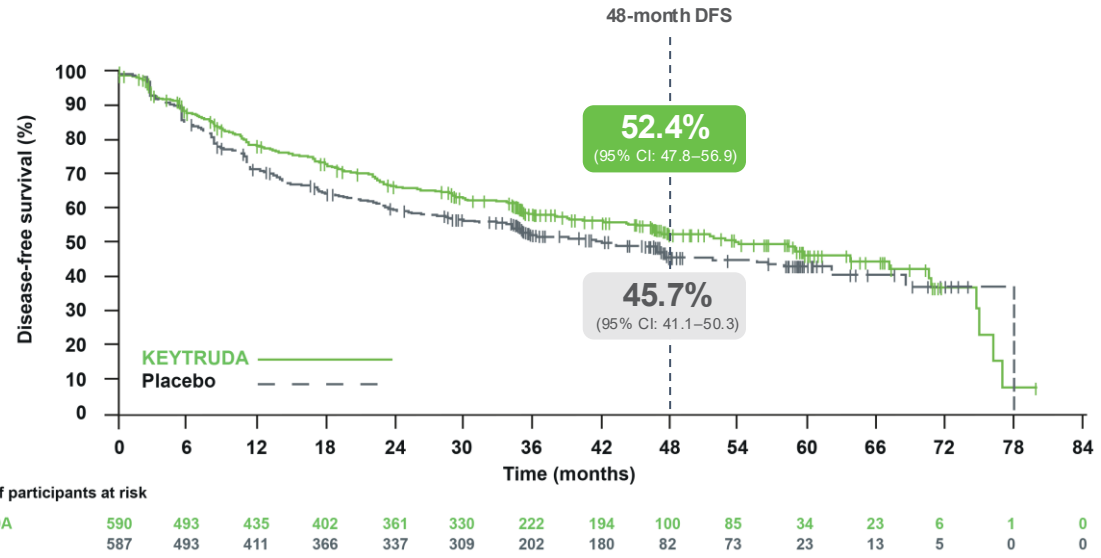
KEYNOTE-091: Disease-free survival (DFS)[1–3]

Final dual primary endpoint analysis of DFS in the ITT population

IA3

KM estimates of DFS by population at IA3 (primary censoring rule)[2,3]

Overall ITT population | PD-L1 TPS ≥50%



NOTE ON THE STUDY POPULATION[1,4]

- The ITT population of KEYNOTE-091 includes 167 patients who did not receive adjuvant platinum-based chemotherapy
- Prior adjuvant platinum-based chemotherapy is a UK license requirement for KEYTRUDA in this setting
- Data are included to provide appropriate context for the exploratory analyses in the licensed subgroup

Summary of DFS by population at IA3[2,3]

	HR (95% CI)*	Median, months	Observed p-value†	Outcome
ITT	0.81 (0.68–0.96)	53.8 vs 43.0	0.00812	Not tested‡
PD-L1 TPS ≥50%	0.83 (0.59–1.16)	67.0 vs 47.6	0.13499§	Not positive¶

*Based on the multivariate Cox regression model with treatment adjusted by the following covariates: Stage (IB vs II vs IIIA), PD-L1 status (≥50% vs 1–49% vs <1%), region (Western Europe vs Eastern Europe vs rest of world vs Asia), histology (squamous vs non-squamous), and smoking status (never vs former/current).[2]
†One-sided p-value based on permutation test with multivariate Cox regression model.[2]
‡The success criterion was met for DFS at IA2.[2]
§P-value boundary: 0.01038.[2]
¶Although DFS in TPS ≥50% can be re-tested at the full alpha level (0.025) after OS hypotheses are rejected, its p-value exceeds the boundary for significance. Consequently, DFS in TPS ≥1% cannot be tested in future analyses, regardless of OS outcomes.[2]

Adjuvant KEYTRUDA demonstrated improved DFS with a **19% reduced risk in recurrence or death** vs placebo in the ITT population (HR: 0.81, p=0.00812)[2,3]

Adapted from Besse B, *et al*. ESMO 2023 and KEYTRUDA Public Assessment Report 2023.[2,3]

IA3: median follow-up was 46.7 months; data cut-off date: 24 January 2023.[2] CI, confidence interval; DFS, disease-free survival; EPAR, European public assessment report; HR, hazard ratio; IA, interim analysis; ITT, intention-to-treat; KM, Kaplan-Meier; NSCLC, non–small cell lung cancer; OS, overall survival; PD-L1, programmed death-ligand 1; TPS, tumour proportion score.

1. KEYTRUDA® (pembrolizumab) Summary of Product Characteristics. United Kingdom. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026. **2.** European Medicines Agency. European public assessment report: KEYTRUDA. Available at: https://www.ema.europa.eu/en/documents/variation-report/keytruda-h-c-003820-ii-0121-epar-assessment-report-variation_en.pdf. Accessed: May 2026. **3.** Besse B. Adjuvant pembrolizumab versus placebo for early-stage NSCLC after resection and optional chemotherapy: updated results from PEARLS/KEYNOTE-091. ESMO Immuno-oncology. 6–8 December 2023. Geneva, Switzerland. **4.** O'Brien M, *et al. Lancet Oncol* 2022;23:1274–1286.

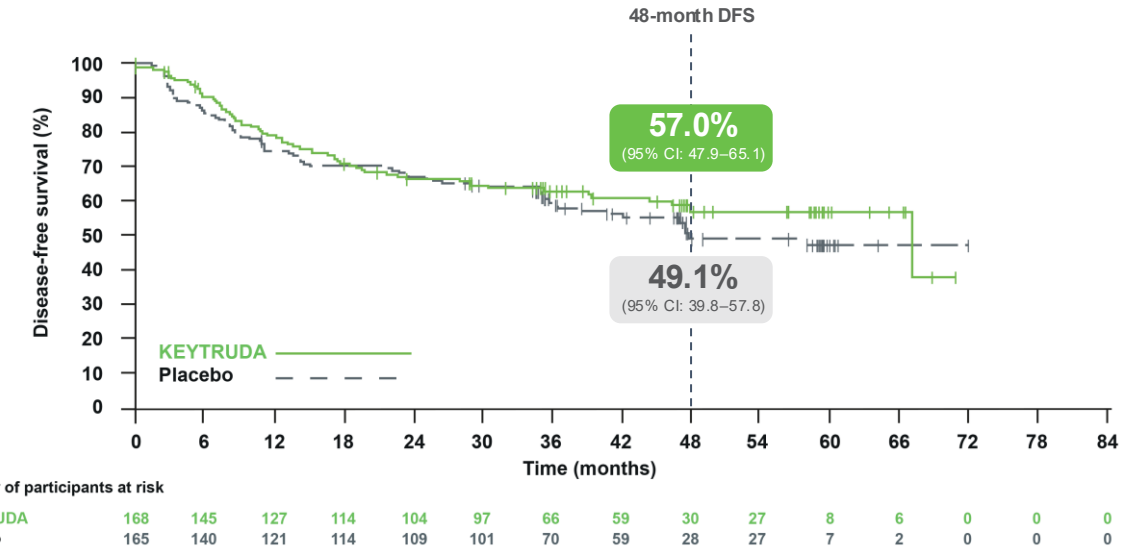
KEYNOTE-091: DFS in ITT patients with PD-L1 TPS ≥50%[1–3]

