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

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MSD Oncology

KEYNOTE-671:

KEYTRUDA® (pembrolizumab) in combination with platinum-containing chemotherapy as neoadjuvant therapy and then continued as adjuvant monotherapy for patients with resectable Stage II, IIIA or IIIB (N2) non-small cell lung carcinoma (NSCLC) (AJCC 8th edition) (KEYTRUDA perioperative treatment)

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 at high risk of recurrence in adults.[1]

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AJCC, American Joint Committee on Cancer; NSCLC, non-small cell lung carcinoma.

1. KEYTRUDA Summary of Product Characteristics. MSD. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: August 2025.

KEYTRUDA® (pembrolizumab)

MSD

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KEYTRUDA early-stage and advanced NSCLC indications[1]

- **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 adjuvant treatment of adults with NSCLC who are at high risk of recurrence following complete resection and platinum-based chemotherapy
- 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 Summary of Product Characteristics. MSD. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: August 2025.

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.

1. West H, *et al. Clin Lung Cancer* 2023;24:260-268.

KEYNOTE-671 indication:

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 at high risk of recurrence in adults[1]

1. KEYTRUDA Summary of Product Characteristics. MSD. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: August 2025.

KEYNOTE-671 study design: Randomised, double-blind, Phase III[1]

Resectable Stage II, IIIA or IIIB (N2) NSCLC (AJCC 8th edition)

- ECOG PS 0–1
- Tumour tissue for PD-L1 evaluation at central lab
- Biopsy of suspicious hilar or mediastinal lymph node(s)
- Untreated, pathologically confirmed (PET scan may be used as surrogate for N1 lymph nodes)*
- No ILD or pneumonitis requiring steroids
- *EGFR/ALKm* permitted

R 1:1 (N=797)

Neoadjuvant phase

IV KEYTRUDA 200 mg Q3W **+ cisplatin** 75 mg/m^2 *combined with either* **pemetrexed**† 500 mg/m^2 OR **gemcitabine**‡ 1000 mg/m^2 for up to 4 cycles

→ Surgery → 4–12w → Adjuvant phase: **KEYTRUDA**§ 200 mg Q3W ≤13 cycles

IV placebo Q3W **+ cisplatin** 75 mg/m^2 *combined with either* **pemetrexed**† 500 mg/m^2 OR **gemcitabine**‡ 1000 mg/m^2 for up to 4 cycles

→ Surgery → 4–12w → **Placebo**§ Q3W ≤13 cycles

Stratification factors:

- Stage (II vs III)
- PD-L1 by 22C3 (TPS <50% vs ≥50%)
- Histology (SQ vs NSQ)
- Region (East Asia vs other)

Dual primary endpoints:

- EFS per investigator review¶ and OS

Key secondary endpoints:

- mPR and pCR per blinded, independent pathology review, and safety

Adapted from Wakelee H, *et al*. N Engl J Med 2023.[1]

*For participants with T2b and T4 tumours.[1] †Permitted for non-squamous disease only.[1] ‡Administered on Days 1 and 8 of cycle; squamous histology only.[1] §Postoperative radiation therapy could be administered for patients with R1-2 resection, extracapsular nodal disease after surgery, and those who do not undergo surgery (followed by adjuvant KEYTRUDA/placebo).[1] ¶EFS defined as time from randomisation to first occurrence of: (i) local PD precluding surgery, (ii) unresectable tumour, (iii) progression or recurrence per RECIST v1.1 by investigator, (iv) death from any cause.[1] AJCC, American Joint Committee on Cancer; *ALKm*, anaplastic lymphoma kinase mutation; DFS, disease-free survival; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EFS, event-free survival; *EGFR*, epidermal growth factor receptor; ILD, interstitial lung disease; IV, intravenous; mPR, major pathological response; N1, involvement of ipsilateral peribronchial and/or ipsilateral hilar lymph nodes (includes direct extension to intrapulmonary nodes);[1] N2, involvement of the ipsilateral mediastinal and/or subcarinal lymph nodes;[1] NSCLC, non-small cell lung carcinoma; NSQ, non-squamous cell carcinoma; OS, overall survival; pCR, pathological complete response; PET, positron emission tomography; PD, progressive disease; PD-L1, programmed death ligand 1; Q3W, every 3 weeks; R, randomised; RECIST, Response Evaluation Criteria in Solid Tumours; SQ, squamous cell carcinoma; TPS, tumour proportion score; w, weeks.

1. Wakelee H, *et al. N Engl J Med* 2023;389:491–503 (including protocol).

KEYNOTE-671: Patient characteristics[1]

Characteristic, n (%)		KEYTRUDA	Placebo
Median age, years (range)		63 (26–83)	64 (35–81)
Sex	Male	279 (70.3)	284 (71.0)
Race	American Indian or Alaska Native	1 (0.3)	0
	Asian	124 (31.2)	125 (31.3)
	Black or African American	6 (1.5)	10 (2.5)
	Multiple	3 (0.8)	10 (2.5)
	White	250 (63.0)	239 (59.8)
	Missing data	13 (3.3)	16 (4.0)
Geographic region	East Asia	123 (31.0)	121 (30.3)
	Not East Asia	274 (69.0)	279 (69.8)
ECOG PS	0	253 (63.7)	246 (61.5)
	1	144 (36.3)	154 (38.5)
Histology	Non-squamous	226 (59.6)	227 (56.8)
	Squamous	171 (43.1)	173 (43.3)

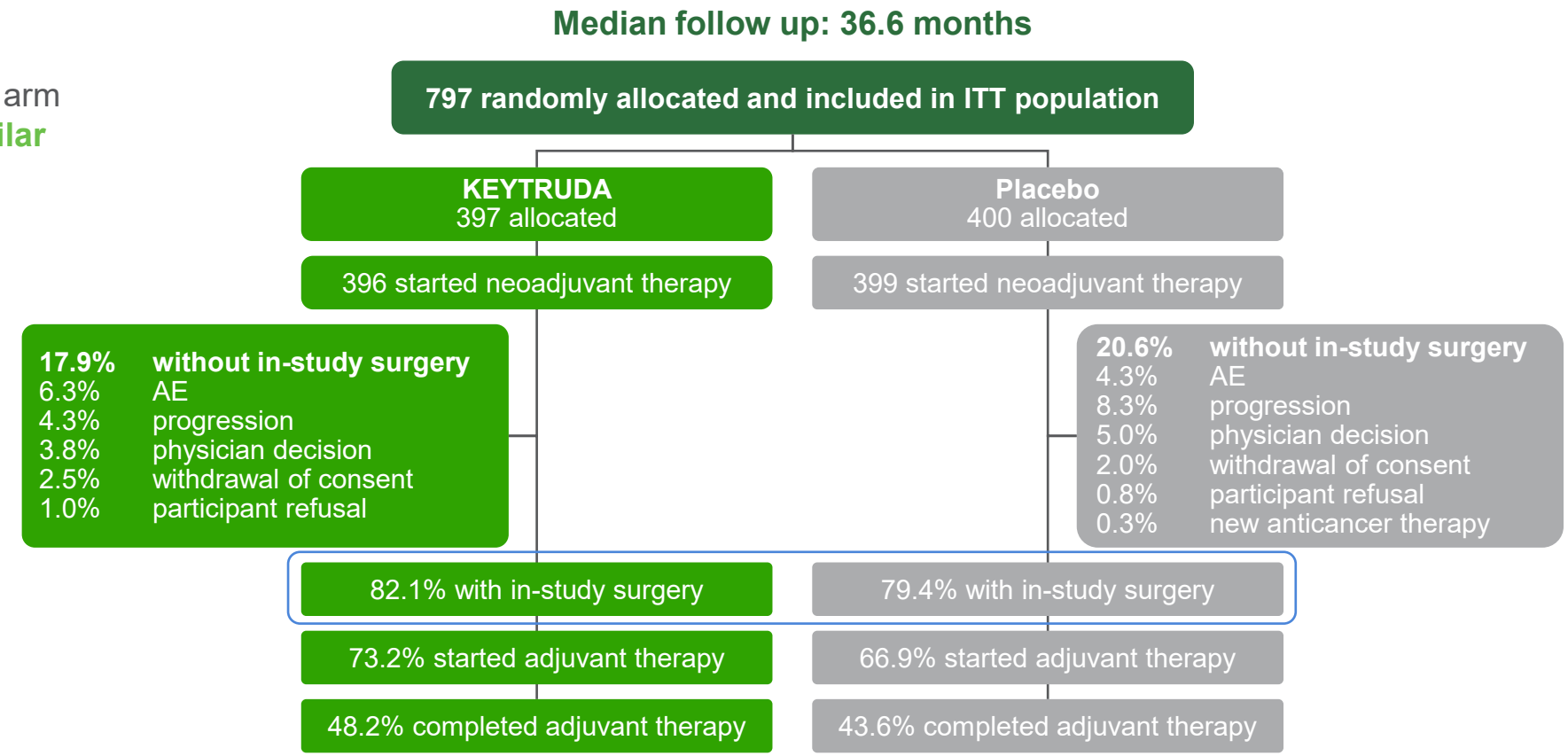
Characteristic, n (%)		KEYTRUDA	Placebo
Smoking status	Current	96 (24.2)	103 (25.8)
	Former	247 (62.2)	250 (62.5)
	Never	54 (13.6)	47 (11.8)
Clinical stage	II	118 (29.7)	121 (30.3)
	IIIA	217 (54.7)	225 (56.3)
	IIIB	62 (15.6)	54 (13.5)
N status*	N0	148 (37.3)	142 (35.5)
	N1	81 (20.4)	71 (17.8)
	N2	168 (42.3)	187 (46.8)
PD-L1 TPS	≥50%	132 (33.2)	134 (33.5)
	1–49%	127 (32.0)	115 (28.8)
	<1%	138 (34.8)	151 (37.8)
Known *EGFR* mutation†		14 (3.5)	19 (4.8)
Known *ALK* translocation†		12 (3.0)	9 (2.3)

