KEYTRUDA® (pembrolizumab) is the first immunotherapy to present 5-year data in three first-line metastatic NSCLC indications licensed in the UK[1–4]

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.

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GB-PDO-03872 | Date of preparation: May 2026

MSD Oncology

KEYNOTE-189

KEYTRUDA plus chemotherapy for the first-line treatment of metastatic, non-squamous, *EGFR/ALK*-wild-type NSCLC

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.[4]

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.

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

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092. **2.** Garassino MC, *et al.* AACR. 29 March–18 April 2019. Atlanta, USA. **3.** Garassino MC, *et al. J Clin Oncol* 2023;41:1992–1998. **4.** KEYTRUDA Summary of Product Characteristics. MSD. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed: May 2026.

KEYTRUDA® (pembrolizumab)

MSD

Links to external sites

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2025 ESMO guidelines recommend KEYTRUDA in combination with chemotherapy for the first-line treatment of non-oncogene-addicted non-squamous mNSCLC irrespective of PD-L1 expression[1,2]

- Highest level of evidence **(I)** and recommendation grade **(A)**
- Established as a **standard treatment option** for patients with any PD-L1 score and PS 0–1, and without contraindications to IO
- KEYTRUDA plus chemotherapy is an IO combination that has an **ESMO-MCBS score of A/4 AT** in this setting
  - The highest possible grades of the ESMO-MCBS are A in the curative setting, and 5 for non-curative indications (for the primary-end point OS). Grades of A and B in the curative setting and 5 and 4 in the non-curative setting indicate substantial clinical benefit.[3]
  - An AT rating was assigned under the v2.0 rules.* Because KN-189 received a curative (A) score, the AT criteria became applicable. With 36% treatment discontinuation, the KN-189 study exceeded the threshold of premature discontinuation of therapy due to AEs in >10%of patients.[3]

*ESMO-MCBS v2.0 introduced an annotation for acute and persistent toxicity (AT) for treatments administered with curative intent. The AT annotation applies when any of the following criteria are met for the experimental arm: 30% prevalence of grade ≥3 adverse events impacting well being; premature discontinuation of therapy due to AEs in >10% of patients; or hospitalization for toxicity in >10% of patients.

ESMO, European Society for Medical Oncology; IO, immuno-oncology; MCBS, magnitude of clinical benefit scale; mNSCLC, metastatic non-small cell lung cancer; OS, overall survival; PD-L1, programmed death-ligand 1.

1. Hendriks LE, *et al.* on behalf of the ESMO Guidelines Committee *Ann Oncol* 2023;34:358–376. **2.** Hendriks LE, *et al.* on behalf of the ESMO Guidelines Committee *Ann Oncol* 2025;36:1223–1227. **3.** ESMO. ESMO-MCBS v2.0 evaluation forms. Available at: https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-evaluation-forms. Accessed: May 2026.

KEYTRUDA metastatic NSCLC indications[1]

- **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 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 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

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; Q3W, every 3 weeks; Q6W, every 6 weeks; TPS, tumour proportion score.

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

KEYNOTE-189

KEYTRUDA plus chemotherapy for the first-line treatment of metastatic, non-squamous, *EGFR*/*ALK*-wild-type NSCLC

Post hoc exploratory pooled analysis

Including KEYNOTE-189 and KEYNOTE-407, 5-year survival with KEYTRUDA plus chemotherapy for mNSCLC with PD-L1 TPS <1%

ALK, anaplastic lymphoma kinase; *EGFR*, epidermal growth factor receptor; mNSCLC, metastatic non-small cell lung cancer; NSCLC, non-small cell lung cancer; PD-L1, programmed death-ligand 1; TPS, tumour proportion score.

KEYNOTE-189 indication:

KEYTRUDA, plus chemotherapy for the first-line treatment of metastatic, non-squamous, *EGFR*/*ALK*-wild-type NSCLC[1]

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

KEYNOTE-189: Definition of analyses

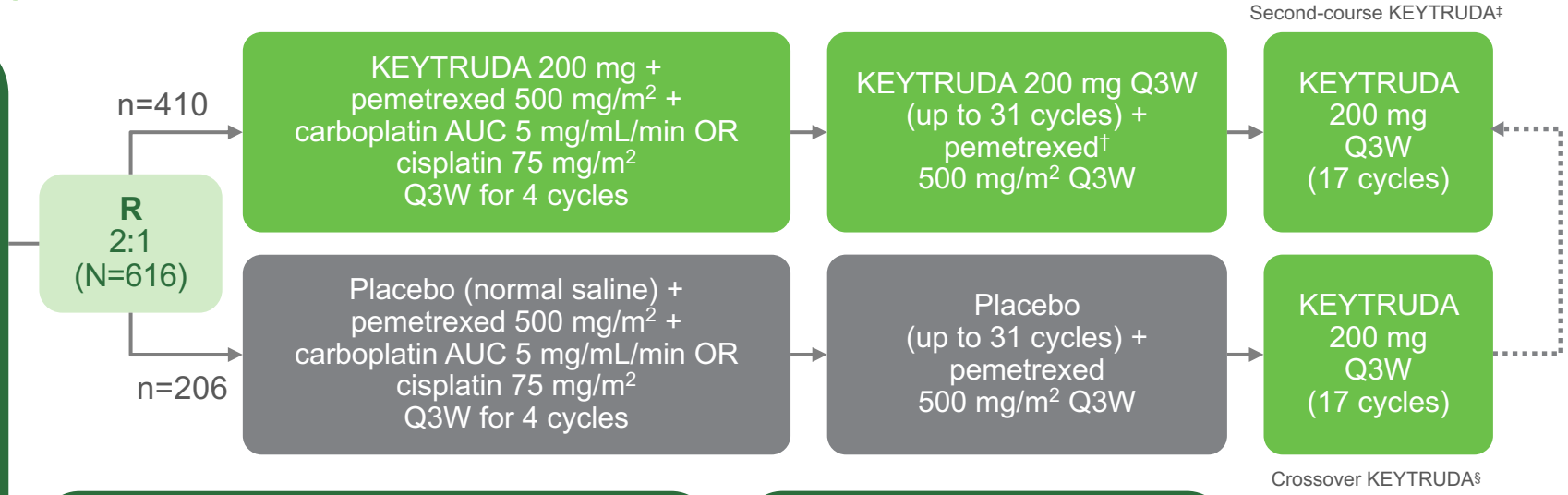
Analysis	Cut-off date	Slide symbol	Median follow-up (range) months
Original/first interim	8 November 2017	1	10.5 (0.2–20.4)[1,2]
Updated analysis	21 September 2018	2	23.1 (18.6–30.9)[3]
5-year follow-up	8 March 2022	3	64.6 (60.1–72.4)[4]

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092. **2.** Garassino MC, *et al. Lancet Oncol* 2020;21:387–397. **3.** Gadgeel S, *et al. J Clin Oncol* 2020;38:1505–1517. **4.** Garassino MC, *et al. J Clin Oncol* 2023;41:1992–1998.

KEYNOTE-189 study design: Multicentre, randomised active-controlled, double-blind, Phase III trial[1–3]

Key eligibility criteria

- Untreated metastatic, non-squamous NSCLC
- No sensitising *EGFR* or *ALK* mutations
- ECOG PS 0 or 1
- Provision of a sample for PD-L1 assessment
- No symptomatic CNS metastases*
- No history of non-infectious pneumonitis requiring use of glucocorticoids, no active autoimmune disease and no systemic immunosuppressive treatment
- <30 Gy of RT to the lung in the previous 6 months



Stratification factors

- PD-L1 expression (TPS¶ ≥1% vs <1%)
- Platinum-based chemotherapy (cisplatin vs carboplatin)
- Smoking history (never vs former/current)

Endpoints

- Primary: OS, PFS‖
- Secondary: ORR, ‖ DOR, ‖ safety#
- Exploratory: Effect of PD-L1 expression on efficacy, PFS2, PROs

Adapted from Gandhi L, *et al.* 2018 & Gray JE, *et al.* 2020.[1,3]

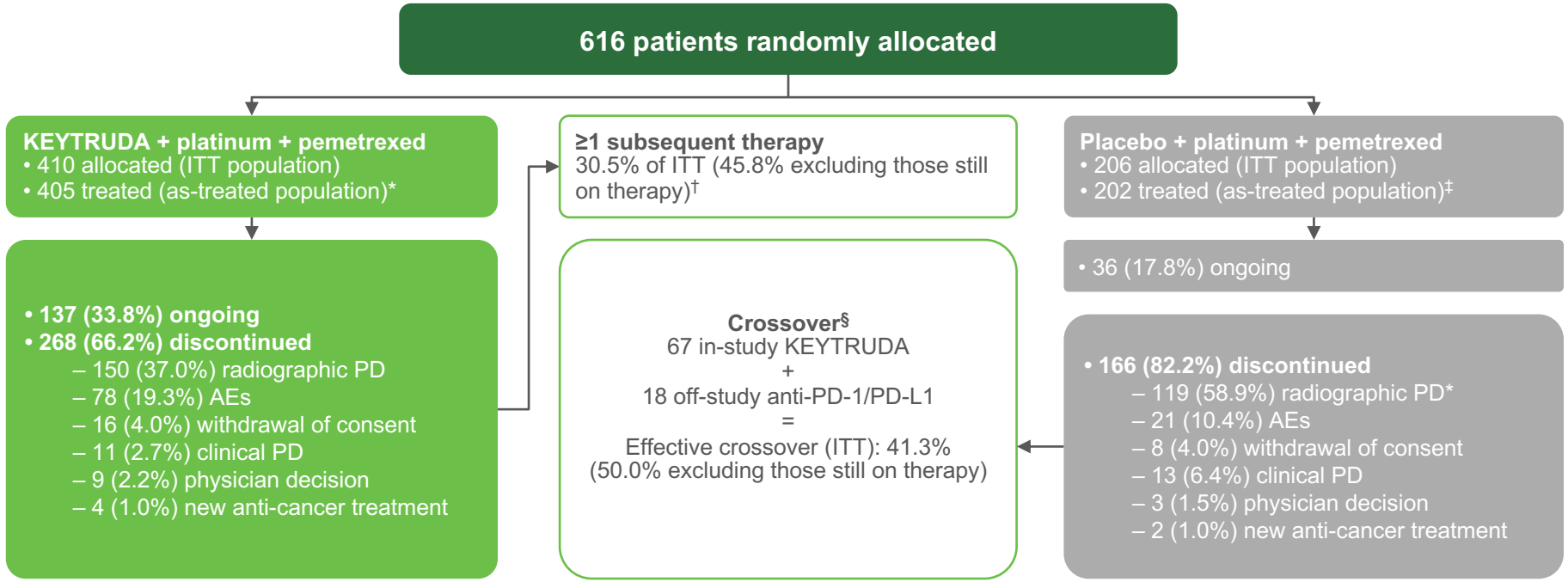
*Patients were permitted to enrol if their brain lesions were previously treated, clinically stable for ≥2 weeks without evidence of new or enlarging lesions, and steroid-free for ≥3 days prior to receiving study treatment.[1] †Efficacy assessed in the ITT population.[1] ‡Patients who had SD or better after completing 35 cycles of KEYTRUDA or had stopped trial treatment after achieving CR and received ≥8 cycles of treatment, but then experienced PD, could receive second-course KEYTRUDA for 17 cycles if they had received no new anti-cancer treatment since the last dose of KEYTRUDA.[1] §To be eligible for crossover to KEYTRUDA monotherapy, PD had to have been verified by blinded, independent, central radiological review and all safety criteria had to have been met.[1] ¶Percentage of tumour cells with membrane PD-L1 staining, as assessed using the PD-L1 IHC 22C3 pharmDx assay.[1] ‖Assessed by blinded, independent central review per RECIST 1.1.[1] #Assessed in all patients who received ≥1 dose of study medication.[1]

ALK, anaplastic lymphoma kinase; AUC, area under the curve; CNS; central nervous system; CR, complete response; DOR, duration of response; ECOG PS; Eastern Cooperative Oncology Group performance status; *EGFR,* epidermal growth factor receptor; IHC, immunohistochemistry; ITT, intention-to-treat; NSCLC, non-small cell lung carcinoma; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PFS2, progression-free survival 2; PRO, patient-reported outcome; Q3W, every 3 weeks; R, randomisation; RECIST, Response Evaluation Criteria in Solid Tumours; RT, radiotherapy; SD, stable disease; TPS, tumour proportion score.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092 (and protocol). **2.** Gandhi L, *et al.* AACR. 14–18 April 2018. Chicago, USA. **3.** Gray JE, *et al.* WCLC. 28–31 January 2021. Virtual.