Final dual primary endpoint analysis of DFS in the PD-L1 TPS ≥50% population

IA3

KM estimates of DFS by population at IA3 (primary censoring rule)[2,3]

Overall ITT population | **PD-L1 TPS ≥50%**



NOTE ON THE STUDY POPULATION[1,4]

- The ITT population of KEYNOTE-091 includes 167 patients who did not receive adjuvant platinum-based chemotherapy
- Prior adjuvant platinum-based chemotherapy is a UK license requirement for KEYTRUDA in this setting
- Data are included to provide appropriate context for the exploratory analyses in the licensed subgroup

Summary of DFS by population at IA3[2,3]

	HR (95% CI)*	Median, months	Observed p-value†	Outcome
ITT	0.81 (0.68–0.96)	53.8 vs 43.0	0.00812	Not tested‡
PD-L1 TPS ≥50%	0.83 (0.59–1.16)	67.0 vs 47.6	0.13499§	Not positive¶

*Based on the multivariate Cox regression model with treatment adjusted by the following covariates: Stage (IB vs II vs IIIA), PD-L1 status (≥50% vs 1–49% vs <1%), region (Western Europe vs Eastern Europe vs rest of world vs Asia), histology (squamous vs non-squamous), and smoking status (never vs former/current).[2]
†One-sided p-value based on permutation test with multivariate Cox regression model.[2]
‡The success criterion was met for DFS at IA2.[2]
§P-value boundary: 0.01038.[2]
¶Although DFS in TPS ≥50% can be re-tested at the full alpha level (0.025) after OS hypotheses are rejected, its p-value exceeds the boundary for significance. Consequently, DFS in TPS ≥1% cannot be tested in future analyses, regardless of OS outcomes.[2]

Adjuvant KEYTRUDA demonstrated improved DFS with a **17% reduced risk in recurrence or death** vs placebo in the PD-L1 TPS ≥50% population (HR: 0.83, p=0.13499)[2,3]

Adapted from Besse B, *et al*. ESMO 2023 and KEYTRUDA Public Assessment Report 2023.[2,3]

IA3: median follow-up was 46.7 months; data cut-off date: 24 January 2023.[2] CI, confidence interval; DFS, disease-free survival; EPAR, European public assessment report; HR, hazard ratio; IA, interim analysis; ITT, intention-to-treat; KM, Kaplan-Meier; NSCLC, non–small cell lung cancer; OS, overall survival; PD-L1, programmed death-ligand 1; TPS, tumour proportion score.

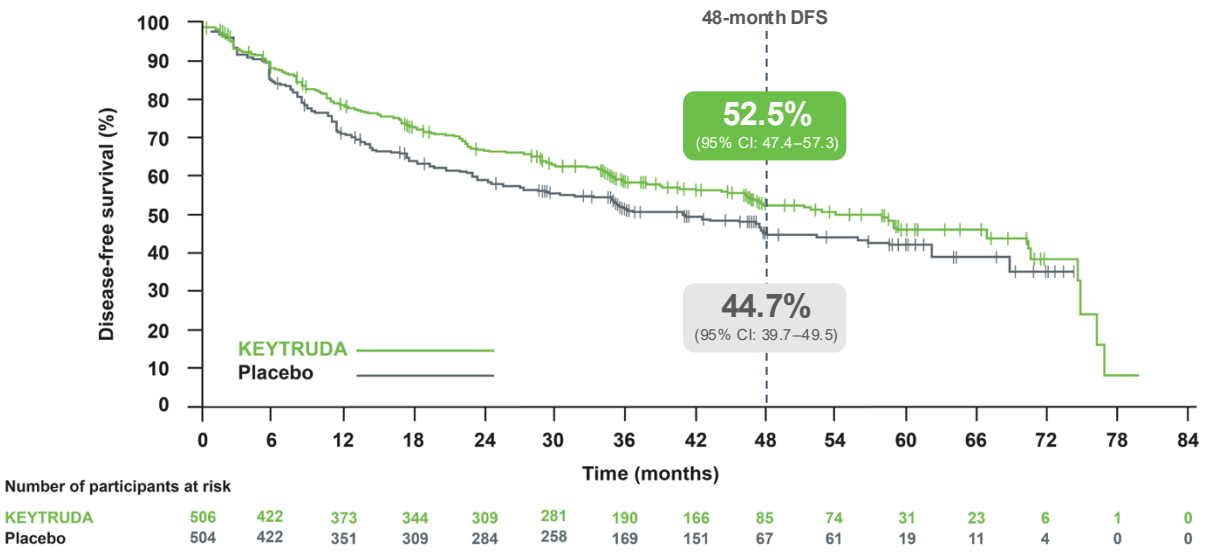
1. KEYTRUDA® (pembrolizumab) Summary of Product Characteristics. United Kingdom. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026. **2.** European Medicines Agency. European public assessment report: KEYTRUDA. Available at: https://www.ema.europa.eu/en/documents/variation-report/keytruda-h-c-003820-ii-0121-epar-assessment-report-variation_en.pdf. Accessed: May 2026. **3.** Besse B. Adjuvant pembrolizumab versus placebo for early-stage NSCLC after resection and optional chemotherapy: updated results from PEARLS/KEYNOTE-091. ESMO Immuno-oncology. 6–8 December 2023. Geneva, Switzerland. **4.** O'Brien M, *et al. Lancet Oncol* 2022;23:1274–1286.

KEYNOTE-091: DFS in patients who had adjuvant chemotherapy[1–3]

Exploratory analysis of DFS

IA3

KM estimates of DFS for prior adjuvant chemotherapy at IA3 (primary censoring rule)[1,3]



Summary of DFS for prior adjuvant chemotherapy at IA3[2]

	Events/patients, % (n/N)	Event rate per 100 person-months, (person-months)	12-month DFS, % (95% CI)
KEYTRUDA	44.5 (225/506)	1.4 (15,754.5)	78.7 (74.8–82.1)
Placebo	52.0 (262/504)	1.8 (14,614.8)	71.0 (66.8–74.7)
HAZARD RATIO: 0.76 (0.64–0.91); p=0.00150*			

Adapted from KN-091 EPAR report 2023.[2]

mDFS for patients who received adjuvant chemotherapy[2]

~4.5 years for KEYTRUDA

vs

~3.4 years for placebo

4.483 years; mDFS: 53.8 (95% CI: 46.2–70.4) months

3.375 years, mDFS: 40.5 (95% CI: 32.9–47.4) months

Adjuvant KEYTRUDA demonstrated improved DFS with a **24% reduced risk in recurrence or death** vs placebo in patients who received prior adjuvant chemotherapy (HR: 0.76, p=0.0014)[1,2]

Adapted from Besse B, *et al*. ESMO 2023.[3]

IA3: median follow-up was 46.7 months; data cut-off date: 24 January 2023.[2] *Hazard ratio based on the multivariate Cox regression model with treatment adjusted by the following covariates: Stage (IB vs II vs IIIA), PD-L1 status (≥50% vs 1–49% vs <1%), region (Western Europe vs Eastern Europe vs rest of world vs Asia), histology (squamous vs non-squamous), and smoking status (never vs former/current); one-sided p-value based on the Wald test in the multivariate Cox regression model.[2] CI, confidence interval; DFS, disease-free survival; EPAR, European public assessment report; IA, interim analysis; KM, Kaplan-Meier; mDFS, median disease-free survival; PD-L1, programmed death-ligand 1.