Adapted from Wakelee H, *et al*. ASCO 2023.[1]

Data cut-off date for IA1: 29 July 2022. Median follow-up: 25.2 months.[1]
*As determined by imaging and biopsy.[1] †*EGFR* and *ALK* status were tested locally per investigator discretion. *EGFR* status was unknown in 68.5% in the KEYTRUDA arm and 63.5% in the placebo arm; *ALK* status was unknown in 70.8% and 64.5%, respectively.[1]
ALK, anaplastic lymphoma kinase; ECOG PS, Eastern Cooperative Oncology Group Performance Status; *EGFR*, epidermal growth factor receptor; IA, interim analysis; PD-L1, programmed death ligand 1; N, nodal involvement; TPS, tumour proportion score.
1. Wakelee H, *et al*. KEYNOTE-671: Randomised, double-blind, Phase 3 study of pembrolizumab or placebo plus platinum-based chemotherapy followed by resection and pembrolizumab or placebo for early-stage NSCLC. ASCO. 2–6 June 2023. Chicago, IL, USA. Abstract: LBA100.

KEYNOTE-671: Treatment disposition[1]

- Most patients underwent in-study surgery (82.1% in the KEYTRUDA arm vs 79.4% in the placebo arm), **similar to other perioperative IO trials[1]**



Adapted from Spicer J, *et al.* STS 2024.[1]

Data cut-off date for IA2: 10 July 2023. Median follow-up: 36.6 months.[1]
*In the KEYTRUDA arm, 307 participants underwent surgery alone, 18 underwent in-study surgery and radiotherapy, and 17 underwent in-study radiotherapy alone. In the placebo arm, 282 participants underwent in-study surgery alone, 35 underwent in-study surgery and radiotherapy, and 18 underwent in-study radiotherapy alone. All percentages are based on the number who received ≥1 dose of neoadjuvant treatment.[1]
IA, interim analysis; IO, immunotherapy; ITT, intention-to-treat; R0, complete resection defined as no invasive cancer at bronchial margin or soft tissue surrounding bronchus, no invasive cancer at pulmonary artery or pulmonary vein margins or surrounding soft tissue, no invasive cancer at medial, lateral, superior and inferior margins of chest wall resection, no minimal margin distance, bronchial dysplasia is considered a negative margin.[1]
1. Spicer J, *et al.* Presented at STS 2024.

KEYNOTE-671: Background[1–4]

In the Phase III KEYNOTE-671 study, neoadjuvant KEYTRUDA + chemotherapy followed by surgery and adjuvant KEYTRUDA **significantly improved OS and EFS** compared with neoadjuvant placebo + chemotherapy and surgery alone in resectable, early-stage NSCLC.

Summary of analyses at IA1, IA2 and IA3

	IA1[1,2] (KEYTRUDA vs placebo)			IA2[3] (KEYTRUDA vs placebo)			IA3[4] (KEYTRUDA vs placebo)		
Median follow-up	25.2 months			36.6 months			41.1 months		
OS, HR (95% CI)	0.73 (0.54–0.99), p=0.02124 (significance boundary not met)			**0.72 (0.56–0.93), p=0.0052 (significance boundary met)**			0.73 (0.58–0.92) (significance boundary met at IA2)		
mOS, months (95% CI)	KEYTRUDA NR (NR–NR)	vs	PLACEBO 45.5 (42.0–NR)	KEYTRUDA NR (NR–NR)	vs	PLACEBO 52.4 (45.7–NR)	KEYTRUDA NR (NR–NR)	vs	PLACEBO NR (50.3–NR)
EFS, HR (95% CI)	**0.58 (0.46–0.72), p<0.001 (significance boundary met)**			0.59 (0.48–0.72) (significance boundary met at IA1)			0.57 (0.47–0.69) (significance boundary met at IA1)		
mEFS, months (95% CI)	KEYTRUDA NR (34.1–NR)	vs	PLACEBO 17.0 (14.3–22.0)	KEYTRUDA 47.2 (32.9–NR)	vs	PLACEBO 18.3 (14.8–22.1)	KEYTRUDA 57.1 (38.0–69.1)	vs	PLACEBO 18.4 (14.8–22.1)

CI, confidence interval; EFS, event-free survival; HR, hazard ratio; IA, interim analysis; m, median; NSCLC; non-small cell lung cancer; OS, overall survival.

1. Wakelee H, *et al.* Presented at ASCO. 2–6 June 2023. Chicago, Illinois, USA. Abstract: LBA100. **2.** Wakelee H, *et al. N Engl J Med* 2023;389:491–503 (plus supplementary appendix).
3. Spicer JD, *et al. Lancet* 2024;404:1240–1252. **4.** Majem M, *et al.* Presented at ESMO I-O 2024. 11–13 December 2024. Geneva, Switzerland. Abstract LBA3.

KEYNOTE-671: 3-year OS in the ITT population (IA1, IA2 and IA3)*[1–3]