KEYNOTE-189: Disposition of study treatment[1]

Median follow-up: 10.5 months.



Adapted from Gandhi L, *et al.* 2018 (and supplementary appendix).[1]

Data cut-off date: 8 November 2017.

*Two AEs, one clinical PD, one death and one protocol violation.[1] †45.8%=125/273, where 273 is derived from the ITT population (410) minus the number of patients with ongoing treatment (137), and 125 is derived from subsequent treatment in 30.5% of the ITT population (410).[2] ‡Two withdrawals of consent, one protocol violation and one physician decision.[1] §An additional 13 patients received other subsequent therapy (6.3% of ITT [7.6% excluding those still on therapy]).[2]

AE, adverse event; ITT, intent-to-treat; PD, progressive disease; PD-1, programmed cell death protein; PD-L1, programmed death-ligand 1.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092 (and supplementary appendix). **2.** Gandhi L, *et al.* AACR. 14–18 April 2018. Chicago, USA.

KEYNOTE-189: Key baseline characteristics[1]

Median follow-up: 10.5 months.

Characteristic, n (%)*	KEYTRUDA–plat–pem (n=410)	Placebo–plat–pem (n=206)
Age, median (range), years	65.0 (34.0–84.0)	63.5 (34.0–84.0)
<65 years	197 (48.0)	115 (55.8)
Male sex†	254 (62.0)	109 (52.9)
ECOG PS‡		
0	186 (45.4)	80 (38.8)
1	221 (53.9)	125 (60.7)
2	1 (0.2)	0
Brain metastases	73 (17.8)	35 (17.0)
Smoking status		
Former/current	362 (88.3)	181 (87.9)
Never	48 (11.7)	25 (12.1)

Characteristic, n (%)*	KEYTRUDA–plat–pem (n=410)	Placebo–plat–pem (n=206)
PD-L1 TPS§		
<1%	127 (31.0)	63 (30.6)
≥1%	260 (63.4)	128 (62.1)
1–49%	128 (31.2)	58 (28.2)
≥50%	132 (32.2)	70 (34.0)
NE¶	23 (5.6)	15 (7.3)
Prior thoracic radiotherapy	28 (6.8)	20 (9.7)
Prior neoadjuvant therapy	5 (1.2)	6 (2.9)
Prior neoadjuvant or adjuvant therapy	25 (6.1)	14 (6.8)

Adapted from Gandhi L, *et al.* 2018.[1]

Data cut-off date: 8 November 2017.

*Unless otherwise stated.[1] †There was a significant between-group difference in the proportion of men (p=0.04).[1] ‡Data regarding ECOG PS status were missing for two patients (0.5%) in the KEYTRUDA + platinum + pemetrexed group, and in one patient (0.5%) in the placebo + platinum + pemetrexed arm.[1] §PD-L1 TPS was defined as the percentage of tumour cells with membranous PD-L1 expression.[1] ¶PD-L1 expression could not be evaluated because specimens had an inadequate number of tumour cells or no tumour cells. For stratification purposes, patients with PD-L1 expression that could not be evaluated were included in the subgroup with PD-L1 TPS <1%; these patients were excluded from analyses of efficacy according to PD-L1 TPS.[1]

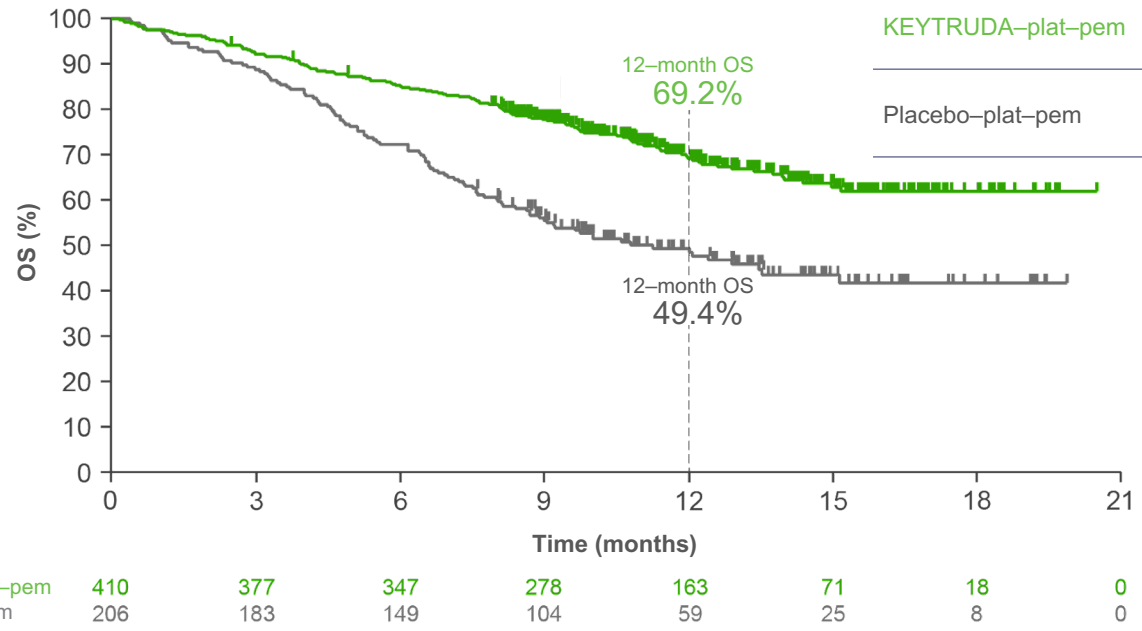
ECOG PS, Eastern Cooperative Oncology Group performance status; NE, not evaluable; PD-L1, programmed death-ligand 1; pem, pemetrexed; plat, platinum; TPS, tumour proportion score.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092.

KEYNOTE-189: 1-year landmark OS in the ITT population (original analysis)*†‡[1,2]

Median follow-up: 10.5 months.

	Events (%)	Median, months (95% CI)	HR (95% CI)	P value
KEYTRUDA–plat–pem	31.0	NR (NE–NE)	0.49 (0.38–0.64)	<0.001
Placebo–plat–pem	52.4	11.3 (8.7–15.1)	–	–



Adapted from Gandhi L, *et al.* 2018 & Gandhi L, *et al.* 2018.[1,2]

Data cut-off date: 8 November 2017.

*OS and PFS were both primary endpoints.[1] †Kaplan-Meier estimate.[1] ‡Overall alpha for study: strictly controlled at one-sided α=0.025, using the graphical method of Maurer and Bretz. The study had 90% power to show an HR of 0.70 for OS at one-sided α=0.0155 (based on 416 deaths) for the comparison between the KEYTRUDA and placebo combination groups. At IA1: one-sided α=0.00128 for OS.[1]

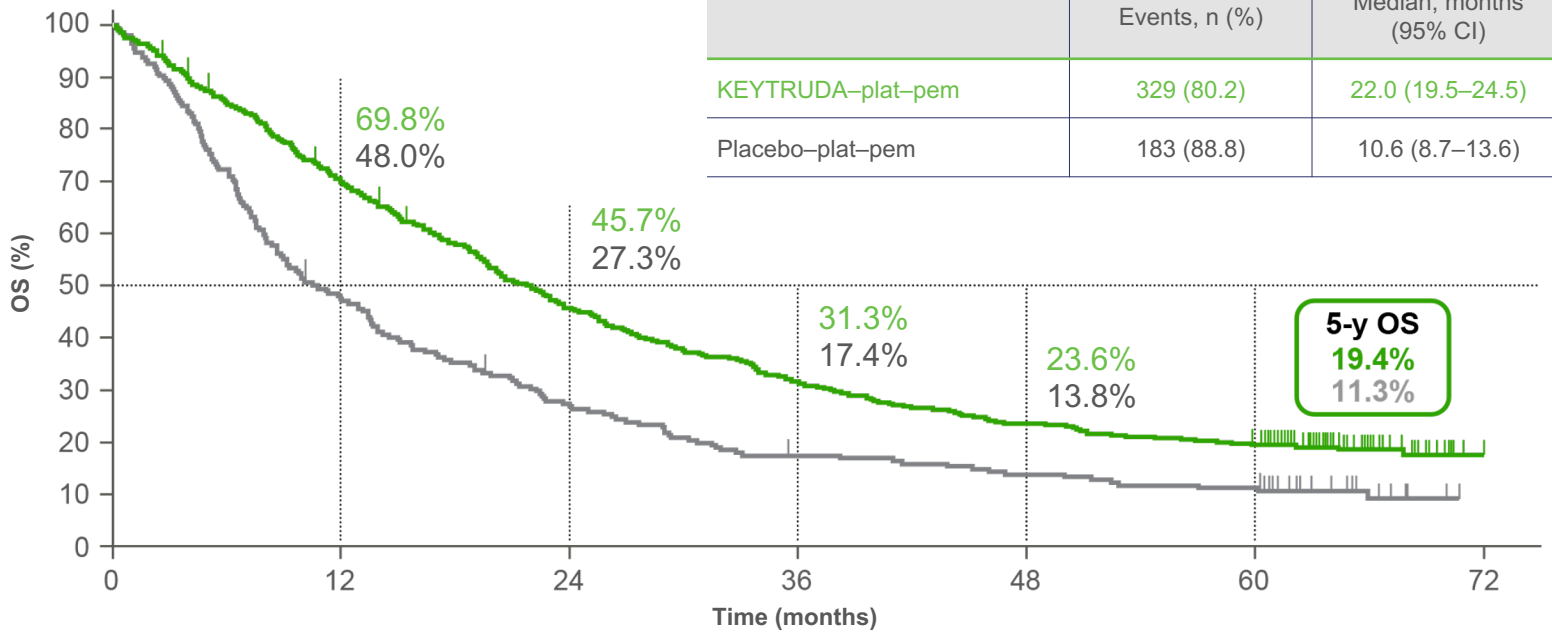
CI, confidence interval; HR, hazard ratio; IA, interim analysis; ITT, intent-to-treat; NE, not evaluable; NR, not reported; OS, overall survival; pem, pemetrexed; PFS, progression-free survival; plat, platinum.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092. **2.** Gandhi L, *et al.* AACR. 14–18 April 2018. Chicago, USA.

KEYNOTE-189: Exploratory analysis – OS in the ITT population (5-year update)*†‡[1]

Median follow-up: 64.6 months. No statistical conclusions can be drawn from this analysis.