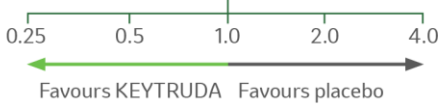
1. KEYTRUDA® (pembrolizumab) Summary of Product Characteristics. United Kingdom. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026. **2.** European Medicines Agency. European public assessment report: KEYTRUDA. Available at: https://www.ema.europa.eu/en/documents/variation-report/keytruda-h-c-003820-ii-0121-epar-assessment-report-variation_en.pdf. Accessed: May 2026. **3.** Besse B. Adjuvant pembrolizumab versus placebo for early-stage NSCLC after resection and optional chemotherapy: updated results from PEARLS/KEYNOTE-091. ESMO Immuno-oncology. 6–8 December 2023. Geneva, Switzerland.

IA3

KEYNOTE-091: DFS in patients who had adjuvant chemotherapy[1]

Exploratory subgroup analysis of DFS

Subgroup	Events/patients (n/N) KEYTRUDA	Placebo	HR (95% CI)
Overall	44.5% (225/506)	52.0% (262/504)	0.76 (0.64–0.91)
Age			
<65 years	42.8% (113/264)	51.2% (129/252)	0.75 (0.58–0.97)
65–74 years	45.0% (95/211)	50.9% (113/222)	0.77 (0.58–1.02)
75–84 years	54.8% (17/31)	66.7% (20/30)	0.70 (0.35–1.39)
Gender			
M	44.0% (149/339)	50.4% (175/347)	0.81 (0.65–1.02)
F	45.5% (76/167)	55.4% (87/157)	0.70 (0.51–0.96)
Race			
White	43.2% (167/387)	49.5% (194/392)	0.80 (0.65–0.98)
All others	50.0% (49/98)	61.7% (58/94)	0.67 (0.45–1.01)
Geographical region			
Western Europe	44.8% (117/261)	53.0% (141/266)	0.75 (0.58–0.96)
Eastern Europe	46.7% (49/105)	47.9% (46/96)	0.84 (0.56–1.26)
Rest of world	32.1% (17/53)	41.8% (23/55)	0.75 (0.38–1.44)
Asia	48.3% (42/87)	59.8% (52/87)	0.71 (0.47–1.08)
Smoking status			
Never smoker	57.5% (46/80)	66.7% (38/57)	0.72 (0.46–1.14)
Former smoker	43.4% (157/362)	49.9% (187/375)	0.81 (0.65–1.00)
Current smoker	34.4% (22/64)	51.4% (37/72)	0.45 (0.25–0.79)



Adapted from KN-091 EPAR report 2023.[1]

DFS benefit with adjuvant KEYTRUDA was **broadly consistent across subgroups**[1]

IA3: median follow-up was 46.7 months; data cut-off date: 24 January 2023.[1] *For overall population and all subgroups, analysis is based on multivariate Cox regression model with treatment adjusted by the following covariates: Stage (IB vs II vs IIIA), PD-L1 status (≥50% vs 1–49% vs <1%), region (Western Europe vs Eastern Europe vs Rest of world vs Asia), histology (squamous vs non-squamous), and smoking status (never vs former/current). If the number of participants in a category of a subgroup variable is less than 50 (except *EGFR* mutation status), or the number of events in a category of a subgroup variable is zero in one treatment arm, or the number of events in a category of a subgroup variable is less than 5 in the pooled arms, the subgroup analysis will not be performed for this category of the subgroup variable.[1] CI, confidence interval; DFS, disease-free survival; *EGFR*, epidermal growth factor receptor; EPAR, European public assessment report; F, female; HR, hazard ratio; IA, interim analysis; M, male; PD-L1, programmed death-ligand 1.

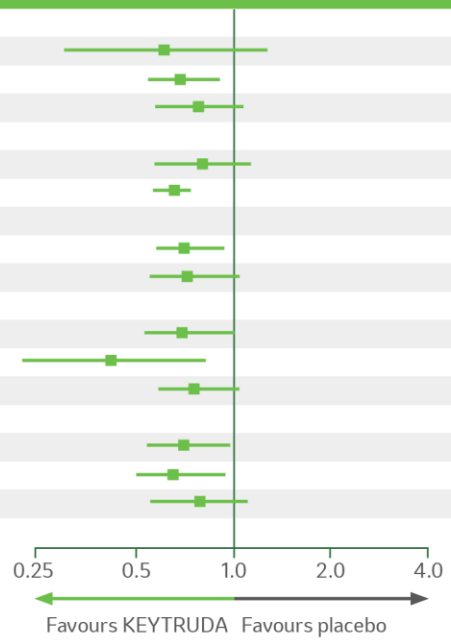
1. European Medicines Agency. European public assessment report: KEYTRUDA. Available at: https://www.ema.europa.eu/en/documents/variation-report/keytruda-h-c-003820-ii-0121-epar-assessment-report-variation_en.pdf. Accessed: May 2026.

IA3

KEYNOTE-091: DFS in patients who had adjuvant chemotherapy[1]

Exploratory subgroup analysis of DFS, *continued*

Subgroup	Events/patients (n/N) KEYTRUDA	Placebo	HR (95% CI)
Stage at baseline per AJCC 7th edition			
IB	31.7% (19/60)	36.8% (21/57)	0.66 (0.33–1.33)
II	40.3% (114/283)	48.5% (143/295)	0.73 (0.57–0.94)
IIIA	56.4% (92/163)	64.0% (96/150)	0.82 (0.61–1.09)
Histology			
Squamous	36.3% (57/157)	40.8% (75/184)	0.85 (0.60–1.20)
Non-squamous	48.1% (168/349)	58.4% (187/320)	0.72 (0.59–0.89)
ECOG PS			
0	44.5% (145/326)	50.7% (148/292)	0.76 (0.61–0.96)
1	44.4% (80/180)	53.8% (114/212)	0.77 (0.57–1.03)
***EGFR* mutation status**			
No	47.4% (90/190)	56.8% (109/192)	0.75 (0.56–1.00)
Yes	55.6% (20/36)	80.0% (24/30)	0.44 (0.22–0.87)
Unknown	41.1% (115/280)	45.7% (129/282)	0.80 (0.62–1.04)
PD-L1 expression			
<1%	46.5% (92/198)	54.5% (108/198)	0.75 (0.56–0.99)
1–49%	46.1% (76/165)	55.2% (91/165)	0.70 (0.51–0.96)
≥50%	39.9% (57/143)	44.7% (63/141)	0.83 (0.57–1.19)