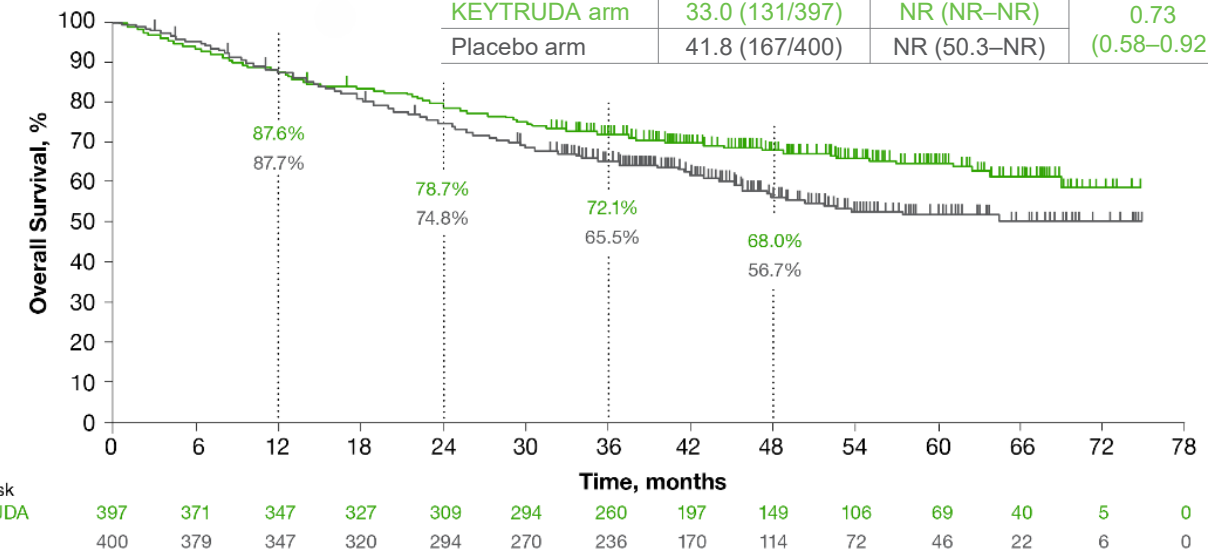
Dual primary endpoint

Median follow-up: 25.2 months (IA1); 36.6 months (IA2); 41.1 months (IA3)

Data cut-off date: 29 July 2022 (IA1); 10 July 2023 (IA2); 19 August 2024 (IA3)

IA3: OS in the ITT population

	Pts w/ Event, % (n/N)	Median (95% CI), mo	HR (95% CI)
KEYTRUDA arm	33.0 (131/397)	NR (NR–NR)	0.73 (0.58–0.92)
Placebo arm	41.8 (167/400)	NR (50.3–NR)	



Adapted from Majem M, *et al*. ESMO 2024.[2]

- **At IA1,** OS was not mature, but showed a favourable trend (HR: 0.73)[1]
- **At IA2,** the prespecified interim analysis for OS, **a statistically significant and clinically meaningful OS benefit was shown** with perioperative KEYTRUDA[3]
  - OS HR was 0.72, representing a 28% reduction in risk of death, with the upper CI clearly below unity[3]
- **At IA3,** perioperative KEYTRUDA continued to provide improved OS vs placebo[2]

Statistical significance for OS was demonstrated at IA2, therefore OS was not formally tested at IA3.[2,3] *OS was defined as time from randomisation to death from any cause.[1]
CI, confidence interval; HR, hazard ratio; IA, interim analysis; ITT, intention-to-treat; mo, months; NR, not reached; OS, overall survival.
1. Wakelee H, *et al.* Presented at ASCO. 2–6 June 2023. Chicago, Illinois, USA. Abstract: LBA100. **2.** Majem M, *et al.* Presented at ESMO I-O 2024. 11–13 December 2024. Geneva, Switzerland. Abstract LBA3. **3** Spicer J, *et al.* Presented at ESMO 2023. Abstract LBA56.

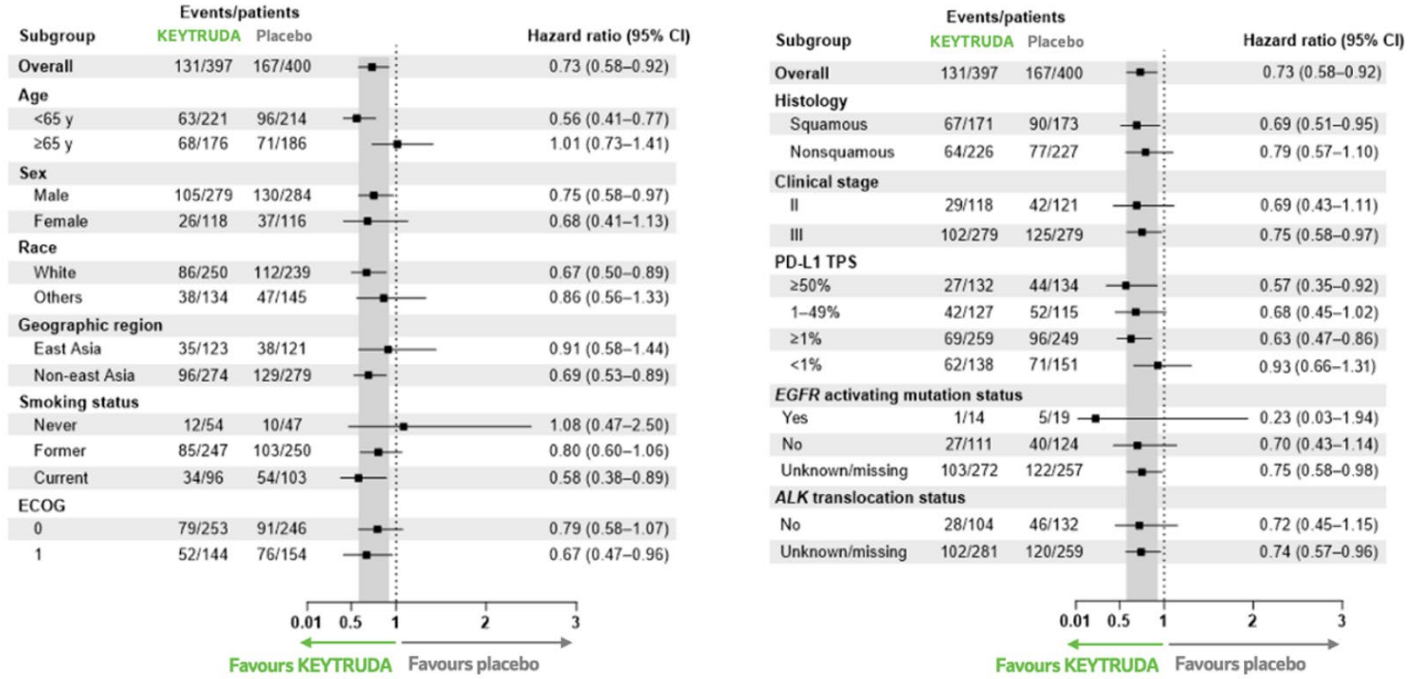
KEYNOTE-671: OS in key subgroups (IA3)*[1,2]

Exploratory analysis

- No statistical conclusions can be drawn from exploratory analyses
- The trend in OS benefit with perioperative KEYTRUDA + chemotherapy vs placebo was observed across many subgroups[1,2]
  - The trend in OS benefit appeared to favour KEYTRUDA regardless of histology and stage†[1,2]
  - At IA3, the relative OS benefit of perioperative KEYTRUDA + chemotherapy vs placebo was similar in participants with Stage II (HR: 0.69; 95% CI: 0.43–1.11) and Stage III (HR: 0.75; 95% CI: 0.58–0.97) disease[2]

IA3 data

OS within the ITT population



Adapted from Majem M, *et al.* ESMO I-O 2024.[2]

IA2: Data cut-off: Jul 10, 2023; Median follow-up: 36.6 months;[1] IA3: Data cut-off: Aug 19, 2024; Median follow-up: 41.1 months.[2]
No conclusions can be drawn from exploratory analyses. *OS was defined as time from randomisation to death from any cause.[1] †Subgroups for Stage IIIA and IIIB and by N status were post hoc, while others were prespecified.[1]
ALK, anaplastic lymphoma kinase; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; *EGFR,* epidermal growth factor receptor; HR, hazard ratio; IA, interim analysis; ITT, intention to treat; OS, overall survival; PD-L1, programmed death-ligand 1; TPS, tumour proportion score.
1. Spicer JD, *et al. Lancet* 2024;404:P1240–1252. **2.** Majem M, *et al.* Presented at ESMO I-O 2024. 11–13 December. Geneva, Switzerland. Abstract LBA3.