	Events, n (%)	Median, months (95% CI)	HR (95% CI)
KEYTRUDA–plat–pem	329 (80.2)	22.0 (19.5–24.5)	0.60 (0.50–0.72) p=not tested
Placebo–plat–pem	183 (88.8)	10.6 (8.7–13.6)	



Number at risk

KEYTRUDA–plat–pem	410	283	184	126	95	77	0
Placebo–plat–pem	206	98	55	34	27	22	0

Adapted from Garassino MC, *et al.* 2023.[1]

Data cut-off date: 8 March 2022.

*OS and PFS were both primary endpoints.[1] †Kaplan-Meier estimate.[1] ‡Statistical significance was met for the primary endpoints in IA1 (2018).[1]

CI, confidence interval; HR, hazard ratio; IA, interim analysis; ITT, intent-to-treat; OS, overall survival; pem, pemetrexed; PFS, progression-free survival; plat, platinum.

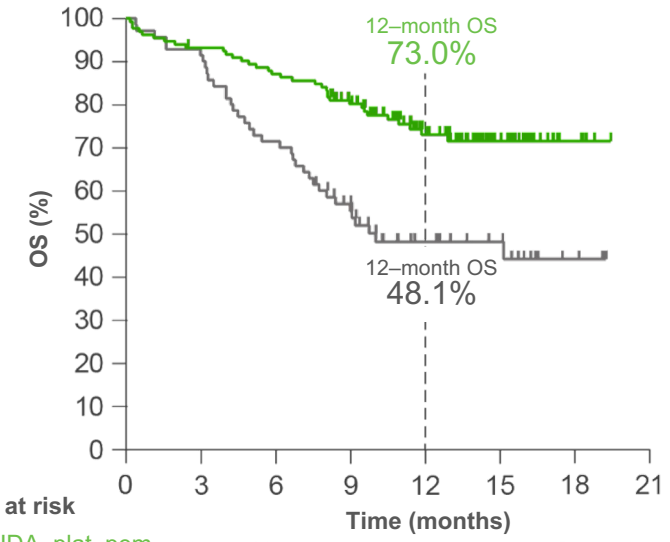
1. Garassino MC, *et al. J Clin Oncol* 2023;41:1992–1998.

KEYNOTE-189: Exploratory endpoint – 1-year landmark OS by PD-L1 TPS (original analysis)*[1,2]

Median follow-up: 10.5 months. No statistical conclusions can be drawn from exploratory endpoints.

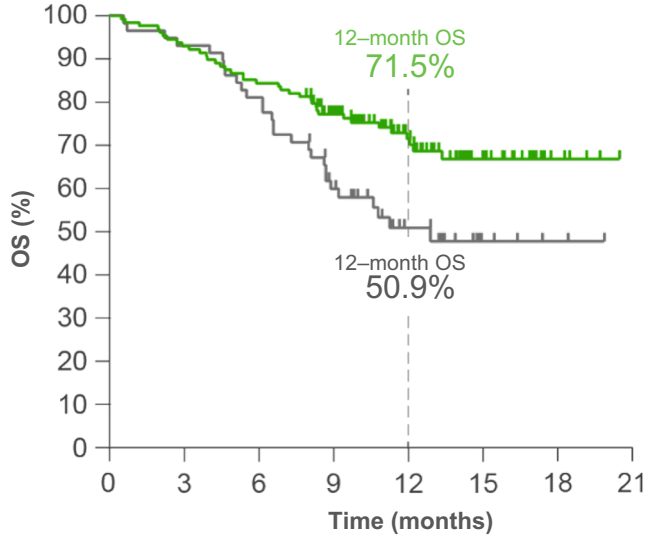
PD-L1 TPS ≥50%

Treatment arm	Events (%)	Median, months (95% CI)	HR (95% CI)	P value†
KEYTRUDA–plat–pem	25.8	NR (NE–NE)	0.42 (0.26–0.68)	0.0001
Placebo–plat–pem	51.4	10.0 (7.5–NE)	–	–



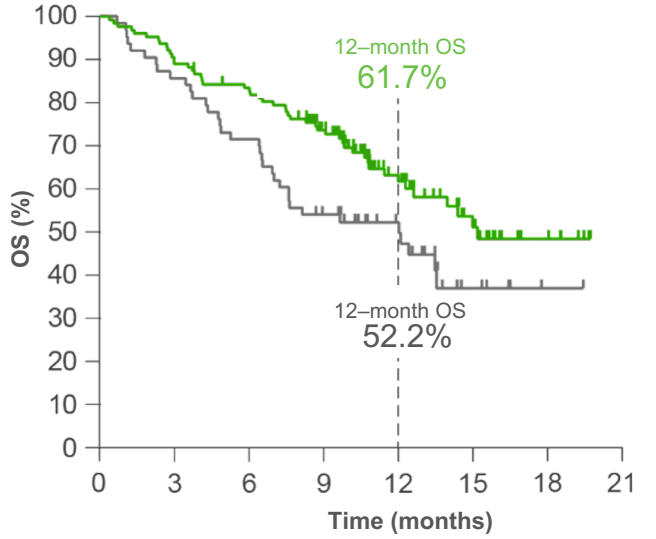
PD-L1 TPS 1–49%

Events (%)	Median, months (95% CI)	HR (95% CI)	P value†
28.9	NR (NE–NE)	0.55 (0.34–0.90)	0.0081
48.3	12.9 (8.7–NE)	–	–



PD-L1 TPS <1%

Events (%)	Median, months (95% CI)	HR (95% CI)	P value†
38.6	15.2 (12.3–NE)	0.59 (0.38–0.92)	0.0095
55.6	12.0 (7.0–NE)	–	–



Number at risk

KEYTRUDA–plat–pem	132	122	114	96	56	25	6	0
Placebo–plat–pem	70	64	50	35	19	13	4	0

KEYTRUDA–plat–pem	128	119	108	84	52	21	5	0
Placebo–plat–pem	58	54	47	32	17	5	2	0

KEYTRUDA–plat–pem	127	113	104	79	42	20	6	0
Placebo–plat–pem	63	54	45	32	21	6	1	0

Adapted from Gandhi L, *et al.* 2018 & Gandhi L, *et al.* 2018.[1,2]

Data cut-off date: 8 November 2017.

*Kaplan-Meier estimate.[1] †Nominal and one-sided.[2]

CI, confidence interval; HR, hazard ratio; NE, not evaluable; NR, not reported; OS, overall survival; PD-L1, programmed death-ligand 1; pem, pemetrexed; plat, platinum; TPS, tumour proportion score.

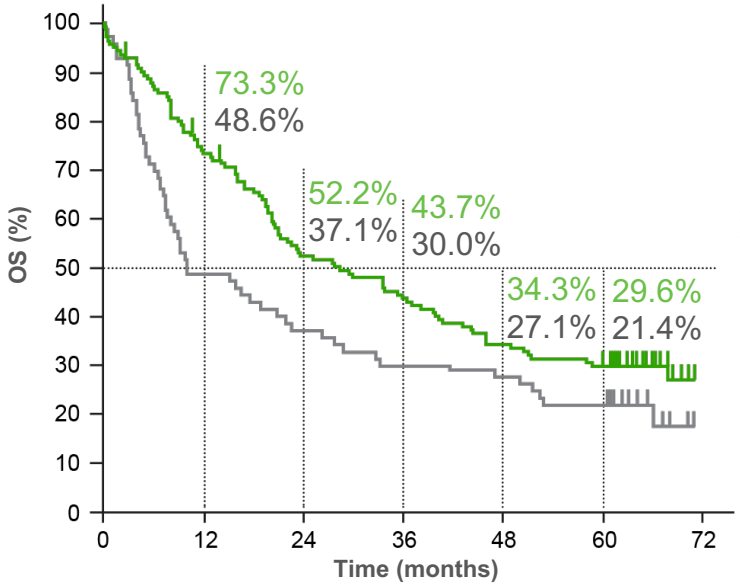
1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092. **2.** Gandhi L, *et al.* AACR. 14–18 April 2018. Chicago, USA.

KEYNOTE-189: Exploratory analysis – OS by PD-L1 TPS (5-year update)*[1]

Median follow-up: 64.6 months. No statistical conclusions can be drawn from this analysis.

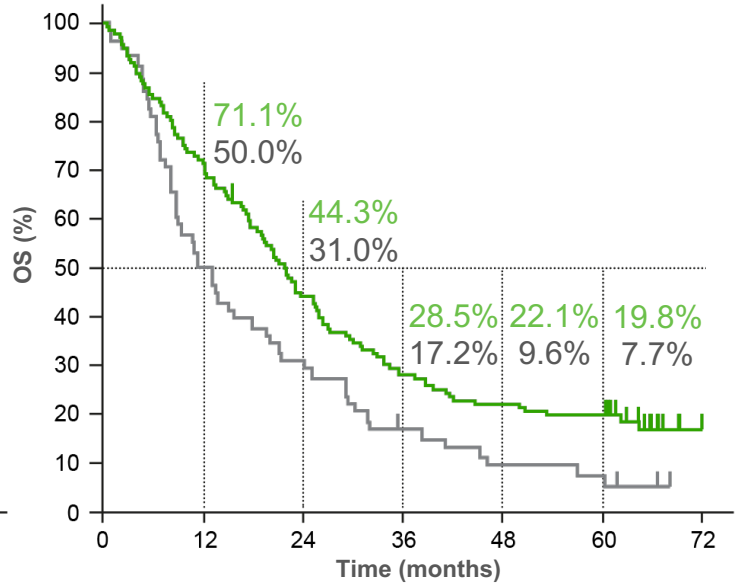
PD-L1 TPS ≥50%

Treatment arm	Events, n (%)	HR (95% CI)	5-year OS rate, % (95% CI)
KEYTRUDA–plat–pem	92 (69.7)	0.68	29.6 (22.0–37.6)
Placebo–plat–pem	56 (80.0)	(0.49–0.96)	21.4 (12.7–31.6)



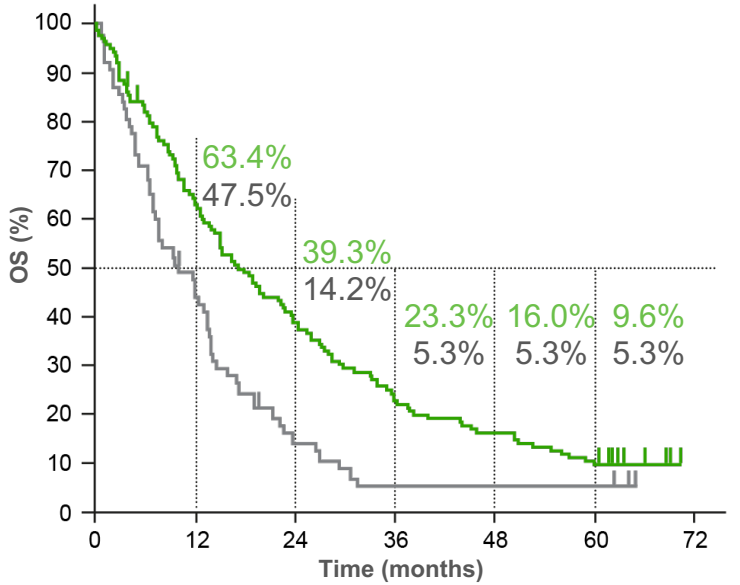
PD-L1 TPS 1–49%

Events, n (%)	HR (95% CI)	5-year OS rate, % (95% CI)
104 (81.3)	0.65	19.8 (13.4–27.1)
54 (93.1)	(0.46–0.90)	7.7 (2.5–16.6)



PD-L1 TPS <1%

Events, n (%)	HR (95% CI)	5-year OS rate, % (95% CI)
113 (89.0)	0.56	9.6 (5.3–15.6)
58 (92.1)	(0.39–0.76)	5.3 (1.4–13.2)