Adapted from KN-091 EPAR report 2023.[1]

DFS benefit with adjuvant KEYTRUDA was **broadly consistent across subgroups**[1]

IA3: median follow-up was 46.7 months; data cut-off date: 24 January 2023.[1] *For overall population and all subgroups, analysis is based on multivariate Cox regression model with treatment adjusted by the following covariates: Stage (IB vs II vs IIIA), PD-L1 status (≥50% vs 1–49% vs <1%), region (Western Europe vs Eastern Europe vs Rest of world vs Asia), histology (squamous vs non-squamous), and smoking status (never vs former/current). If the number of participants in a category of a subgroup variable is less than 50 (except *EGFR* mutation status), or the number of events in a category of a subgroup variable is zero in one treatment arm, or the number of events in a category of a subgroup variable is less than 5 in the pooled arms, the subgroup analysis will not be performed for this category of the subgroup variable.[1] AJCC, American Joint Committee on Cancer; CI, confidence interval; DFS, disease-free survival; ECOG PS, Eastern Cooperative Oncology Group performance status; *EGFR*, epidermal growth factor receptor; EPAR, European public assessment report; HR, hazard ratio; IA, interim analysis; PD-L1, programmed death-ligand 1.

1. European Medicines Agency. European public assessment report: KEYTRUDA. Available at: https://www.ema.europa.eu/en/documents/variation-report/keytruda-h-c-003820-ii-0121-epar-assessment-report-variation_en.pdf. Accessed: May 2026.

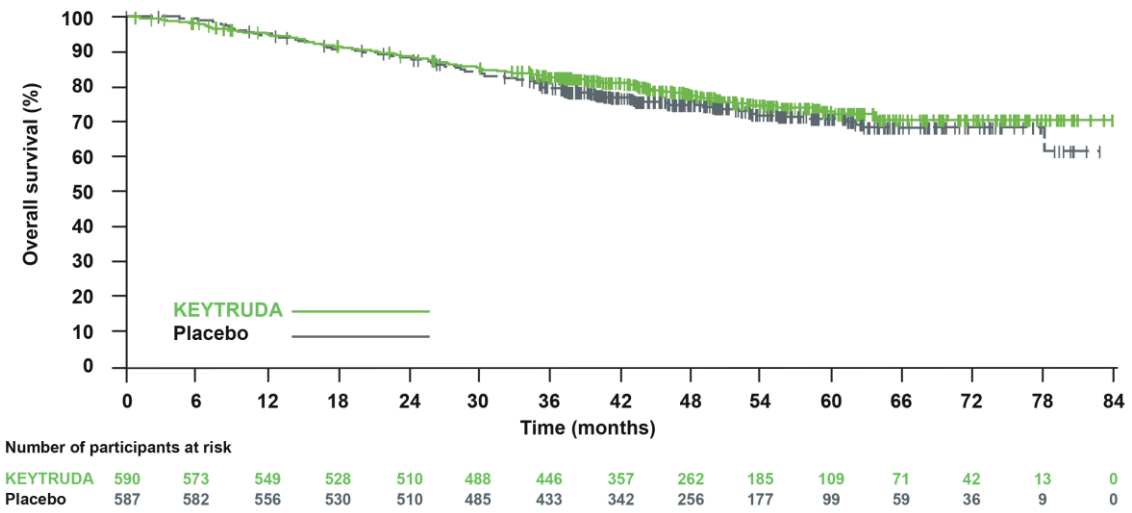
KEYNOTE-091: Overall survival (OS)[1–3]

Secondary endpoint analysis of OS in the ITT population

IA3

KM estimates of OS by population at IA3[2]

Overall ITT population | PD-L1 TPS ≥50%



NOTE ON THE STUDY POPULATION[1,3]

- The ITT population of KEYNOTE-091 includes 167 patients who did not receive adjuvant platinum-based chemotherapy
- Prior adjuvant platinum-based chemotherapy is a UK license requirement for KEYTRUDA in this setting
- Data are included to provide appropriate context for the exploratory analyses in the licensed subgroup

Summary of OS by population at IA3[2]

	HR (95% CI)*	Median, months	Observed p-value†	Outcome
ITT	0.87 (0.69–1.10)	NR vs NR	0.11792	Not positive‡
PD-L1 TPS ≥50%	0.93 (0.57–1.50)	NR vs NR	0.3778	Not positive‡

*Based on the multivariate Cox regression model with treatment adjusted by the following covariates: Stage (IB vs II vs IIIA), PD-L1 status (≥50% vs 1–49% vs <1%), region (Western Europe vs Eastern Europe vs rest of world vs Asia), histology (squamous vs non-squamous), and smoking status (never vs former/current).[2]
†One-sided p-values for OS endpoints are based on the Wald test in the multivariate Cox regression model.[2]
‡Significance to be tested again during next interim analysis.[2]

Adapted from KN-091 EPAR report 2023.[2]

IA3: median follow-up was 46.7 months; data cut-off date: 24 January 2023.[2] CI, confidence interval; EPAR, European public assessment report; HR, hazard ratio; IA, interim analysis; ITT, intention-to-treat; KM, Kaplan-Meier; NR, not reached; NSCLC, non–small cell lung carcinoma; OS, overall survival; PD-L1, programmed death-ligand 1; TPS, tumour proportion score.

1. KEYTRUDA® (pembrolizumab) Summary of Product Characteristics. United Kingdom. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026. **2.** European Medicines Agency. European public assessment report: KEYTRUDA. Available at: https://www.ema.europa.eu/en/documents/variation-report/keytruda-h-c-003820-ii-0121-epar-assessment-report-variation_en.pdf. Accessed: May 2026. **3.** O'Brien M, *et al. Lancet Oncol* 2022;23:1274–1286.

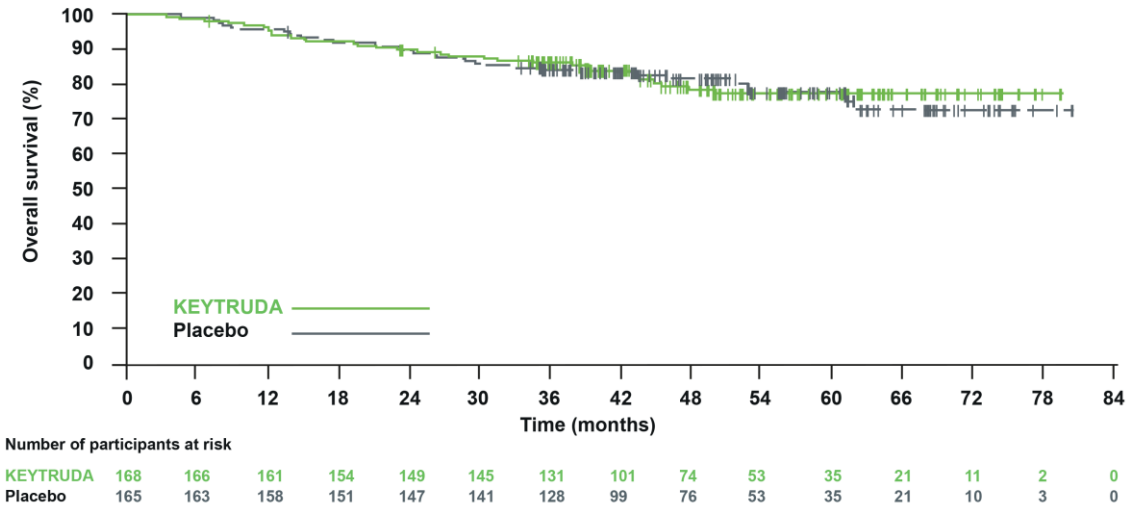
KEYNOTE-091: OS in patients with PD-L1 TPS ≥50%[1–3]