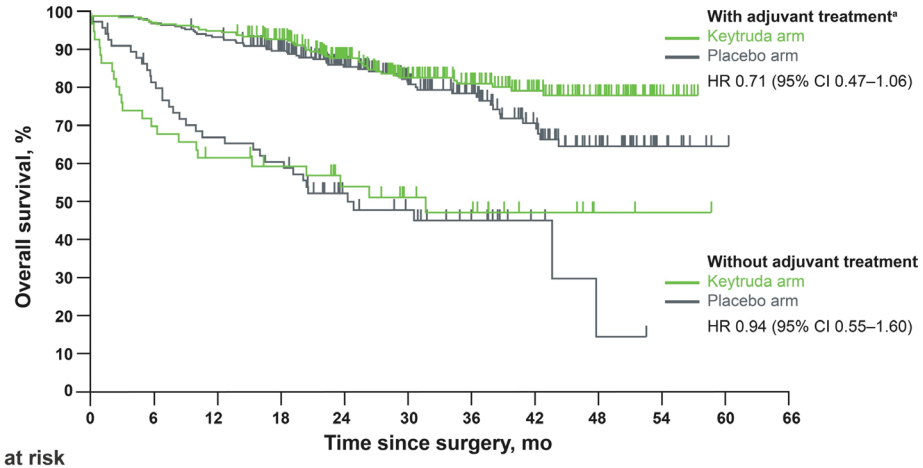
KEYNOTE-671: OS benefit of adjuvant treatment[1–3]

Exploratory analysis

No statistical conclusions can be drawn from exploratory analyses. The possibility that both the neoadjuvant and adjuvant treatment phases contributed to the overall benefit cannot be eliminated.

- 73.2% (290/396) of participants in the neoadjuvant KEYTRUDA + chemotherapy arm started adjuvant therapy vs 66.9% (267/399) of participants in the placebo + chemotherapy arm[1]
- 48.2% (191/396) of participants in the neoadjuvant KEYTRUDA + chemotherapy arm completed adjuvant treatment vs 43.6% (n=174/399) of participants in the placebo + chemotherapy/placebo arm completed adjuvant treatment[2]
- Exploratory data suggests that KEYTRUDA demonstrated a 29% relative reduction in the risk of death vs placebo (HR: 0.71; 95% CI: 0.47–1.06) in patients who received adjuvant treatment*[3]
- Exploratory data suggests that KEYTRUDA + chemotherapy demonstrated a 6% relative reduction in the risk of death vs placebo + chemotherapy (HR: 0.94; 95% CI: 0.55–1.60) in patients who did not receive adjuvant treatment*[3]

IA2 data **OS in patients who received or did not receive adjuvant therapy**



Number at risk (number censored)

With adjuvant treatment	Keytruda arm	276 (0)	271 (0)	265 (0)	245 (14)	183 (64)	139 (98)	102 (133)	71 (162)	45 (187)	10 (222)	0 (232)	0 (232)
	Placebo arm	253 (0)	248 (0)	238 (1)	212 (18)	158 (63)	112 (102)	85 (126)	52 (152)	26 (174)	8 (192)	1 (199)	0 (200)
Without adjuvant treatment	Keytruda arm	49 (0)	34 (1)	29 (2)	25 (5)	19 (9)	14 (13)	12 (14)	6 (20)	2 (24)	1 (25)	0 (26)	0 (26)
	Placebo arm	64 (0)	51 (2)	42 (2)	38 (2)	24 (11)	18 (15)	11 (21)	4 (28)	1 (29)	0 (30)	0 (30)	0 (30)

Adapted from Garassino M, *et al.* Presented at ESMO 2024.[3]

IA1: Data cut-off: Jul 29, 2022; Median follow-up: 25.2 months;[1] IA2: Data cut-off: Jul 10, 2023; Median follow-up: 36.6 months.[2]
*Among patients who started adjuvant treatment, HRs for EFS and OS from the start of adjuvant therapy were 0.55 (95% CI: 0.42–0.72; N=548) and 0.71 (95% CI: 0.49–1.03; N=557), respectively.[3]
CI, confidence interval; EFS, event-free survival; HR, hazard ratio; IA, interim analysis; mo, months; OS, overall survival; rNSCLC, resectable non-small cell lung cancer.

1. Wakelee H, *et al. N Engl J Med* 2023;389:491–503. **2.** Spicer JD, *et al. Lancet* 2024;404:P1240–1252.
3. Garassino M, *et al.* Presented at ESMO 2024.13–17 September 2024. Barcelona, Spain. Abstract OP121.

KEYNOTE-671: 3-year EFS in the ITT population (IA1, IA2 and IA3)*[1–4]

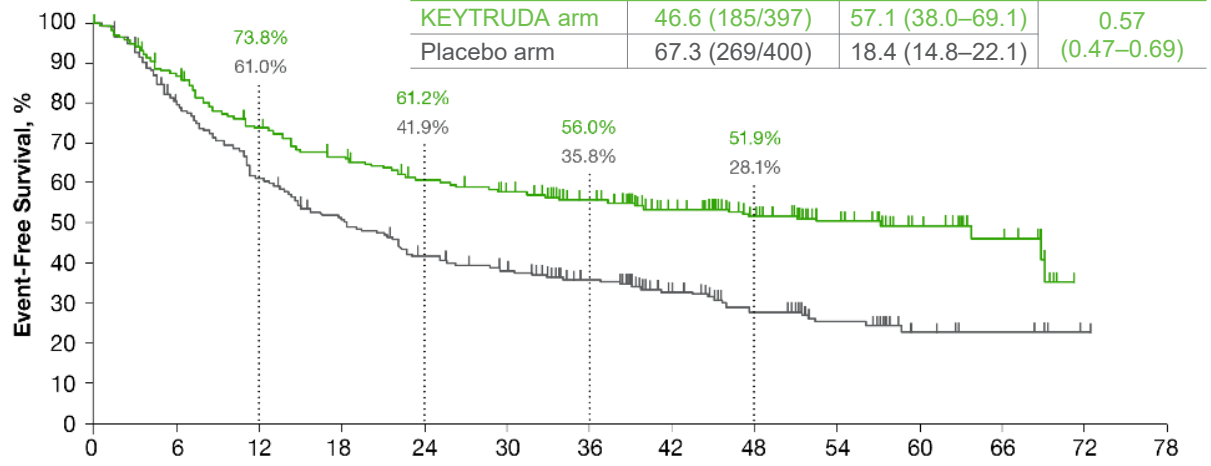
Dual primary endpoint

Median follow-up: 25.2 months (IA1); 36.6 months (IA2); 41.1 months (IA3)

Data cut-off date: 29 July 2022 (IA1); 10 July 2023 (IA2); 19 August 2024 (IA3)

IA3: EFS in the ITT population

	Pts w/ Event, % (n/N)	Median (95% CI), mo	HR (95% CI)
KEYTRUDA arm	46.6 (185/397)	57.1 (38.0–69.1)	0.57 (0.47–0.69)
Placebo arm	67.3 (269/400)	18.4 (14.8–22.1)	



No. at risk

KEYTRUDA	397	340	284	255	229	209	175	135	95	63	27	15	0	0
Placebo	400	309	235	195	157	141	112	79	47	28	13	10	1	0

Adapted from Majem M, *et al*. ESMO 2024.[3]

- At **IA1,** EFS benefit in the overall population was **shown to be statistically significant and clinically meaningful**[1,2]
  - EFS HR was 0.58 (95% CI: 0.46–0.72); p<0.001[2]
  - Median EFS was not reached in the perioperative KEYTRUDA arm and was 17 months in the placebo arm[2]
- At **IA2,** with an additional 11 months of follow-up, **benefit was sustained with HR 0.59**[4]
  - Median EFS was more than doubled, being 47.2 months with KEYTRUDA vs 18.3 months with placebo[4]
  - 3-year EFS was 54% with pembrolizumab vs 35% with placebo[4]
- At **IA3,** with an additional 16 months of follow-up, **benefit was sustained with HR 0.57**[3]

Statistical testing for EFS was demonstrated at IA1, and therefore EFS was not formally tested at IA3.[1,3] *Event-free survival defined as time from randomisation to first occurrence of local progression precluding planned surgery, unresectable tumour, progression or recurrence per RECIST version 1.1 by investigator assessment, or death from any cause.[2]

CI, confidence interval; EFS, event-free survival; HR, hazard ratio; ITT, intention-to-treat.