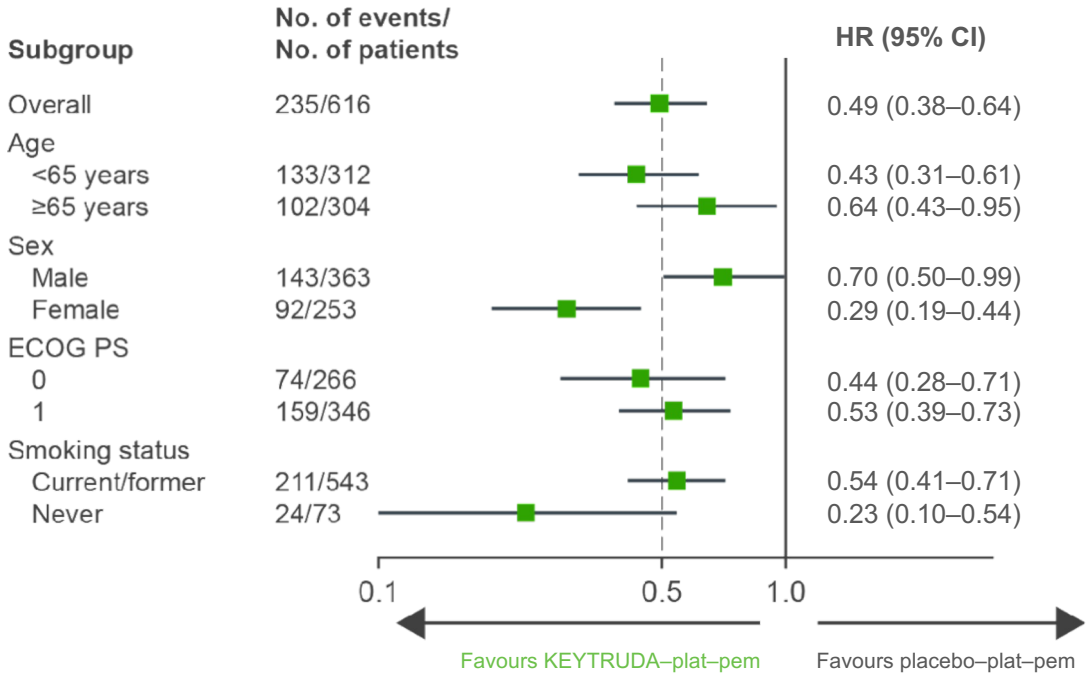
Number at risk							
KEYTRUDA–plat–pem	132	95	67	56	44	37	0
Placebo–plat–pem	70	34	26	21	19	15	0
KEYTRUDA–plat–pem	128	91	56	36	28	25	0
Placebo–plat–pem	58	29	18	9	5	4	0
KEYTRUDA–plat–pem	127	79	49	29	20	12	0
Placebo–plat–pem	63	29	8	3	3	3	0

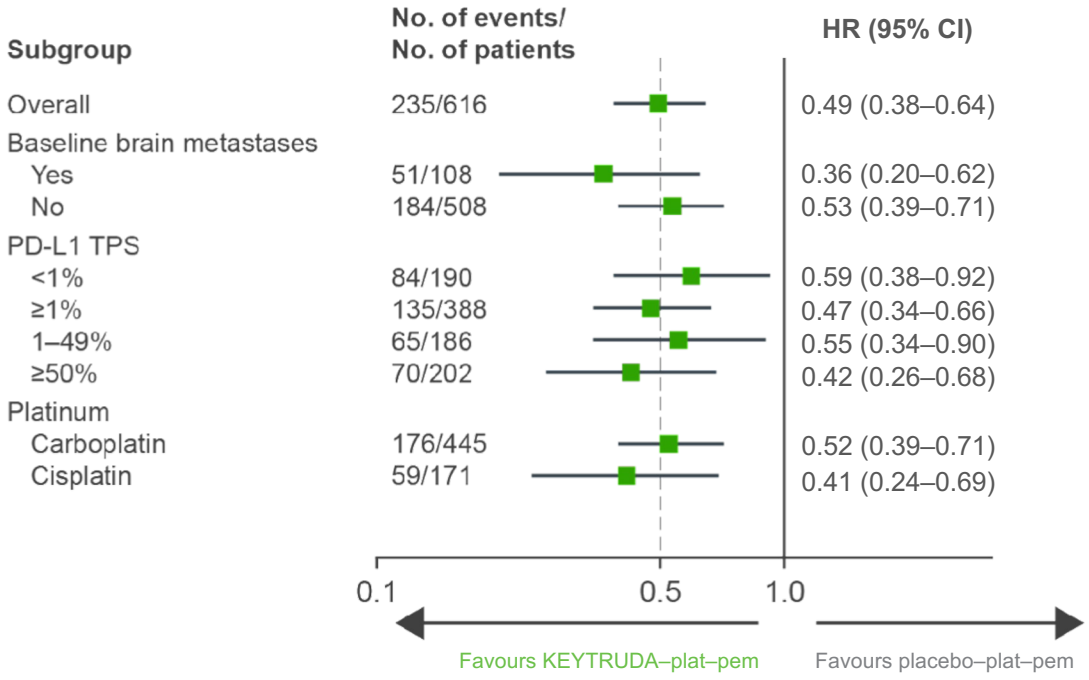
Adapted from Garassino MC, *et al.* 2023.[1]

Data cut-off date: 8 March 2022.
*Kaplan-Meier estimate.[1]
CI, confidence interval; HR, hazard ratio; OS, overall survival; PD-L1, programmed death-ligand 1; pem, pemetrexed; plat, platinum; TPS, tumour proportion score.
1. Garassino MC, *et al. J Clin Oncol* 2023;41:1992–1998.

KEYNOTE-189: Exploratory endpoint – OS in key subgroups (original analysis)[1]

Median follow-up: 10.5 months. No statistical conclusions can be drawn from exploratory endpoints.





Adapted from Ghandi L, *et al*. 2018.[1]

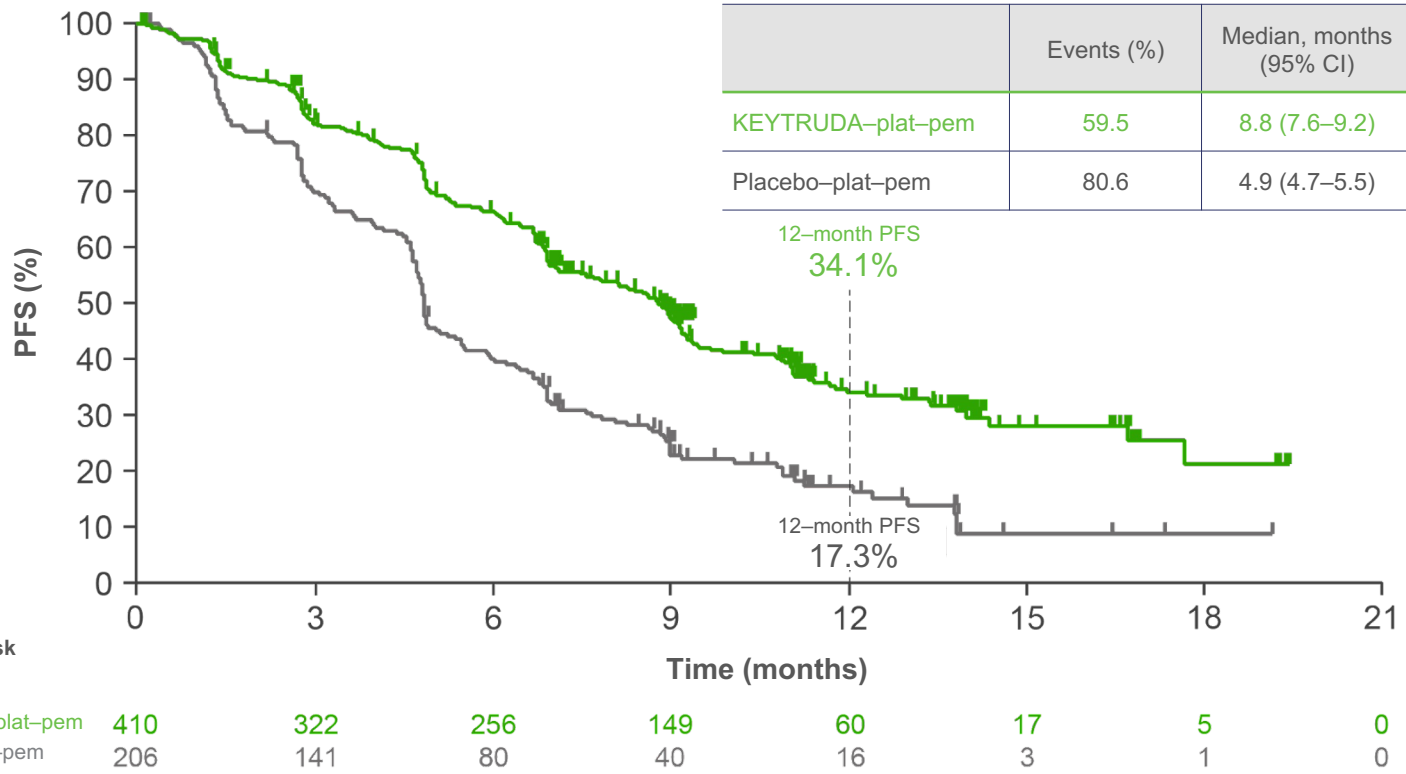
Data cut-off date: 8 November 2017.

CI, confidence interval; HR, hazard ratio; ECOG PS, Eastern Cooperative Oncology Group performance status; OS, overall survival; PD-L1, programmed death-ligand 1; TPS, tumour proportion score.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092.

KEYNOTE-189: 1-year landmark PFS in the ITT population (original analysis)*†‡§[1,2]

Median follow-up: 10.5 months.



	Events (%)	Median, months (95% CI)	HR (95% CI)	P value
KEYTRUDA–plat–pem	59.5	8.8 (7.6–9.2)	0.52 (0.43–0.64)	<0.001
Placebo–plat–pem	80.6	4.9 (4.7–5.5)	–	–

Adapted from Gandhi L, *et al.* 2018 & Gandhi L, *et al.* 2018.[1,2]

Data cut-off date: 8 November 2017.