Secondary endpoint analysis of OS in the PD-L1 TPS ≥50% population

IA3

KM estimates of OS by population at IA3[2]

Overall ITT population | **PD-L1 TPS ≥50%**



NOTE ON THE STUDY POPULATION[1,3]

- The ITT population of KEYNOTE-091 includes 167 patients who did not receive adjuvant platinum-based chemotherapy
- Prior adjuvant platinum-based chemotherapy is a UK license requirement for KEYTRUDA in this setting
- Data are included to provide appropriate context for the exploratory analyses in the licensed subgroup

Summary of OS by population at IA3[2]

	HR (95% CI)*	Median, months	Observed p-value†	Outcome
ITT	0.87 (0.69–1.10)	NR vs NR	0.11792	Not positive‡
PD-L1 TPS ≥50%	0.93 (0.57–1.50)	NR vs NR	0.3778	Not positive‡

*Based on the multivariate Cox regression model with treatment adjusted by the following covariates: Stage (IB vs II vs IIIA), PD-L1 status (≥50% vs 1–49% vs <1%), region (Western Europe vs Eastern Europe vs rest of world vs Asia), histology (squamous vs non-squamous), and smoking status (never vs former/current).[2]
†One-sided p-values for OS endpoints are based on the Wald test in the multivariate Cox regression model.[2]
‡Significance to be tested again during next interim analysis.[2]

Adapted from KN-091 EPAR report 2023.[2]

IA3: median follow-up was 46.7 months; data cut-off date: 24 January 2023.[2] CI, confidence interval; EPAR, European public assessment report; HR, hazard ratio; IA, interim analysis; ITT, intention-to-treat; KM, Kaplan-Meier; NR, not reached; NSCLC, non–small cell lung carcinoma; OS, overall survival; PD-L1, programmed death-ligand 1; TPS, tumour proportion score.

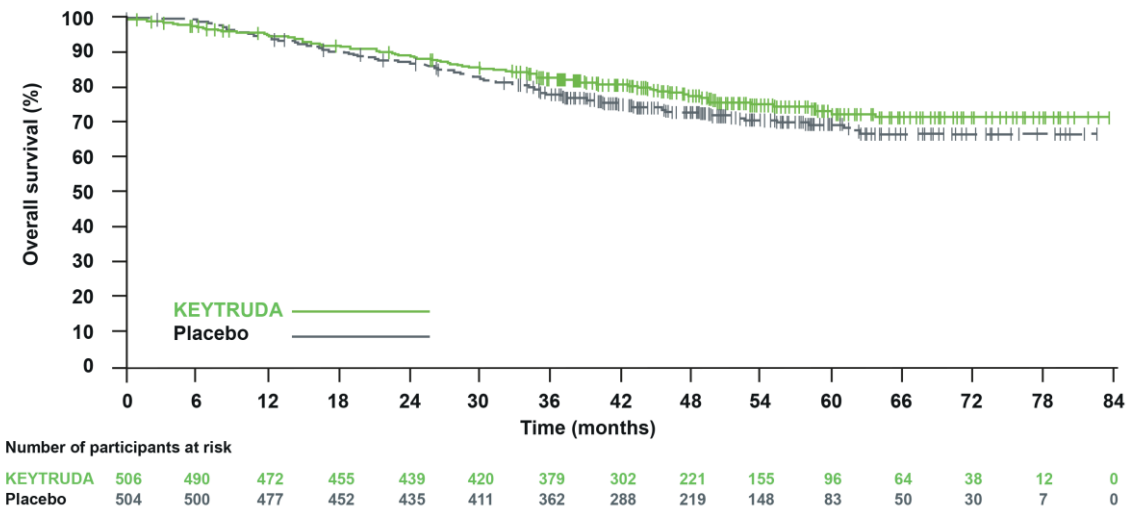
1. KEYTRUDA® (pembrolizumab) Summary of Product Characteristics. United Kingdom. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026. **2.** European Medicines Agency. European public assessment report: KEYTRUDA. Available at: https://www.ema.europa.eu/en/documents/variation-report/keytruda-h-c-003820-ii-0121-epar-assessment-report-variation_en.pdf. Accessed: May 2026. **3.** O'Brien M, *et al. Lancet Oncol* 2022;23:1274–1286.

KEYNOTE-091: OS in patients who had adjuvant chemotherapy[1]

Exploratory analysis of DFS

IA3

KM estimates of OS for prior adjuvant chemotherapy at IA3



Summary of OS for prior adjuvant chemotherapy at IA3

	Median, months	Events/patients, % (n/N)	Event rate per 100 person-months, (person-months)	12-month OS, % (95% CI)
KEYTRUDA	NR	22.3 (113/506)	0.5 (22810.0)	95.6 (93.4–97.1)
Placebo	NR	27.4 (138/504)	0.6 (22313.1)	95.0 (92.7–96.6)
HAZARD RATIO: 0.79 (0.62–1.01); p=0.03224*				

Adapted from KN-091 EPAR report 2023.[2]

Adapted from KN-091 EPAR report 2023.[1]

IA3: median follow-up was 46.7 months; data cut-off date: 24 January 2023.[1] *Hazard ratio based on the multivariate Cox regression model with treatment adjusted by the following covariates: Stage (IB vs II vs IIA), PD-L1 status (≥50% vs 1-49% vs <1%), region (Western Europe vs Eastern Europe vs rest of world vs Asia), histology (squamous vs non-squamous), and smoking status (never vs former/current).[1] †One-sided p-value based on the Wald Test in the multivariate Cox regression model.[1] CI, confidence interval; DFS, disease-free survival; EPAR, European public assessment report; IA, interim analysis; ITT, intention-to-treat; KM, Kaplan-Meier; NR, not reached; NSCLC, non-small cell lung carcinoma; OS, overall survival; PD-L1, programmed death-ligand 1.

1. KEYTRUDA® (pembrolizumab) Summary of Product Characteristics. United Kingdom. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026. **2.** European Medicines Agency. European public assessment report: KEYTRUDA. Available at: https://www.ema.europa.eu/en/documents/variation-report/keytruda-h-c-003820-ii-0121-epar-assessment-report-variation_en.pdf. Accessed: May 2026.