1. Wakelee H, *et al*. Presented at ASCO. 2–6 June 2023. Chicago, Illinois, USA. Abstract: LBA100. **2.** Wakelee H, *et al. N Engl J Med* 2023;389:491–503. **3.** Majem M, *et al*. Presented at ESMO I-O 2024. 11–13 December 2024. Geneva, Switzerland. Abstract LBA3. **4.** Spicer J, *et al*. Presented at ESMO 2023.

KEYNOTE-671: EFS in key subgroups (IA3)*[1–3]

Exploratory analysis

- No statistical conclusions can be drawn from exploratory analyses
- The EFS benefit with perioperative KEYTRUDA + chemotherapy vs placebo was relatively **consistent across most subgroups and regardless of PD-L1 expression[1–3]**
  - The EFS benefit appeared to be similar regardless of histology and stage†[1–3]
  - The EFS benefit was observed regardless of PD-L1 status[1–3]
  - At IA3, in the PD-L1 TPS subgroup analysis, the greatest EFS benefit was observed in participants with PD-L1 TPS ≥50% (HR: 0.44; 95% CI: 0.30–0.63)[3]
  - At IA3, an EFS benefit was observed in participants with PD-L1 TPS <1% (HR: 0.72; 95% CI: 0.54–0.97)[3]

IA3 data

EFS within the ITT population

Subgroup	Events/patients KEYTRUDA	Events/patients Placebo	Hazard ratio (95% CI)
Overall	185/397	269/400	0.57 (0.47–0.69)
Age			
<65 y	96/221	146/214	0.51 (0.39–0.66)
≥65 y	89/176	123/186	0.65 (0.50–0.86)
Sex			
Male	135/279	193/284	0.60 (0.48–0.75)
Female	50/118	76/116	0.49 (0.35–0.71)
Race			
White	117/250	161/239	0.56 (0.44–0.71)
Others	60/134	96/145	0.57 (0.41–0.79)
Geographic region			
East Asia	54/123	80/121	0.58 (0.41–0.81)
Non-east Asia	131/274	189/279	0.56 (0.45–0.71)
Smoking status			
Never	27/54	28/47	0.73 (0.43–1.24)
Former	108/247	166/250	0.55 (0.43–0.70)
Current	50/96	75/103	0.54 (0.38–0.77)
ECOG			
0	111/253	165/246	0.54 (0.43–0.69)
1	74/144	104/154	0.62 (0.46–0.83)

Subgroup	Events/patients KEYTRUDA	Events/patients Placebo	Hazard ratio (95% CI)
Overall	185/397	269/400	0.57 (0.47–0.69)
Histology			
Squamous	74/171	124/173	0.49 (0.36–0.65)
Nonsquamous	111/226	145/227	0.65 (0.50–0.83)
Clinical stage			
II	40/118	71/121	0.50 (0.34–0.74)
III	145/279	198/279	0.58 (0.47–0.72)
PD-L1 TPS			
≥50%	44/132	81/134	0.44 (0.30–0.63)
1–49%	61/127	80/115	0.54 (0.39–0.76)
≥1%	105/259	161/249	0.50 (0.39–0.64)
<1%	80/138	108/151	0.72 (0.54–0.97)
***EGFR* activating mutation status**			
Yes	6/14	15/19	0.32 (0.12–0.83)
No	47/111	80/124	0.54 (0.37–0.77)
Unknown/missing	132/272	174/257	0.60 (0.48–0.75)
***ALK* translocation status**			
No	45/104	46/132	0.48 (0.34–0.69)
Unknown/missing	133/281	120/259	0.60 (0.48–0.76)

Adapted from Majem M, *et al.* ESMO I-O 2024.[3]

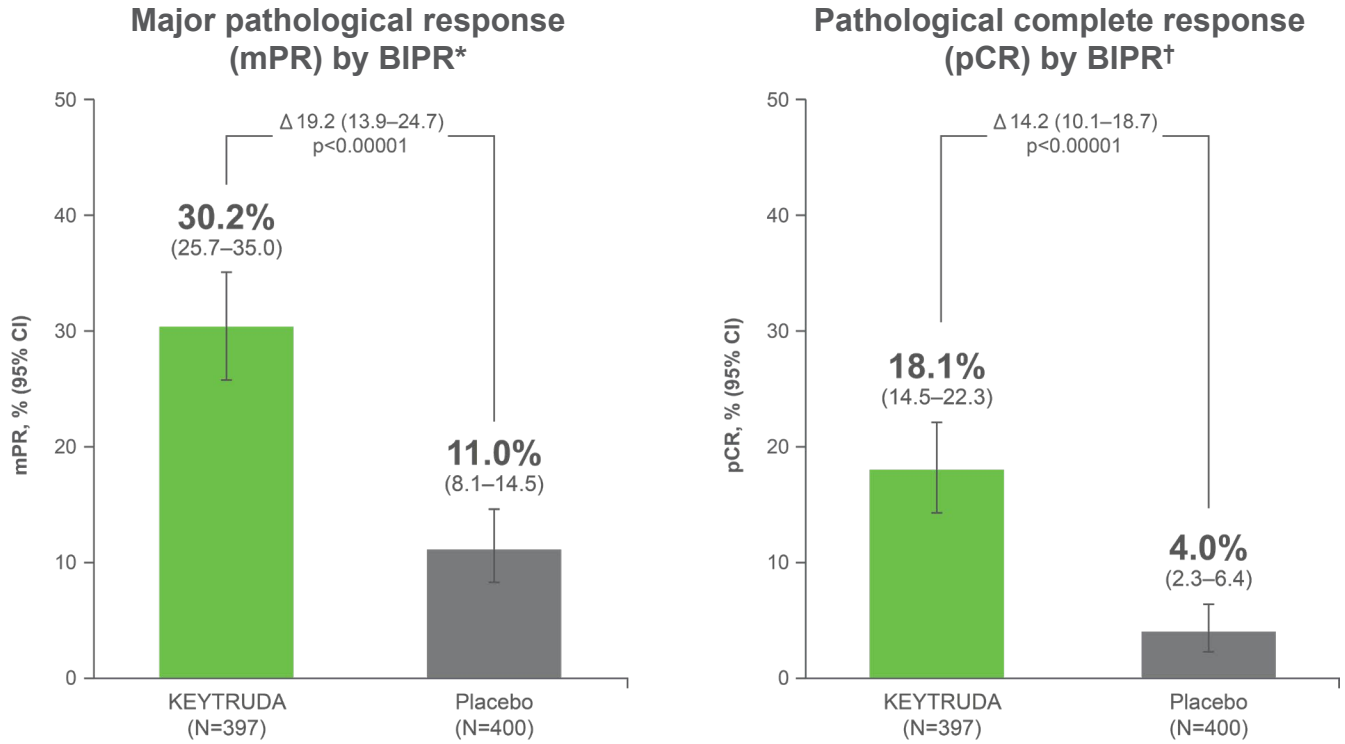
IA1: Data cut-off: Jul 29, 2022; Median follow-up: 25.2 months;[1] IA2: Data cut-off: Jul 10, 2023; Median follow-up: 36.6 months;[2] IA3: Data cut-off: Aug 19, 2024; Median follow-up: 41.1 months.[3]
No conclusions can be drawn from exploratory analyses. *EFS is defined as the time from randomisation to the first occurrence of local progression that precluded the planned surgery, unresectable tumour, progression or recurrence according to RECIST v1.1, or death from any cause.[1–3] †Subgroups for Stage IIIA and IIIB and by N status were post hoc, while others were prespecified.[2]
ALK, anaplastic lymphoma kinase; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; EFS, event-free survival; *EGFR,* epidermal growth factor receptor; HR, hazard ratio; IA, interim analysis; ITT, intention to treat; PD-L1, programmed death-ligand 1; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1; TPS, tumour proportion score.
1. Wakelee H, *et al. N Engl J Med* 2023;389(6):491–503. **2.** Spicer JD, *et al. Lancet* 2024;404:P1240–1252. **3.** Majem M, *et al.* Presented at ESMO I-O 2024. 11–13 December 2024. Geneva, Switzerland. Abstract LBA3.