*OS and PFS were both primary endpoints.[1] †Kaplan-Meier estimate.[1] ‡Assessed using RECIST by blinded, independent, central radiological review.[1] §Overall alpha for study: strictly controlled at one-sided α=0.025, using the graphical method of Maurer and Bretz. The study had 90% power to show an HR of 0.70 for PFS at one-sided α=0.0095 (based on 468 deaths) for the comparison between the KEYTRUDA and placebo combination groups. At IA1: one-sided α=0.00559 for PFS[1]

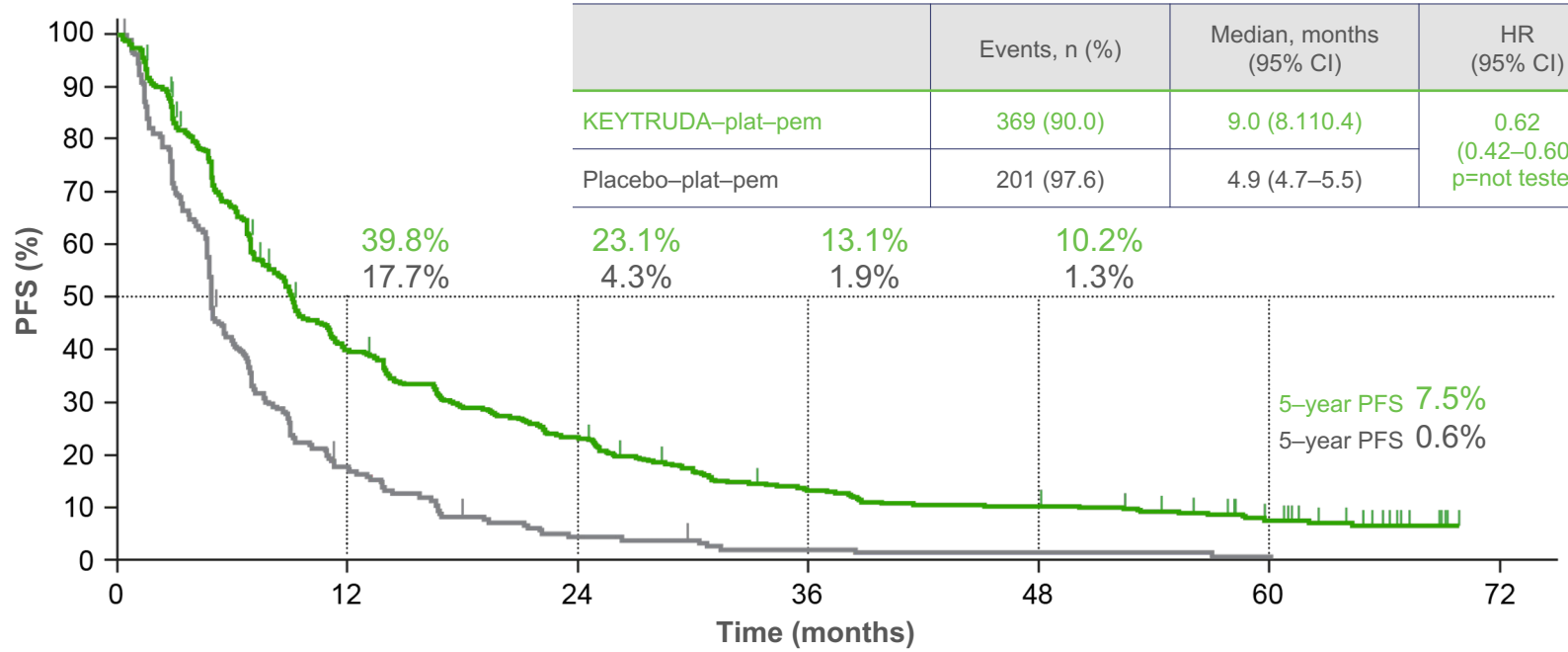
CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; OS, overall survival; PD-L1, programmed death-ligand 1; pem, pemetrexed; PFS, progression-free survival; plat, platinum; RECIST, Response Evaluation Criteria in Solid Tumours; TPS, tumour proportion score.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092. **2.** Gandhi L, *et al.* AACR. 14–18 April 2018. Chicago, USA.

KEYNOTE-189: Exploratory analysis – PFS in the ITT population (5-year update)*†‡§[1]

Median follow-up: 56.9 months. No statistical conclusions can be drawn from this analysis.

	Events, n (%)	Median, months (95% CI)	HR (95% CI)
KEYTRUDA–plat–pem	369 (90.0)	9.0 (8.110.4)	0.62 (0.42–0.60) p=not tested
Placebo–plat–pem	201 (97.6)	4.9 (4.7–5.5)	



Number at risk

KEYTRUDA–plat–pem	410	158	91	49	37	21	0
Placebo–plat–pem	206	35	8	3	2	1	0

Adapted from Garassino MC, *et al.* 2023.[1]

Data cut-off date: 8 March 2022.

*OS and PFS were both primary endpoints.[1] †Kaplan-Meier estimate.[1] ‡Statistical significance was met for the primary endpoints in IA1 (2018).[1] §Assessed using RECIST by blinded, independent, central radiological review.[1]

CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; OS, overall survival; pem, pemetrexed; PFS, progression-free survival; plat, platinum; RECIST, Response Evaluation Criteria in Solid Tumours.

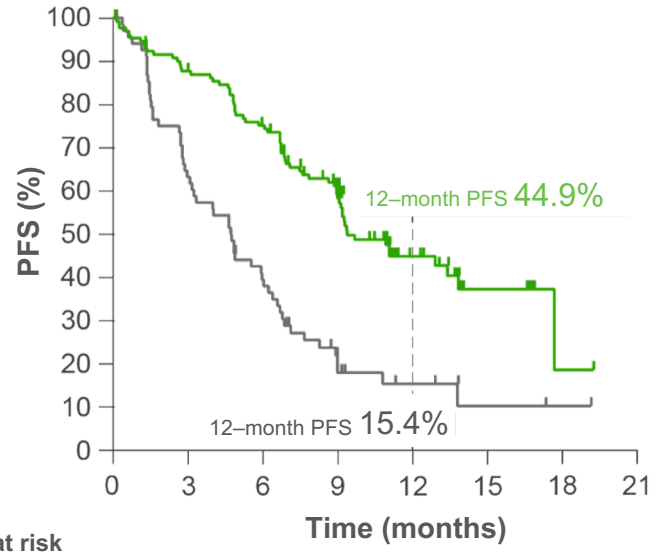
1. Garassino MC, *et al. J Clin Oncol* 2023;41:1992–1998.

KEYNOTE-189: Exploratory endpoint – 1-year landmark PFS by PD-L1 TPS (original analysis)*[1,2]

Median follow-up: 10.5 months. No statistical conclusions can be drawn from exploratory endpoints.

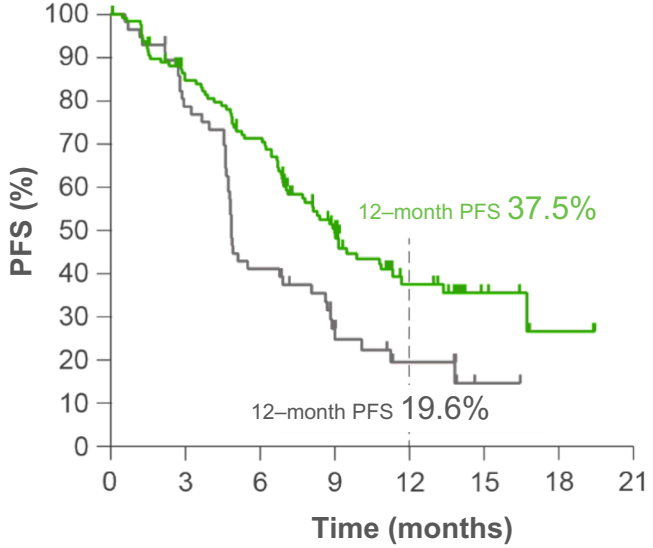
PD-L1 TPS ≥50%

Treatment arm	Events (%)	Median, months (95% CI)	HR (95% CI)	P value†
KEYTRUDA–plat–pem	51.5	9.4 (9.0–13.8)	0.36 (0.25–0.52)	0.00001
Placebo–plat–pem	80.0	4.7 (3.1–6.0)	–	–



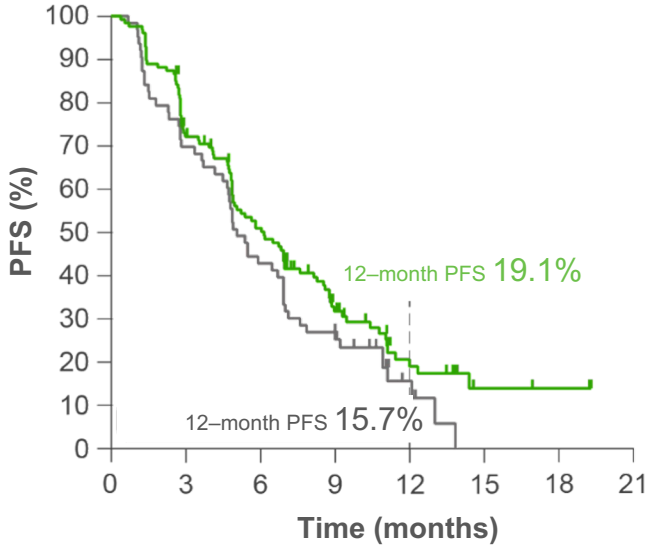
PD-L1 TPS 1–49%

Events (%)	Median, months (95% CI)	HR (95% CI)	P value†
54.7	9.0 (7.1–11.3)	0.55 (0.37–0.81)	0.0010
75.9	4.9 (4.7–6.9)	–	–



PD-L1 TPS <1%

Events (%)	Median, months (95% CI)	HR (95% CI)	P value†
72.4	6.1 (4.9–7.6)	0.75 (0.53–1.05)	0.0476
85.7	5.1 (4.5–6.9)	–	–



Number at risk

KEYTRUDA–plat–pem	132	112	95	60	23	7	1	0
Placebo–plat–pem	70	43	26	11	5	2	1	0

KEYTRUDA–plat–pem	128	101	84	47	21	6	2	0
Placebo–plat–pem	58	44	23	11	6	1	0	0

KEYTRUDA–plat–pem	127	88	60	31	12	3	2	0
Placebo–plat–pem	63	44	27	16	4	0	0	0

Adapted from Gandhi L, *et al.* 2018 & Gandhi L, *et al.* 2018.[1,2]

Data cut-off date: 8 November 2017.

*Assessed using RECIST by blinded, independent, central radiological review.[1] †Nominal and one-sided.[2]

CI, confidence interval; HR, hazard ratio; PD-L1, programmed death-ligand 1; pem, pemetrexed; PFS, progression-free survival; plat, platinum; RECIST, Response Evaluation Criteria in Solid Tumours; TPS, tumour proportion score.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092. **2.** Gandhi L, *et al.* AACR. 14–18 April 2018. Chicago, USA.

KEYNOTE-189: Exploratory analysis – PFS by PD-L1 TPS (5-year update)*†[1]

Median follow-up: 64.6 months. No statistical conclusions can be drawn from this analysis.

PD-L1 TPS ≥50%

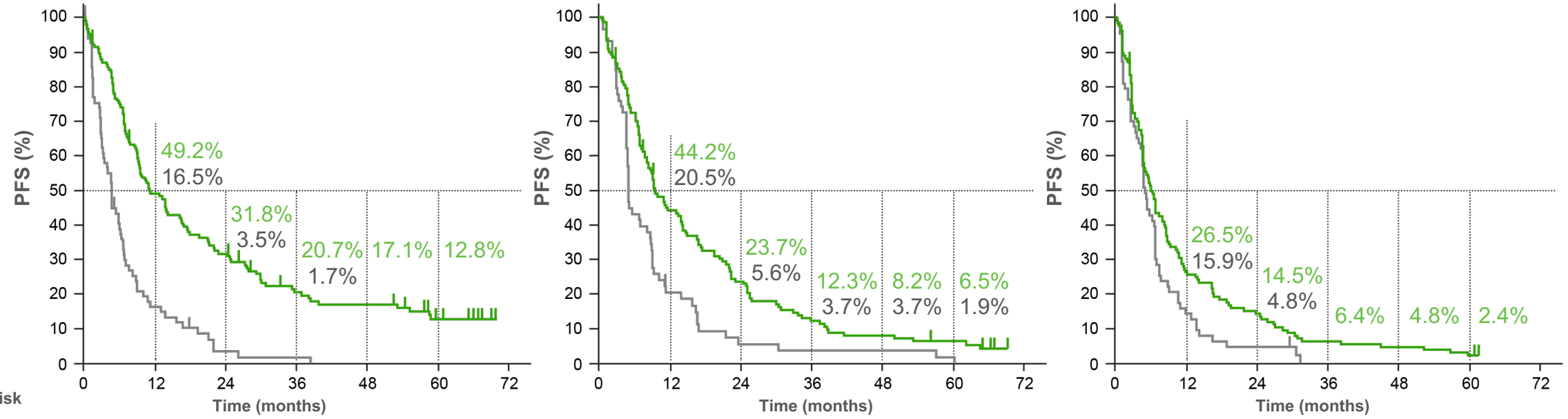
Treatment group	Events, n (%)	Median, months (95% CI)	HR (95% CI)	5-year PFS rate, % (95% CI)
KEYTRUDA–plat–pem	109 (82.6)	11.3 (9.1–16.5)	0.35	12.8 (7.4–19.8)
Placebo–plat–pem	67 (95.7)	4.8 (3.1–6.2)	(0.25–0.49)	–