KEYNOTE-091: Summary of 4-year efficacy data[1]

IA3

Summary of primary endpoints and secondary efficacy endpoints at IA3, after 46.7 months median follow-up[1]

		Population	Events, n (IF)	Median, months	HR (95% CI)*	Observed p-value†	Outcome
Dual primary endpoints	DFS	ITT	561 (102%)	53.8 vs 43.0	0.81 (0.68–0.96)	0.00812	Not tested (success criterion met at IA2)
	DFS	TPS ≥50%	140 (99%)	67.0 vs 47.6	0.83 (0.59–1.16)	0.13499‡	Not positive
Key secondary endpoints	DFS	TPS ≥1%	331 (102%)	58.7 vs 42.8	0.78 (0.62–0.97)	0.01327	Not tested
	OS	ITT	290	NR vs NR	0.87 (0.69–1.10)	0.11792	Not positive; to be tested again at next IA
	OS	TPS ≥50%†	67	NR vs NR	0.93 (0.57–1.50)	0.37780	Not positive; to be tested again at next IA
	OS	TPS ≥1%†	165	NR vs NR	0.83 (0.61–1.13)	0.12390	Not tested; to be tested once positive in TPS ≥50%

NOTE ON THE STUDY POPULATION[2,3]

- The ITT population of KEYNOTE-091 includes 167 patients who did not receive adjuvant platinum-based chemotherapy
- Prior adjuvant platinum-based chemotherapy is a UK license requirement for KEYTRUDA in this setting
- Data are included to provide appropriate context for the exploratory analyses in the licensed subgroup

Adapted from KN-091 EPAR report 2023.[1]

IA3: median follow-up was 46.7 months; data cut-off date: 24 January 2023.[1] *Based on the multivariate Cox regression model with treatment adjusted by the following covariates: Stage (IB vs II vs IIIA), PD-L1 status (≥50% vs 1-49% vs <1%), region (Western Europe vs Eastern Europe vs rest of world vs Asia), histology (squamous vs non-squamous), and smoking status (never vs former/current).[1] †One-sided p-values for DFS endpoints are based on the permutation test with the multivariate Cox regression model; one-sided p-values for OS endpoints are based on the Wald test in the multivariate Cox regression model.[1] ‡P-value boundary: 0.01038.[1] CI, confidence interval; DFS, disease-free survival; EPAR, European public assessment report; HR, hazard ratio; IA, interim analysis; IF, information fraction; ITT, intention-to-treat; NR, not reached; OS, overall survival; PD-L1, programmed death-ligand 1; TPS, tumour proportion score.

1. European Medicines Agency. European public assessment report: KEYTRUDA. Available at: https://www.ema.europa.eu/en/documents/variation-report/keytruda-h-c-003820-ii-0121-epar-assessment-report-variation_en.pdf. Accessed: May 2026. **2.** KEYTRUDA® (pembrolizumab) Summary of Product Characteristics. United Kingdom. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026. **3.** O'Brien M, *et al. Lancet Oncol* 2022;23:1274–1286.

IA2

KEYNOTE-091: Safety profile (as-treated population)[1]

Median follow-up: 35.6 months. Data cut-off date: 20 September 2021.

Adverse events of any cause and grade (occurring in ≥5% of patients) in both KEYTRUDA and placebo group

	KEYTRUDA (n=580)				Placebo (n=581)			
AE, n (%)	Grade 1–2	Grade 3	Grade 4	Grade 5	Grade 1–2	Grade 3	Grade 4	Grade 5
Any event	358 (62%)	166 (29%)	21 (4%)	11 (2%)	379 (65%)	130 (22%)	14 (2%)	6 (1%)
Increased bodyweight	127 (22%)	6 (1%)	0	0	159 (27%)	9 (2%)	0	0
Pruritus	124 (21%)	1 (<1%)	0	0	72 (12%)	2 (<1%)	0	0
Hypothyroidism	119 (21%)	1 (<1%)	0	0	27 (5%)	0	0	0
Arthralgia	104 (18%)	4 (1%)	0	0	74 (13%)	1 (<1%)	0	0
Diarrhoea	99 (17%)	7 (1%)	0	0	81 (14%)	2 (<1%)	0	0
Fatigue	95 (16%)	1 (<1%)	0	0	86 (15%)	3 (<1%)	0	0
Cough	86 (15%)	1 (<1%)	0	0	98 (17%)	0	0	0
Hypertension	32 (6%)	35 (6%)	0	0	42 (7%)	32 (6%)	0	0
Dyspnoea	58 (10%)	8 (1%)	0	0	65 (11%)	7 (1%)	0	0
Hyperthyroidism	61 (11%)	1 (<1%)	0	0	17 (3%)	0	0	0
Upper respiratory tract infection	53 (9%)	0	0	0	55 (9%)	0	0	0
Nausea	51 (9%)	1 (<1%)	0	0	37 (6%)	0	0	0
Nasopharyngitis	50 (9%)	0	0	0	32 (6%)	0	0	0
Rash	47 (8%)	2 (<1%)	0	0	29 (5%)	0	0	0
Increased alanine aminotransferase	42 (7%)	4 (1%)	0	0	31 (5%)	3 (1%)	0	0
Back pain	44 (8%)	1 (<1%)	0	0	46 (8%)	0	0	0
Headache	43 (7%)	2 (<1%)	0	0	45 (8%)	1 (<1%)	0	0

Adapted from O'Brien M, *et al*. 2022.[1]

The 4 doses were 2 mg/kg bodyweight every 3 weeks, 200 mg every 3 weeks, or 10 mg/kg bodyweight every 2 or 3 weeks.[1]
DFS, disease-free survival; IA, interim analysis; NSCLC, non–small cell lung cancer.

1. O'Brien M, *et al. Lancet Oncol* 2022;23:1274–1286.

IA2

KEYNOTE-091: Safety profile (as-treated population)

The adverse event profile observed with KEYTRUDA was similar to that in previous studies of KEYTRUDA monotherapy, including of locally advanced or metastatic NSCLC and of adjuvant therapy for melanoma and renal-cell carcinoma.[1]

The most common adverse events (occurring in ≥5% of patients) of any grade in both KEYTRUDA and placebo group (continued)[1]

	KEYTRUDA (n=580)				Placebo (n=581)			
AE, n (%)	Grade 1–2	Grade 3	Grade 4	Grade 5	Grade 1–2	Grade 3	Grade 4	Grade 5
Asthenia	41 (7%)	3 (1%)	0	0	29 (5%)	3 (1%)	0	0
Maculopapular rash	40 (7%)	3 (1%)	0	0	20 (3%)	0	0	0
Increased aspartate aminotransferase	39 (7%)	2 (<1%)	0	0	28 (5%)	4 (1%)	0	0
Decreased appetite	40 (7%)	1 (<1%)	0	0	26 (4%)	1 (<1%)	0	0
Decreased bodyweight	39 (7%)	0	0	0	25 (4%)	0	0	0
Increased blood creatinine	38 (7%)	0	0	0	32 (6%)	0	0	0
Myalgia	35 (6%)	2 (<1%)	0	0	15 (3%)	0	0	0
Productive cough	37 (6%)	0	0	0	15 (3%)	0	0	0
Constipation	35 (6%)	0	0	0	41 (7%)	0	0	0
Influenza-like illness	34 (6%)	0	0	0	32 (6%)	0	0	0
Pneumonitis	27 (5%)	5 (1%)	2 (<1%)	0	12 (2%)	4 (1%)	0	0
Pyrexia	31 (5%)	1 (<1%)	0	0	33 (6%)	1 (<1%)	0	0
Dry skin	31 (5%)	0	0	0	21 (4%)	0	0	0
Pain in extremity	18 (3%)	0	0	0	30 (5%)	1 (<1%)	0	0
Paraesthesia	18 (3%)	0	0	0	32 (6%)	0	0	0