KEYNOTE-671: pCR and mPR[1,2]

Secondary analysis

- **Significantly higher rates of pathologic response** were seen in the KEYTRUDA arm[1,2]
  - Note that the majority of patients did not achieve a pCR (~82%) or an mPR (~70%)[1,2]
  - pCR and mPR were assessed by blinded review and defined by IASLC criteria*†[1,2]

IA1 data



Adapted from Wakelee H, *et al.* ASCO 2023.[1]

Data cut-off date for IA1: 29 July 2022. Median follow-up: 25.2 months.[2]
*Per IASLC criteria, mPR was defined as ≤10% viable tumour cells in resected primary tumour and lymph nodes.[1] †Per IASLC criteria, pCR was defined as 0% viable tumour cells in resected primary tumour and lymph nodes.[1]
BIPR, blinded independent pathological review; CI, confidence interval; IASLC, International Association for the Study of Lung Cancer; IA, interim analysis; irPRC, immune-related pathologic response criteria; mPR, major pathologic response; pCR, pathological complete response.
1. Wakelee H, *et al.* KEYNOTE-671: Randomised, double-blind, Phase 3 study of pembrolizumab or placebo plus platinum-based chemotherapy followed by resection and pembrolizumab or placebo for early-stage NSCLC. ASCO. 2–6 June 2023. Chicago, IL, USA. Abstract: LBA100.
2. Wakelee H, *et al. N Engl J Med* 2023;389:491–503.

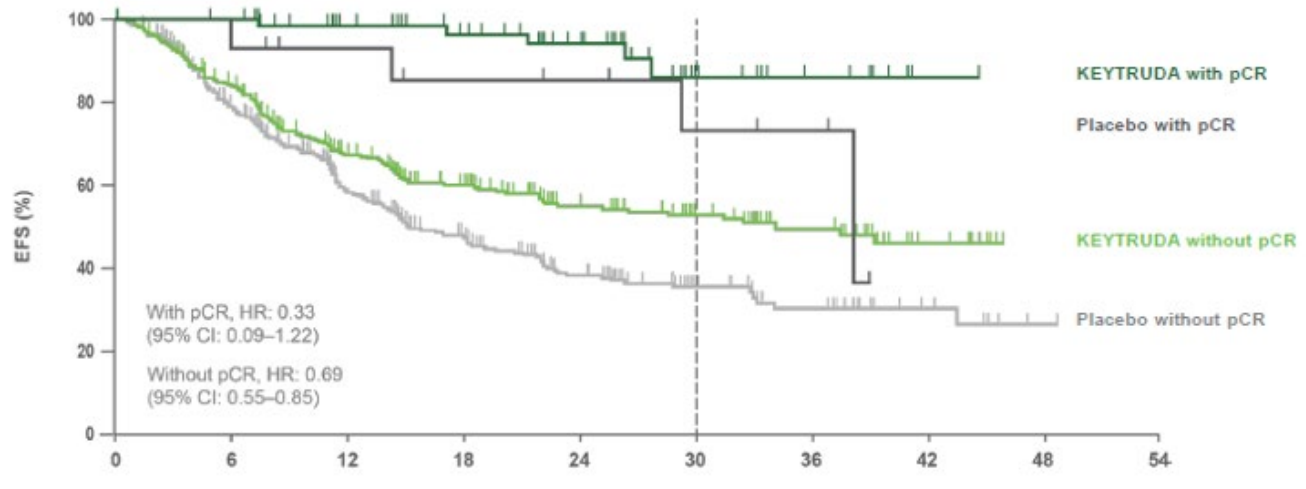
KEYNOTE-671: EFS by pCR[1,2]

Exploratory analysis

- Exploratory data from IA1* showed EFS benefit in the perioperative KEYTRUDA group **regardless of whether participants had a complete pathologic response or not**[1,2]
  - With pCR, HR: 0.33; without pCR, HR: 0.69[1]
- The EFS benefit in those without pCR is particularly important as it suggests a specific benefit from adjuvant KEYTRUDA

As seen in other trials there is evidence to support pCR as a surrogate endpoint for survival[3]
- However, the majority of patients do not achieve a pCR or mPR and a high unmet medical need exists for this group[1,2]

IA1 data



Number at risk

KEYTRUDA with pCR	72	72	59	46	33	15	8	1	0	0
Placebo with pCR	16	14	12	10	9	5	4	0	0	0
KEYTRUDA without pCR	325	258	177	126	84	57	34	10	0	0
Placebo without pCR	384	280	171	114	65	33	20	9	1	0

Adapted from Wakelee H, *et al. N Engl J Med* 2023.[2]

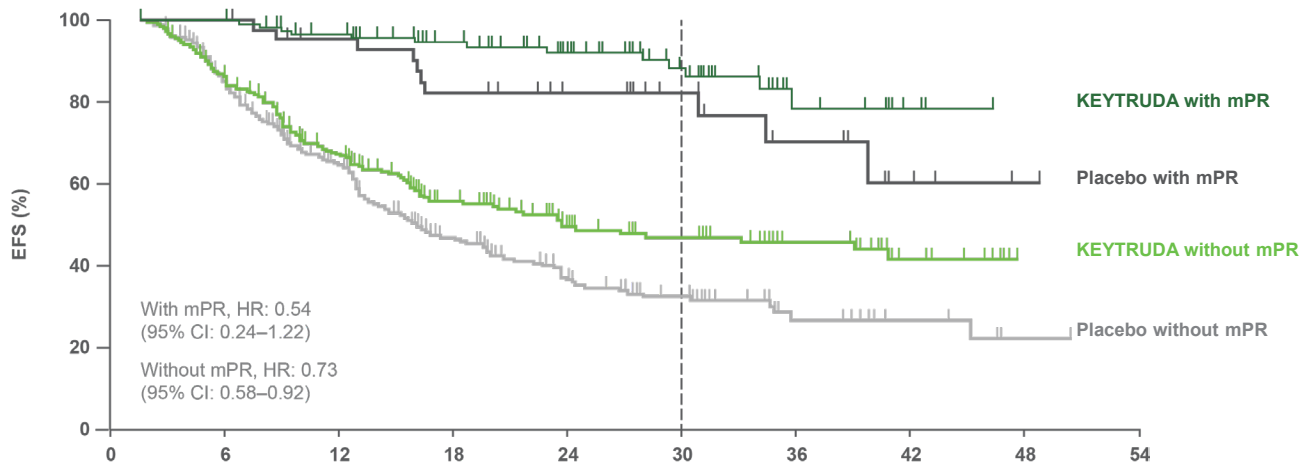
Data cut-off date for IA1: 29 July 2022. Median follow-up: 25.2 months.[2]
*Exploratory analysis from IA1 was not updated at IA2 as the updated EFS in the ITT was consistent with IA1.[1,2]
CI, confidence interval; EFS, event-free survival; HR, hazard ratio; IA, interim analysis; ITT, intention-to-treat; pCR, pathological complete response.
1. Wakelee H, *et al.* KEYNOTE-671: Randomised, double-blind, Phase 3 study of pembrolizumab or placebo plus platinum-based chemotherapy followed by resection and pembrolizumab or placebo for early-stage NSCLC. ASCO. 2–6 June 2023. Chicago, IL, USA. Abstract: LBA100.
2. Wakelee H, *et al. N Engl J Med* 2023;389:491–503. **3.** Deutsch JS, *et al. Nat Med* 2024;30:218–228.