PD-L1 TPS 1–49%

Events, n (%)	Median, months (95% CI)	HR (95% CI)	5-year PFS rate, % (95% CI)
118 (92.2)	9.4 (8.1–13.8)	0.57	6.5 (3.1–11.8)
57 (98.3)	4.9 (4.7–8.6)	(0.41–0.80)	1.9 (0.2–8.7)

PD-L1 TPS <1%

Events, n (%)	Median, months (95% CI)	HR (95% CI)	5-year PFS rate, % (95% CI)
122 (96.1)	6.2 (4.9–8.3)	0.67	2.4 (0.7–6.3)
62 (98.4)	5.1 (4.5–6.8)	(0.49–0.92)	–



Number at risk

KEYTRUDA–plat–pem	132	63	40	23	19	10	0
Placebo–plat–pem	70	11	2	1	0	0	0

KEYTRUDA–plat–pem	128	54	29	15	10	6	0
Placebo–plat–pem	58	11	3	2	2	1	0

KEYTRUDA–plat–pem	127	33	18	8	6	3	0
Placebo–plat–pem	63	10	3	0	0	0	0

Adapted from Garassino MC, *et al.* 2023.[1]

Data cut-off date: 8 March 2022.

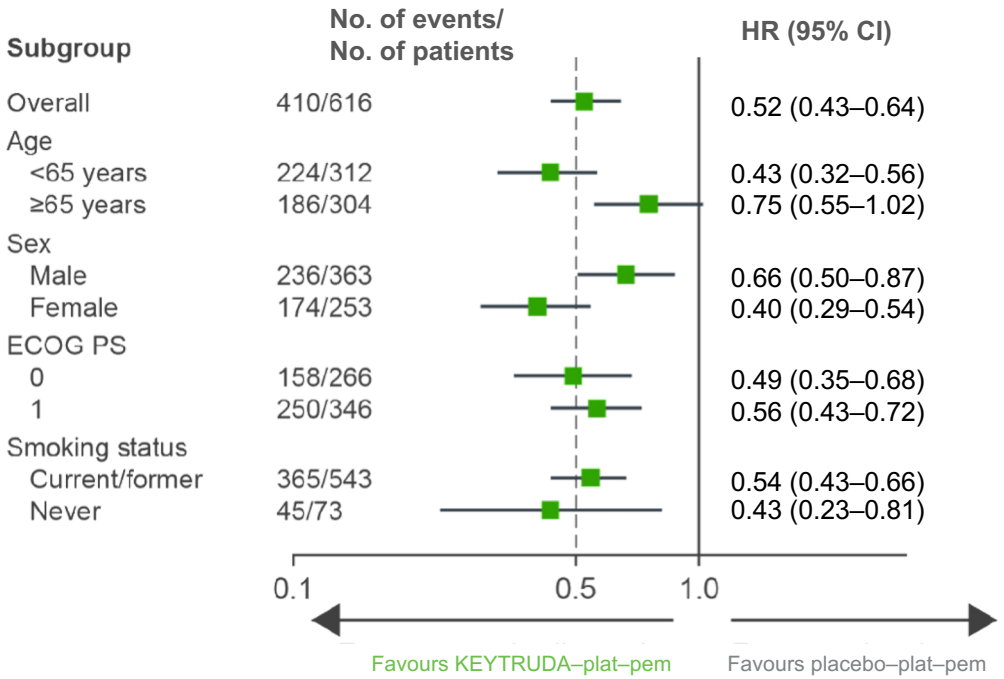
*Assessed using RECIST by blinded, independent, central radiological review.[1] †Kaplan-Meier estimate.[1]

CI, confidence interval; HR, hazard ratio; PD-L1, programmed death-ligand 1; pem, pemetrexed; PFS, progression-free survival; plat, platinum; RECIST, Response Evaluation Criteria in Solid Tumours; TPS, tumour proportion score.

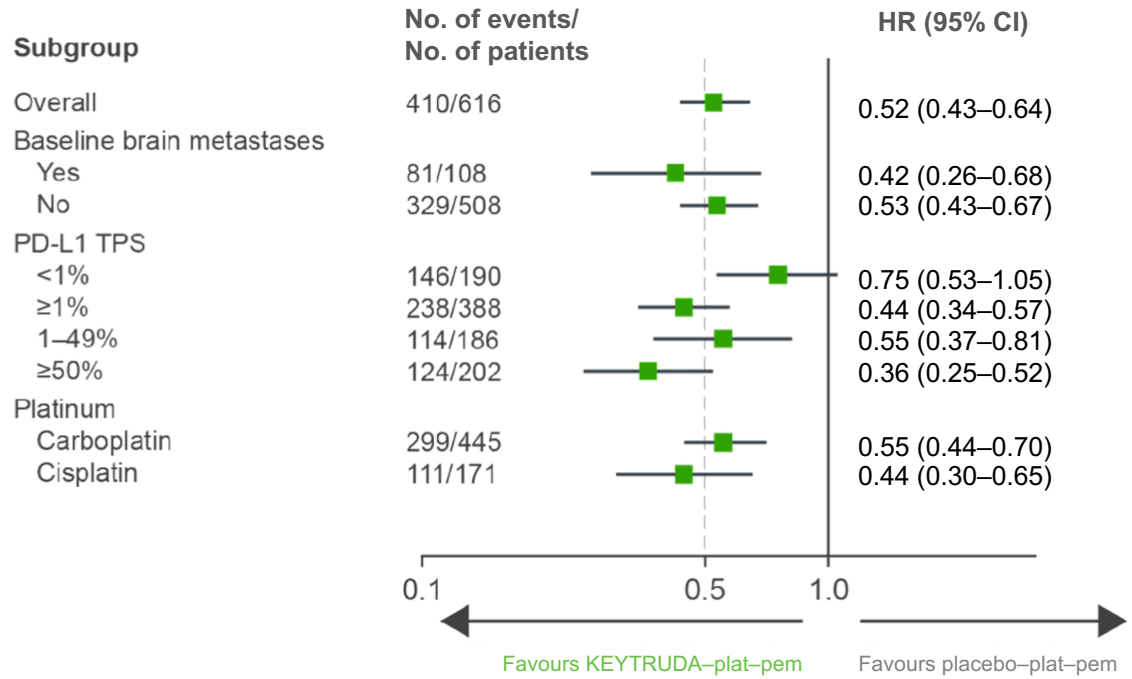
1. Garassino MC, *et al. J Clin Oncol* 2023;41:1992–1998.

KEYNOTE-189: Exploratory endpoint – PFS in key subgroups (original analysis)*[1]

Median follow-up: 10.5 months. No statistical conclusions can be drawn from exploratory endpoints.



HR for disease progression or death (95% CI)



HR for disease progression or death (95% CI)

Adapted from Ghandi L, *et al*. 2018.[1]

Data cut-off date: 8 November 2017.

*Assessed using RECIST by blinded, independent, central radiological review.[1]

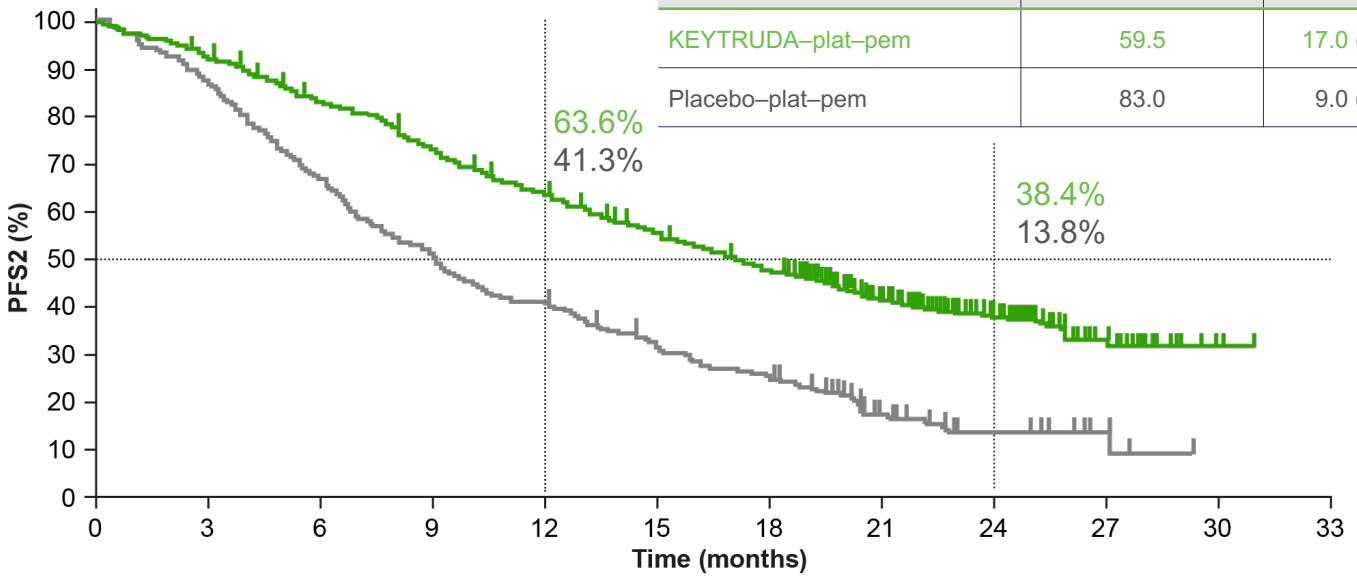
CI, confidence interval; HR, hazard ratio; PD-L1, programmed death-ligand 1; pem, pemetrexed; PFS, progression-free survival; plat, platinum; RECIST, Response Evaluation Criteria in Solid Tumours; TPS, tumour proportion score.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092.

KEYNOTE-189: Exploratory endpoint – PFS2 (updated analysis)*†[1]

Median follow-up: 23.1 months. PFS2 defined as the time from randomisation to second or subsequent tumour progression on next line of treatment or death. No statistical conclusions can be drawn from exploratory endpoints.

	Events (%)	Median, months (95% CI)	HR (95% CI)
KEYTRUDA–plat–pem	59.5	17.0 (15.1–19.4)	0.49 (0.40–0.59)
Placebo–plat–pem	83.0	9.0 (7.6–10.4)	–



Number at risk												
KEYTRUDA–plat–pem	0	377	336	294	253	217	185	115	67	26	2	0
Placebo–plat–pem	6	180	139	105	84	61	50	23	10	3	0	0

Adapted from Gadgeel S, *et al.* 2020.[1]

Data cut-off date: 21 September 2018.
*Assessed using RECIST by investigator review.[1] †Kaplan-Meier estimate.[1]
CI, confidence interval; HR, hazard ratio; pem, pemetrexed; PFS2, progression-free survival 2; plat, platinum; RECIST, Response Evaluation Criteria in Solid Tumours.
1. Gadgeel S, *et al. J Clin Oncol* 2020;38:1505–1517.