Adapted from O'Brien M, *et al*. 2022.[1]

The 4 doses were 2 mg/kg bodyweight every 3 weeks, 200 mg every 3 weeks, or 10 mg/kg bodyweight every 2 or 3 weeks.[1]
NSCLC, non–small cell lung cancer.

1. O'Brien M, *et al. Lancet Oncol* 2022;23:1274–1286.

IA2

KEYNOTE-091: Safety profile (as-treated population)

Overall summary of adverse events at 35.6 months follow-up[1]

Potentially immune-mediated adverse events and infusion reactions of any incidence in the safety population[1]

	KEYTRUDA (n=580)				Placebo (n=581)			
AE, n (%)	Grade 1–2	Grade 3	Grade 4	Grade 5	Grade 1–2	Grade 3	Grade 4	Grade 5
Any event	180 (31%)	38 (7%)	6 (1%)	2 (<1%)	64 (11%)	11 (2%)	0	0
Hypothyroidism	119 (21%)	1 (<1%)	0	0	27 (5%)	0	0	0
Hyperthyroidism	61 (11%)	1 (<1%)	0	0	17 (3%)	0	0	0
Pneumonitis	32 (6%)	6 (1%)	2 (<1%)	0	13 (2%)	4 (1%)	0	0
Severe skin reactions	5 (1%)	11 (2%)	0	0	2 (<1%)	2 (<1%)	0	0
Colitis	10 (2%)	4 (1%)	0	0	4 (1%)	1 (<1%)	0	0
Adrenal insufficiency	6 (1%)	4 (1%)	0	0	0	0	0	0
Hepatitis	1 (<1%)	5 (1%)	4 (<1%)	0	2 (<1%)	2 (<1%)	0	0
Hypophysitis	4 (1%)	3 (1%)	0	0	0	0	0	0
Thyroiditis	6 (1%)	0	0	0	1(<1%)	0	0	0
Infusion reactions	5 (1%)	0	0	0	4 (<1%)	0	0	0
Myocarditis	1 (<1%)	2 (<1%)	0	2 (<1%)	0	1 (<1%)	0	0
Nephritis	4 (<1%)	0	0	0	0	0	0	0
Pancreatitis	2 (<1%)	0	0	0	1 (<1%)	1 (<1%)	0	0
Myositis	1 (<1%)	0	0	0	0	0	0	0
Sarcoidosis	0	1 (<1%)	0	0	0	0	0	0
Type 1 diabetes	0	1 (<1%)	0	0	0	0	0	0
Vasculitis	0	1 (<1%)	0	0	0	0	0	0

Adapted from O'Brien M, *et al*. 2022.[1]

Potentially immune-mediated adverse events and infusion reactions were based on a list of terms prepared by the sponsor and were considered regardless of attribution to trial treatment by the investigator. In addition to the specific preferred terms listed, related terms were included.[1] The 4 doses were 2 mg/kg bodyweight every 3 weeks, 200 mg every 3 weeks, or 10 mg/kg bodyweight every 2 or 3 weeks.[1]

NSCLC, non–small cell lung cancer.

1. O'Brien M, *et al. Lancet Oncol* 2022;23:1274–1286.

KEYNOTE-091: Safety profile

Overall summary of adverse events at 46.7 months follow-up[1,2]

IA3

The most common adverse events (occurring in ≥15% of patients in the as-treated population by IA3)[1]

AE, n (%)	KEYTRUDA (n=580)	Placebo (n=581)
Any event, any grade	556 (95.9)	529 (91.0)
Any event, Grade ≥3	198 (34.1)	150 (25.8)
Increased body weight	132 (22.8)	168 (28.9)
Pruritus	125 (21.6)	74 (12.7)
Hypothyroidism	120 (20.7)	27 (4.6)
Arthralgia	107 (18.4)	72 (12.4)
Diarrhoea	106 (18.3)	83 (14.3)
Fatigue	96 (16.6)	89 (15.3)
Cough	87 (15.0)	98 (16.9)

Adapted from Besse B. 2023.[1]

Incidence rates of treatment-related AEs

Any grade, any cause:

- 75.2% (436/580) vs 52.5% (305/581)

Grade ≥3, any cause:

- 15.3% (89/580) vs 4.3% (25/581)*

The AE profile of KEYTRUDA observed during KEYNOTE-091 was similar to that in previous studies of KEYTRUDA monotherapy, including of locally advanced or metastatic NSCLC and of adjuvant therapy for melanoma and renal-cell carcinoma.[2]

IA3: median follow-up was 46.7 months; data cut-off date: 24 January 2023.[3] *Grade 5 treatment-related AEs occurred in four patients in the KEYTRUDA group: myocarditis (n=2), cardiogenic shock, pneumonia, septic shock, sudden death (n=1). There were no Grade 5 treatment-related AEs in the placebo group.[1] AE, adverse event; IA, interim analysis; NSCLC, non–small cell lung carcinoma.

1. Besse B. Adjuvant pembrolizumab versus placebo for early-stage NSCLC after resection and optional chemotherapy: updated results from PEARLS/KEYNOTE-091. ESMO Immuno-oncology. 6–8 December 2023. Geneva, Switzerland. **2.** O'Brien M, *et al. Lancet Oncol* 2022;23:1274–1286. **3.** European Medicines Agency. European public assessment report: KEYTRUDA. Available at: https://www.ema.europa.eu/en/documents/variation-report/keytruda-h-c-003820-ii-0121-epar-assessment-report-variation_en.pdf. Accessed: May 2026.