KEYNOTE-671: EFS by mPR[1,2]

Exploratory analysis

- Exploratory data from IA1* showed EFS benefit in the perioperative KEYTRUDA group **regardless of whether participants had a major pathological response or not**[1,2]
  - With mPR, HR: 0.54; without mPR, HR: 0.73[1]

IA1 data



Number at risk

KEYTRUDA with mPR	120	117	99	79	60	30	15	1	0	0
Placebo with mPR	44	42	36	28	22	12	10	2	0	0
KEYTRUDA without mPR	277	213	137	93	57	42	27	10	0	0
Placebo without mPR	356	252	147	96	52	26	14	7	1	0

Adapted from Wakelee H, *et al. N Engl J Med* 2023.[2]

Data cut-off date for IA1: 29 July 2022. Median follow-up: 25.2 months.[2]
*Exploratory analysis from IA1 was not updated at IA2 as the updated EFS in the ITT was consistent with IA1.[1,2]
CI, confidence interval; EFS, event-free survival; HR, hazard ratio; IA, interim analysis; ITT, intention-to-treat; mPR, major pathologic response.
1. Wakelee H, *et al.* KEYNOTE-671: Randomised, double-blind, Phase 3 study of pembrolizumab or placebo plus platinum-based chemotherapy followed by resection and pembrolizumab or placebo for early-stage NSCLC. ASCO. 2–6 June 2023. Chicago, IL, USA. Abstract: LBA100.
2. Wakelee H, *et al. N Engl J Med* 2023;389:491–503.

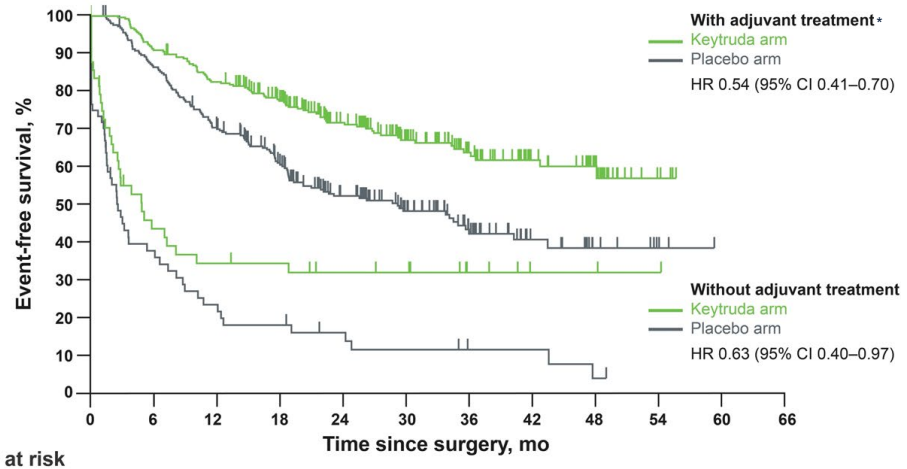
KEYNOTE-671: EFS benefit of adjuvant treatment[1–3]

Exploratory analysis

No statistical conclusions can be drawn from exploratory analyses. The possibility that both the neoadjuvant and adjuvant treatment phases contributed to the overall benefit cannot be eliminated.

- 73.2% (290/396) of participants in the neoadjuvant KEYTRUDA + chemotherapy arm started adjuvant therapy vs 66.9% (267/399) of participants in the placebo + chemotherapy arm[1]
- 48.2% (191/396) of participants in the neoadjuvant KEYTRUDA + chemotherapy arm completed adjuvant treatment vs 43.6% (n=174/399) of participants in the placebo + chemotherapy/ placebo arm completed adjuvant treatment[2]
- Exploratory data suggests that KEYTRUDA demonstrated a 46% relative reduction in the risk of an event vs placebo (HR: 0.54; 95% CI: 0.41–0.70) in patients who received adjuvant treatment*[3]
- Exploratory data suggests that KEYTRUDA + chemotherapy demonstrated a 37% relative reduction in the risk of an event vs placebo + chemotherapy (HR: 0.63; 95% CI: 0.40–0.97) in patients who did not receive adjuvant treatment*[3]

IA2 data **EFS in patients who received or did not receive adjuvant therapy**



Number at risk (number censored)

With adjuvant treatment	Keytruda arm	276 (0)	250 (1)	225 (3)	191 (24)	139 (63)	99 (95)	64 (126)	38 (150)	24 (163)	4 (182)	0 (186)	0 (186)
	Placebo arm	253 (0)	216 (3)	173 (5)	136 (21)	91 (48)	64 (69)	39 (89)	18 (108)	8 (117)	3 (122)	0 (125)	0 (125)
Without adjuvant treatment	Keytruda arm	49 (0)	19 (4)	15 (4)	14 (5)	11 (7)	10 (8)	5 (13)	2 (16)	2 (16)	1 (17)	0 (18)	0 (18)
	Placebo arm	64 (0)	21 (5)	13 (5)	10 (5)	7 (7)	5 (7)	3 (9)	3 (9)	1 (9)	0 (10)	0 (10)	0 (10)

Adapted from Garassino M, *et al.* Presented at ESMO 2024.[3]

IA1: Data cut-off: Jul 29, 2022; Median follow-up: 25.2 months;[1] IA2: Data cut-off: Jul 10, 2023; Median follow-up: 36.6 months.[2]
*Among patients who started adjuvant treatment, HRs for EFS and OS from the start of adjuvant therapy were 0.55 (95% CI: 0.42–0.72; N=548) and 0.71 (95% CI: 0.49–1.03; N=557), respectively.[3]
CI, confidence interval; EFS, event-free survival; HR, hazard ratio; IA, interim analysis; mo, months; OS, overall survival; rNSCLC, resectable non-small cell lung cancer.

1. Wakelee H, *et al. N Engl J Med* 2023;389:491–503. **2.** Spicer JD, *et al. Lancet* 2024;404:P1240–1252.
3. Garassino M, *et al.* Presented at ESMO 2024.13–17 September 2024. Barcelona, Spain. Abstract OP121.

KEYNOTE-671: Surgical outcomes[1,2]

- Most patients who received at least one dose of neoadjuvant therapy underwent in-trial surgery (82.1% in the KEYTRUDA group vs 79.4% in the placebo group)[1,2]
- Among those who underwent surgery, the most common surgical procedure was lobectomy (78.8% vs 75.1%), and the **majority of patients had complete (R0) resection (92.0% vs 84.2%)[1,2]**

IA1 data

Summary of surgical outcomes, n (%)		KEYTRUDA (n=325)	Placebo (n=317)
In-study surgery*	Resected	320 (98.5)	302 (95.3)
	Complete – R0	299 (92.0)	267 (84.2)
	Incomplete – R1	17 (5.2)	31 (9.8)
	Incomplete – R2	4 (1.2)	4 (1.3)
	Unresected	5 (1.5)	15 (4.7)
Surgical procedure	Lobectomy	256 (78.8)	238 (75.1)
	Pneumonectomy	37 (11.4)	39 (12.3)
	Bilobectomy	26 (8.0)	26 (8.2)
	Exploratory thoracotomy	4 (1.2)	13 (4.1)
	Other	2 (0.6)†	1 (0.3)‡
30-day mortality		6 (1.8)§	2 (0.6)¶

Adapted from Wakelee H, *et al.* ASCO 2023.[2]

Data cut-off date for IA1: 29 July 2022. Median follow-up: 25.2 months.[1]
*An additional 8 participants in the KEYTRUDA arm and 7 participants in the placebo arm underwent off-study surgery.[1] †Lung segmentectomy (n=1), lung wedge resection (n=1).[1] ‡Lymph node dissection only (planned surgery was lung lobectomy; need for more extensive surgery discovered during surgery, but consent was not granted).[1] §Pulmonary embolism (n=2), pulmonary haemorrhage due to arterial injury during surgery (n=1), pulmonary sepsis (n=1), respiratory failure (n=1) and septic shock (n=1).[1] ¶Respiratory failure (n=1) and pneumonia (n=1).[1]
AE, adverse event; IA, interim analysis; R0, complete resection defined as no invasive cancer at bronchial margin or soft tissue surrounding bronchus, no invasive cancer at pulmonary artery or pulmonary vein margins or surrounding soft tissue, no invasive cancer at medial, lateral, superior and inferior margins of chest wall resection, no minimal margin distance, bronchial dysplasia is considered a negative margin.[1] R1, microscopic invasive cancer at bronchial, pulmonary vein or pulmonary arterial margins or surrounding soft tissue, carcinoma *in situ* at bronchial margin; R2, gross residual disease.
1. Wakelee H, *et al. N Engl J Med* 2023;389:491–503 (and supplementary appendix). **2.** Wakelee H, *et al.* KEYNOTE-671: Randomised, double-blind, Phase 3 study of pembrolizumab or placebo plus platinum-based chemotherapy followed by resection and pembrolizumab or placebo for early-stage NSCLC. ASCO. 2–6 June 2023. Chicago, IL, USA. Abstract: LBA100.