KEYNOTE-189: Exploratory endpoint – PFS2 by PD-L1 TPS (updated analysis)*†‡[1]

Median follow-up: 23.1 months. No statistical conclusions can be drawn from exploratory endpoints.

PD-L1 TPS ≥50%

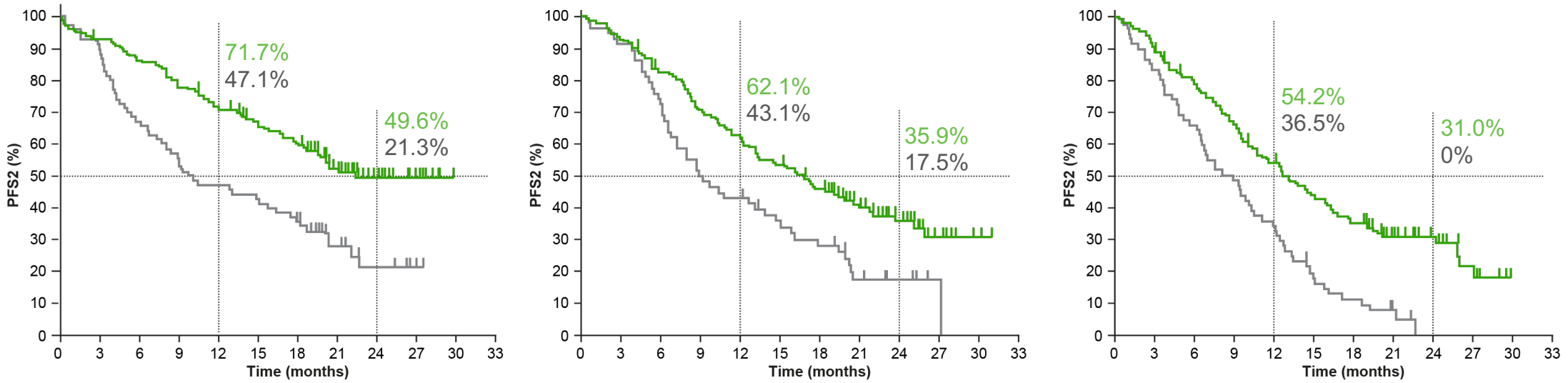
Treatment arm	Events (%)	Median, months (95% CI)	HR (95% CI)
KEYTRUDA–plat–pem	47.0	22.5 (18.5–NR)	0.47 (0.33–0.69)
Placebo–plat–pem	72.9	9.9 (7.4–16.4)	–

PD-L1 TPS 1–49%

Events (%)	Median, months (95% CI)	HR (95% CI)
61.7	16.9 (12.7–20.5)	0.59 (0.41–0.86)
81.0	9.1 (6.8–13.9)	–

PD-L1 TPS <1%

Events (%)	Median, months (95% CI)	HR (95% CI)
69.3	12.6 (10.2–15.9)	0.46 (0.33–0.66)
93.7	8.9 (6.5–10.5)	–



Adapted from Gadgeel S, *et al.* 2020.[1]

Data cut-off date: 21 September 2018.

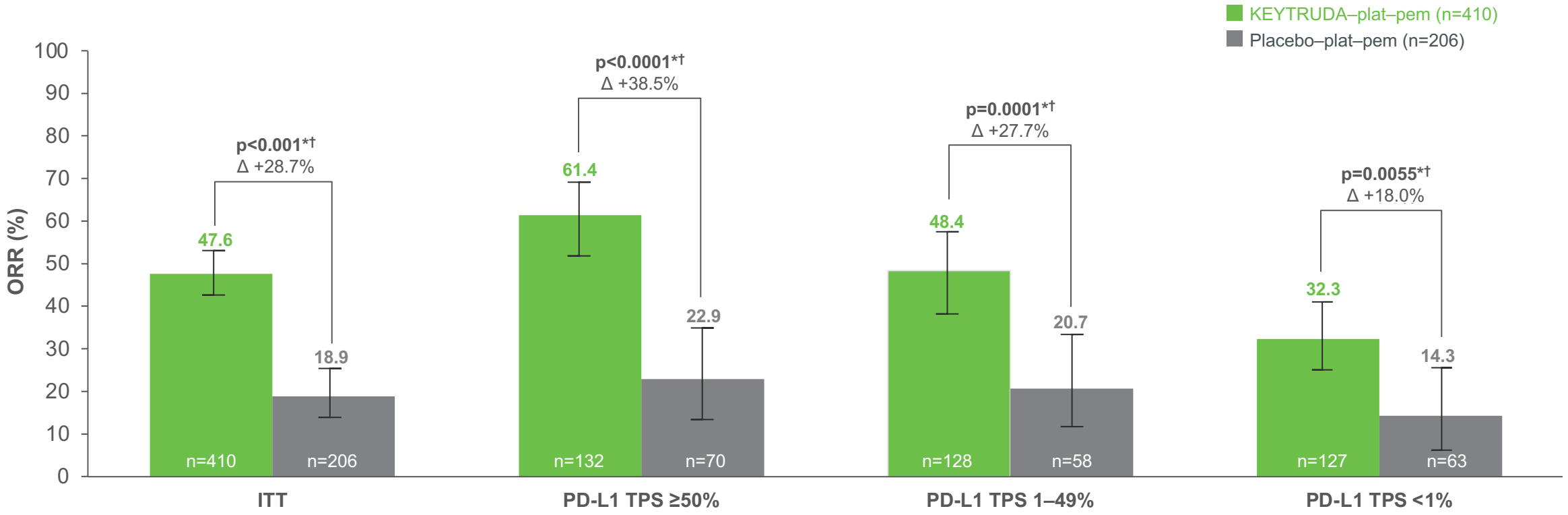
*Defined as the time from randomisation to second or subsequent tumour progression on next line of treatment or death.[1] †Assessed using RECIST by investigator review.[1] ‡Kaplan-Meier estimate.[1]

CI, confidence interval; HR, hazard ratio; NR, not reached; PD-L1, programmed death-ligand 1; pem, pemetrexed; PFS2, progression-free survival 2; plat, platinum; RECIST, Response Evaluation Criteria in Solid Tumours; TPS, tumour proportion score.

1. Gadgeel S, *et al. J Clin Oncol* 2020;38:1505–1517.

KEYNOTE-189: ORR in the ITT population*[1] and exploratory endpoint ORR by PD-L1 TPS (original analysis)*[1,2]

Median follow-up: 10.5 months. No statistical conclusions can be drawn from exploratory endpoints.



Adapted from Gandhi L, *et al.* 2018 & Gandhi L, *et al.* 2018.[1,2]

Data cut-off date: 8 November 2017.

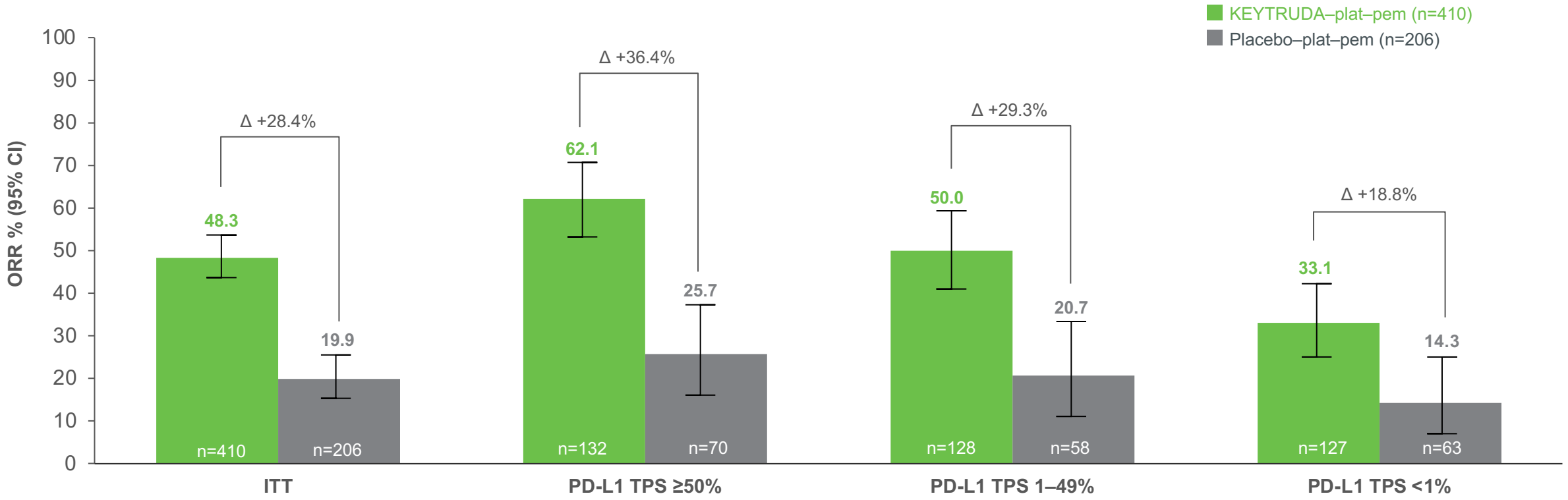
*Assessed using RECIST by blinded, independent, central radiological review.[1] †Nominal and one-sided.[2]

ITT, intent-to-treat; ORR, objective response rate; PD-L1, programmed death-ligand 1; pem, pemetrexed; plat, platinum; RECIST, Response Evaluation Criteria in Solid Tumours; TPS, tumour proportion score.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092 (and supplementary appendix). **2.** Gandhi L, *et al.* AACR. 14–18 April 2018. Chicago, USA.

KEYNOTE-189: Exploratory analysis – ORR in the ITT population and exploratory endpoint ORR by PD-L1 TPS (5-year update)*[1]

Median follow-up: 64.6 months. No statistical conclusions can be drawn from this analysis.



Adapted from . Garassino MC, *et al.* 2023.[1]

Data cut-off date: 8 March 2022.

*Assessed using RECIST by blinded, independent, central radiological review.[1]

ITT, intent-to-treat; ORR, objective response rate; PD-L1, programmed death-ligand 1; pem, pemetrexed; plat, platinum; RECIST, Response Evaluation Criteria in Solid Tumours; TPS, tumour proportion score.

1. Garassino MC, *et al. J Clin Oncol* 2023;41:1992–1998.

KEYNOTE-189: DOR and DCR in the ITT population (original analysis)*[1,2]

Median follow-up: 10.5 months.

Best response and DOR

Best response,† n (%)	KEYTRUDA–plat–pem (n=410)	Placebo–plat–pem (n=206)
CR	2 (0.5)	1 (0.5)
PR	193 (47.1)	38 (18.4)
SD	152 (37.1)	106 (51.5)
PD	36 (8.8)	36 (17.5)
DOR, months	**KEYTRUDA–plat–pem (n=195)**	**Placebo–plat–pem (n=39)**
Median	11.2	7.8
Range‡	1.1+ to 18.0+	2.1+ to 16.4+
	KEYTRUDA–plat–pem	**Placebo–plat–pem**
DCR, %§	84.6	70.4

Adapted from Gandhi L, *et al.* 2018 & Gandhi L, *et al.* 2018.[1,2]

Data cut-off date: 8 November 2017.