KEYNOTE-091: Safety profile

Immune-mediated adverse events (IMAEs) and infusion reactions at 46.7 months follow-up[1]

IA3

The most common IMAEs and infusion reactions (occurring in ≥1% of patients in the as-treated population by IA3)*[1]

IMAE (any grade), n (%)	KEYTRUDA (n=580)	Placebo (n=581)
Hypothyroidism	120 (20.7)	27 (4.6)
Hyperthyroidism	62 (10.7)	17 (2.9)
Pneumonitis	40 (6.9)	17 (2.9)
Severe skin reactions	16 (2.8)	4 (0.7)
Colitis	14 (2.4)	5 (0.9)
Adrenal insufficiency	10 (1.7)	0
Hepatitis	9 (1.6)	4 (0.7)
Hypophysitis	7 (1.2)	0
Thyroiditis	6 (1.0)	1 (0.2)

Adapted from Besse B. 2023.[2]

Incidence rates of IMAEs and infusion reactions

Any grade, any cause:

- 39.1% (227/580) vs 13.1% (76/581)

Grade ≥3, any cause:

- 7.9% (46/580) vs 1.9% (11/581)

The AE profile of KEYTRUDA observed during KEYNOTE-091 was similar to that in previous studies of KEYTRUDA monotherapy, including of locally advanced or metastatic NSCLC and of adjuvant therapy for melanoma and renal-cell carcinoma.[2]

IA3: median follow-up was 46.7 months; data cut-off date: 24 January 2023.[3] *Immune-mediated adverse events and infusion reactions were based on a list of preferred terms intended to capture known risks of KEYTRUDA and were considered regardless of attribution to study treatment by the investigator.[1] AE, adverse event; IA, interim analysis; IMAE, immune-mediated adverse event; NSCLC, non–small cell lung carcinoma.

1. Besse B. Adjuvant pembrolizumab versus placebo for early-stage NSCLC after resection and optional chemotherapy: updated results from PEARLS/KEYNOTE-091. ESMO Immuno-oncology. 6–8 December 2023. Geneva, Switzerland. **2.** O'Brien M, *et al. Lancet Oncol* 2022;23:1274–1286.

Safety profile of KEYTRUDA monotherapy[1]

The safety of KEYTRUDA monotherapy has been evaluated in 7631 patients across tumour types and across four doses (SmPC last updated: 04 December 2025)*

In patients receiving KEYTRUDA monotherapy:

Most adverse events (AEs) reported were either Grade 1 or 2 in severity.

The most frequent were:

- Fatigue (31%)
- Diarrhoea (22%)
- Nausea (20%)

The most serious AEs were IMAEs and infusion-related reactions.

Incidence rates of IMAEs in the adjuvant setting:

- Any grade (37%); Grade ≥3 (9%)

Incidence rates of IMAEs in the metastatic setting:

- Any grade (25%); Grade ≥3 (6%)

No new safety signals were identified in the adjuvant setting.

In patients with NSCLC and other tumour types receiving KEYTRUDA as monotherapy in the adjuvant setting (n=2060), the incidence of hypothyroidism was 18.5%; the incidence of hyperthyroidism was 11%.†

*The 4 doses were 2 mg/kg body weight every 3 weeks, 200 mg every 3 weeks, or 10 mg/kg body weight every 2 or 3 weeks. Median observation time was 8.5 months (range:1 day to 39 months).[1] †AE rates from a pooled dataset of patients with melanoma, NSCLC or RCC who were treated with adjuvant KEYTRUDA monotherapy.[1] AE, adverse event; IMAE, immune-mediated adverse event; NSCLC, non–small cell lung carcinoma; RCC, renal cell carcinoma; SmPC, Summary of Product Characteristics.

1. KEYTRUDA® (pembrolizumab) Summary of Product Characteristics. United Kingdom. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026.

KEYNOTE-091: Summary

A key to more possibilities for appropriate patients with completely resected NSCLC following platinum-based chemotherapy

Efficacy of KEYTRUDA in KEYNOTE-091[1]

After 46.7 months median follow-up, vs placebo, **adjuvant KEYTRUDA monotherapy reduced the risk of disease recurrence or death (DFS) by:**

19% in the ITT population

HR: 0.81; 95% CI: 0.68–0.96;* p=0.00812† (primary endpoint; statistically significant)

17% in patients with PD-L1 TPS ≥50%

HR: 0.83; 95% CI: 0.59–1.16;* p=0.13499† (primary endpoint; not statistically significant)

24% in those who received prior adjuvant chemotherapy

HR: 0.76; 95% CI: 0.64–0.91;* p=0.00150‡ (exploratory endpoint)

In patients who received adjuvant chemotherapy:[1]

- DFS was extended by ~4.5 years with KEYTRUDA vs ~3.4 years with placebo (53.8 months vs 40.5 months)§
- OS results are not yet mature, but a positive trend is emerging in favour of KEYTRUDA (22.3% vs 27.4% OS event rate)

Safety profile of KEYTRUDA in KEYNOTE-091[1–4]

After 46.7 months median follow-up, no new safety signals were identified.[1,4]

KEYNOTE-091 data were comparable to other safety reports of KEYTRUDA monotherapy, except for hypothyroidism and hyperthyroidism.[2,3]

TRAE incidence rates with KEYTRUDA vs placebo:[4]

- Any grade: 75.2% vs 52.5%; Grade ≥3: 15.3% vs 4.3%

IMAE incidence rates with KEYTRUDA vs placebo:[4]

- Any grade: 39.1% vs 13.1%; Grade ≥3: 7.9% vs 1.9%

NOTE ON THE STUDY POPULATION[2,3]

- The ITT population of KEYNOTE-091 includes 167 patients who did not receive adjuvant platinum-based chemotherapy
- Prior adjuvant platinum-based chemotherapy is a UK license requirement for KEYTRUDA in this setting
- Data are included to provide appropriate context for the exploratory analyses in the licensed subgroup

*Based on the multivariate Cox regression model with treatment adjusted by the following covariates: Stage (IB vs II vs IIIA), PD-L1 status (≥50% vs 1–49% vs <1%), region (Western Europe vs Eastern Europe vs rest of world vs Asia), histology (squamous vs non-squamous), and smoking status (never vs former/current).[1] †One-sided p-value based on permutation test with multivariate Cox regression model.[1] ‡One-sided p-value based on the Wald test in the multivariate Cox regression model.[1] §4.483 years (53.8 months); 3.375 years (40.5 months).[1]
CI, confidence interval; DFS, disease-free survival; HR, hazard ratio; ITT, intention-to-treat; NSCLC, non–small cell lung carcinoma; OS, overall survival; PD-L1, programmed death-ligand 1; TRAE, treatment-related adverse event; TPS, tumour proportion score.

1. European Medicines Agency. European public assessment report: KEYTRUDA. Available at: https://www.ema.europa.eu/en/documents/variation-report/keytruda-h-c-003820-ii-0121-epar-assessment-report-variation_en.pdf. Accessed: May 2026. **2.** KEYTRUDA® (pembrolizumab) Summary of Product Characteristics. United Kingdom. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026. **3.** O'Brien M, *et al. Lancet Oncol* 2022;23:1274–1286 **4.** Besse B. Adjuvant pembrolizumab versus placebo for early-stage NSCLC after resection and optional chemotherapy: updated results from PEARLS/KEYNOTE-091. ESMO Immuno-oncology. 6–8 December 2023. Geneva, Switzerland.

KEYTRUDA offers flexibility of dosing[1]

Administered as an IV infusion

Over 30 minutes

200 mg Q3W or 400 mg Q6W

The 200 mg Q3W (once every 3 weeks) 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 every 6 weeks) dosing for monotherapy and combination therapy.[1]

IV, intravenous; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. KEYTRUDA Summary of Product Characteristics. MSD. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026.