KEYNOTE-671: Safety[1]

- **Most TRAEs occurred in the neoadjuvant phase,** consistent with neoadjuvant chemotherapy being the main contributor[1]
  - Addition of KEYTRUDA did not substantially increase the rate of any-grade TRAEs (Δ+2.0%), high-grade TRAEs (Δ+4.1%), or discontinuation due to AEs (Δ+1.7%)[1]
- The rate of TRAEs in the adjuvant phase was lower than in the neoadjuvant phase, indicating that **adjuvant KEYTRUDA is generally well-tolerated**[1]
  - Adjuvant KEYTRUDA was associated with an increase in any TRAEs (Δ+22.7%) and high-grade TRAEs (Δ+4.4%)[1]
  - At IA1, more patients received and completed adjuvant therapy with KEYTRUDA than placebo (Δ+5.1%)[1]
  - Only a small proportion discontinued adjuvant therapy due to AEs (9.3% vs 3.3%)[1]

IA1 data

Completion/discontinuation by treatment phase[1]		KEYTRUDA (n=396)	Placebo (n=399)
Neoadjuvant phase, n (%)	Completed 4 cycles	295 (74.5)	297 (74.4)
	Discontinued due to AEs	8 (2.0)	1 (0.3)
Surgery phase, n (%)	Underwent surgery	325 (82.1)	317 (79.4)
	Did not proceed to adjuvant due to AEs	19 (4.8)	10 (2.5)
Adjuvant phase, n (%)	Received adjuvant	290 (73.2)	267 (66.9)
	Completed adjuvant	160 (40.4)	141 (35.3)
	Discontinued due to AEs	37 (9.3)	13 (3.3)

Adapted from Wakelee H, *et al. N Engl J Med* 2023. Supplementary appendix.[1]

Data cut-off date for IA1: 29 July 2022. Median follow-up: 25.2 months.[1]
AE, adverse event; IA, interim analysis; TRAE, treatment-related adverse event.
1. Wakelee H, *et al. N Engl J Med* 2023;389:491–503 (and supplementary appendix).

KEYNOTE-671: 3-year AE summary in the as-treated population (IA3)[1]

IA3 data

AE summary across treatment phases	KEYTRUDA (n=396)	Placebo (n=399)
Treatment-related AEs	383 (96.7)	381 (95.5)
Grade 3–5	179 (45.2)	151 (37.8)
Serious	73 (18.4)	59 (14.8)
Led to death	4 (1.0)	3 (0.8)
Led to treatment discontinuation of any drug	77 (19.4)	53 (13.3)
Immune-mediated AEs and infusion reactions*	103 (26.0)	37 (9.3)
Grade 3–5	25 (6.3)	7 (1.8)
Serious	24 (6.1)	7 (1.8)
Led to death	1 (0.3)	0
Led to treatment discontinuation of any drug	24 (6.1)	3 (0.8)

Adapted from Majem M, *et al.* ESMO 2024.[1]

- Profile of the perioperative KEYTRUDA regimen (plus chemotherapy) was **consistent with safety profiles of the individual components**, and no new safety signals were seen[2]
- At IA3, the addition of KEYTRUDA did not substantially increase the rate of any-grade TRAEs vs placebo[1]
  - Grade 3–5 TRAEs occurred in 45.2% (179/396) of the perioperative KEYTRUDA participants and 37.8% (151/399) of the placebo participants[1]
  - TRAEs led to discontinuation of all treatment in 19.4% (77/396) of participants in the perioperative KEYTRUDA arm and 13.3% (53/399) in the placebo arm[1]
  - There were 5 TRAE- or imAE-related deaths in the perioperative KEYTRUDA arm and 3 in the placebo arm[1]

Data cut-off date for IA3: 19 August 2024. Median follow-up: 41.1 months.[1]
*Immune-mediated AEs 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; TRAE, treatment-related adverse event.
1. Majem M, *et al.* Presented at ESMO I-O 2024. Geneva, Switzerland. Abstract LBA3. **2.** Spicer J, *et al.* Presented at ESMO 2023; abstract LBA56.

KEYNOTE-671: Summary[1–5]

A key to more possibilities for appropriate patients with resectable NSCLC

Efficacy of KEYTRUDA in KEYNOTE-671[1–4]

- EFS benefit in the perioperative KEYTRUDA group was sustained over 3 years.[1–4] KEYTRUDA reduced the relative risk of an event vs placebo by:
  - **43%** in the ITT population (HR: 0.57; 95% CI: 0.41–0.69)[4]
  - **56%** in participants with PD-L1 TPS ≥50% (HR: 0.44; 95% CI: 0.30–0.63)[4]
- The reduction in relative risk with KEYTRUDA was also observed regardless of whether participants had a major or complete pathologic response:*[1,2]
  - With pCR HR: 0.33; without pCR HR: 0.69
  - With mPR HR: 0.54; without mPR HR: 0.73
- An OS benefit in the perioperative KEYTRUDA group was observed[3] KEYTRUDA reduced the relative risk of death vs placebo by:
  - **28%** in the ITT population (HR: 0.72; 95% CI: 0.56–0.93)[3]
- Positive trends in the data suggest that this benefit was sustained over 3 years[3]

Safety profile of KEYTRUDA in KEYNOTE-671[1–5]

After 41.1 months median follow-up, no new safety signals were identified[1–3]

- Grade 3–5 treatment-related adverse events were seen in 45.2% of those treated with KEYTRUDA vs 37.8% who received placebo[1–4]
- The safety of KEYTRUDA as monotherapy has been evaluated in 7631 patients across tumour types in clinical studies. The most frequent adverse reactions with KEYTRUDA were fatigue (31%), diarrhoea (22%) and nausea (20%)[5]

*Exploratory analysis from IA1 was not updated at IA2, as the updated EFS in the ITT was consistent with IA1.[2,3] The possibility that both the neoadjuvant and adjuvant treatment phases contributed to the overall benefit cannot be eliminated.

CI, confidence interval; EFS, event-free survival; HR, hazard ratio; IA, interim analysis; ITT, intention-to-treat; OS, overall survival; mPR, major pathologic response; pCR, pathological complete response.

1. Wakelee H, *et al.* KEYNOTE-671: Randomised, double-blind, Phase 3 study of pembrolizumab or placebo plus platinum-based chemotherapy followed by resection and pembrolizumab or placebo for early-stage NSCLC. ASCO. 2–6 June 2023. Chicago, IL, USA. Abstract: LBA100. **2.** Wakelee H, *et al. N Engl J Med* 2023;389:491–503. **3.** Spicer JB, *et al.* Overall survival in the KEYNOTE-671 study of perioperative pembrolizumab for early-stage NSCLC. ESMO. 20–24 October 2023. Madrid, Spain. Abstract: LBA56. **4.** Majem M, *et al.* Presented at ESMO I-O 2024. 11–13 December 2024. Geneva, Switzerland. Abstract LBA3. **5.** KEYTRUDA Summary of Product Characteristics. MSD. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: August 2025.

KEYTRUDA offers flexibility of dosing[1]

Administered as an IV infusion

Over 30 minutes

200 mg Q3W or 400 mg Q6W

Assessment of regimens

The recommended dose of KEYTRUDA in adults is either 200 mg every 3 weeks or 400 mg every 6 weeks administered as an intravenous infusion over 30 minutes.

For use in combination, see the Summary of Product Characteristics (SmPC) for the concomitant therapies.[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: August 2025.