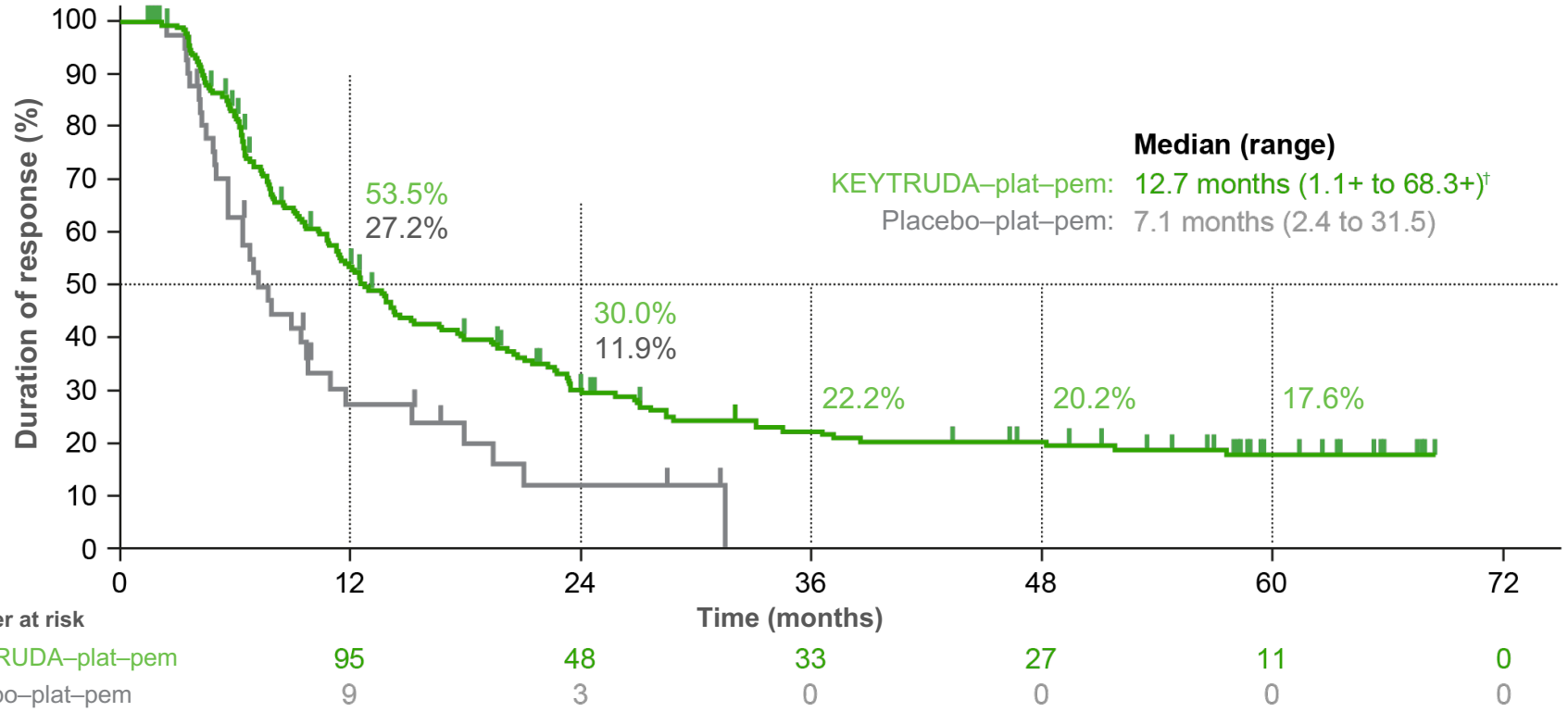
*Assessed using RECIST by blinded, independent, central radiological review.[1] †An additional 27 (6.6%) patients in the KEYTRUDA + platinum + pemetrexed arm and 25 (12.1%) in the placebo + platinum + pemetrexed arm did not have ≥2 evaluable sets of radiographic images.[2] ‡+ denotes a response that was ongoing at the analysis cut-off date.[2] §The proportion of patients with a confirmed complete or partial response or stable disease.[1]

CR, complete response; DCR, disease control rate; DOR, duration of response; ITT, intent-to-treat; PD, progressive disease; pem, pemetrexed; plat, platinum; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours; SD, stable disease.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092 (and supplementary appendix). **2.** Gandhi L, *et al.* AACR. 14–18 April 2018. Chicago, USA.

KEYNOTE-189: Exploratory analysis – DOR in the ITT population (5-year update)*[1]

Median follow-up: 64.6 months. No statistical conclusions can be drawn from this analysis.



Adapted from Garassino MC, *et al.* 2023.[1]

Data cut-off date: 6 March 2022.
*Kaplan-Meier estimate.[1] †+ denotes a response that was ongoing at the analysis cut-off date.[1]
DOR, duration of response; ITT, intent-to-treat; pem, pemetrexed; plat, platinum.
1. Garassino MC, *et al. J Clin Oncol* 2023;41:1992–1998.

KEYNOTE-189: Exploratory analysis – DOR by PD-L1 TPS (5-year update)*[1]

Median follow-up: 64.6 months. No statistical conclusions can be drawn from this analysis.

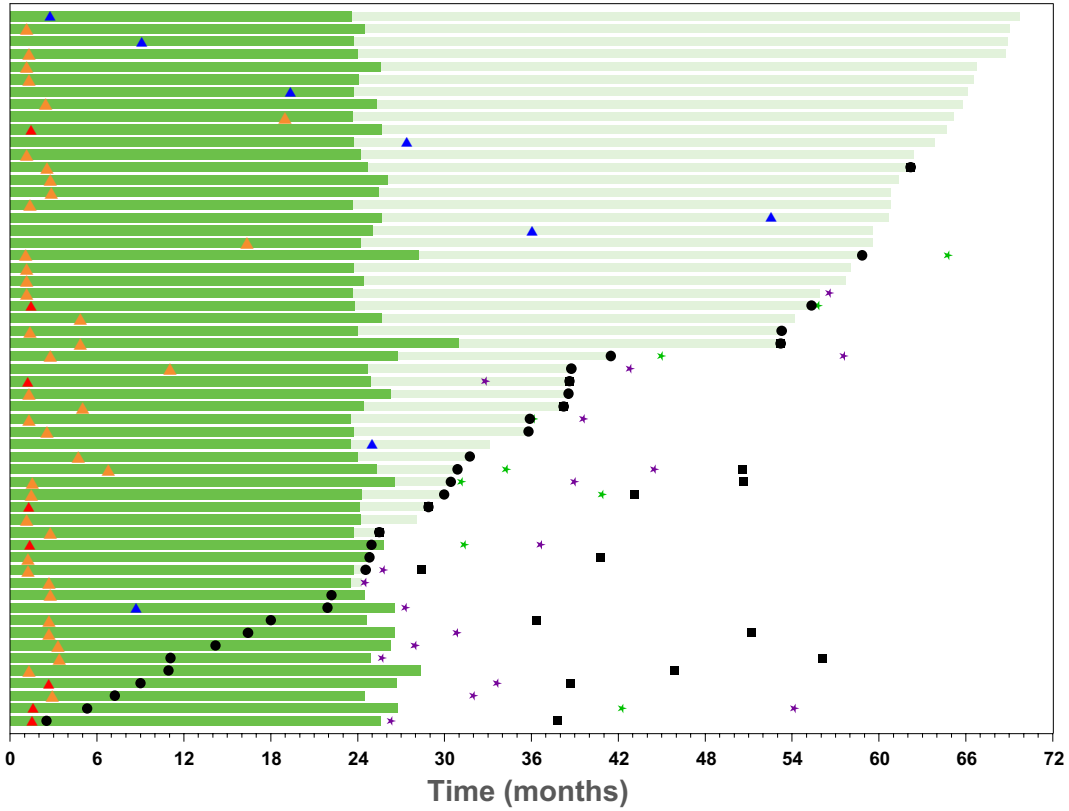
	PD-L1 TPS ≥50%		PD-L1 TPS 1%-49%		PD-L1 TPS <1%	
	KEYTRUDA–plat–pem	Placebo–plat–pem	KEYTRUDA–plat–pem	Placebo–plat–pem	KEYTRUDA–plat–pem	Placebo–plat–pem
DOR Median (range), months†	15.3 (1.2+ to 68.3+)	7.1 (3.4 to 31.5)	13.6 (2.1+ to 67.6+)	7.6 (2.4 to 31.0+)	10.8 (1.1+ to 59.4+)	7.8 (4.1 to 28.3+)

Adapted from Garassino MC, *et al.* 2023.[1]

Data cut-off date: 8 March 2022.
*Kaplan-Meier estimate.[1] †+ denotes a response that was ongoing at the analysis cut-off date.[1]
DOR, duration of response; PD-L1, programmed death-ligand 1; pem, pemetrexed; plat, platinum; TPS, tumour proportion score.
1. Garassino MC, *et al. J Clin Oncol* 2023;41:1992–1998.

KEYNOTE-189: Exploratory analysis – outcomes in patients who completed 35 cycles of KEYTRUDA (5-year update)[1,2]

Median follow-up: 56.9 months. No statistical conclusions can be drawn from this analysis.



	(n=57)
ORR (95% CI),* %	86.0 (74.2–93.7)
Best overall response, n (%)	
CR	8 (14.0)
PR	41 (71.9)
Median DOR (range),† months	57.7 (4.2 to 68.3+)
3-year OS rate after completing 35 cycles‡	71.9%
Alive without PD or subsequent therapy, n (%)	23 (40.4)

Adapted from Garassino MC, *et al.* 2023.[1]

Data cut-off date: 8 March 2022.

*Assessed using RECIST by blinded, independent, central radiological review.[1] †Kaplan-Meier estimate.[1] ‡Approximately 5 years after randomisation.[1]

CI, confidence interval; CR, complete response; DOR, duration of response; ORR, objective response rate; OS, overall survival; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours; SD, stable disease.

1. Garassino MC, *et al. J Clin Oncol* 2023;41:1992–1998; **2.** Garassino MC, *et al.* ESMO. 9–13 September 2022. Paris, France.

KEYNOTE-189: Exposure to study treatment in the as-treated population (original analysis)[1,2]

Median follow-up: 10.5 months.

	KEYTRUDA–plat–pem (n=405)	Placebo–plat–pem (n=202)
Treatment duration, mean (± SD), months	7.4 (4.7)	5.4 (4.3)
Treatment cycles, n		
Mean (± SD)	10.9 (6.4)	8.1 (5.7)
Median (range)	10.0 (1–30)	7 (1–26)
4 cycles of platinum, n (%)	334 (82.5)	150 (74.3)
≥5 cycles of pemetrexed, n (%)	310 (76.5)	135 (66.8)
≥5 cycles of KEYTRUDA or placebo, n (%)	320 (79.0)	138 (68.3)

Adapted from Gandhi L, *et al.* 2018 & Gandhi L, *et al.* 2018.[1,2]

Data cut-off date: 8 November 2017.
Pem, pemetrexed; plat, platinum; SD, standard deviation.
1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092. **2.** Gandhi L, *et al.* AACR. 14–18 April 2018. Chicago, USA.

KEYNOTE-189: Summary of AEs in the as-treated population (original analysis)*[1]

Median follow-up: 10.5 months.

AE, n (%)	KEYTRUDA–plat–pem (n=405)	Placebo–plat–pem (n=202)
All causes	404 (99.8)	200 (99.0)
Grade 3–5†	272 (67.2)	133 (65.8)
Led to death	27 (6.7)	12 (5.9)
Led to discontinuation		
All treatment‡	56 (13.8)	16 (7.9)
Any treatment component	112 (27.7)	30 (14.9)
Immune-mediated§	92 (22.7)	24 (11.9)
Grade 3–5†	36 (8.9)	9 (4.5)
Led to death	3 (0.7)¶	0

Adapted from Gandhi L, *et al.* 2018.[1]

Data cut-off date: 8 November 2017.

*All patients who had undergone randomisation and received ≥1 dose of the assigned combination therapy. AEs that occurred during crossover from the placebo-combination group to KEYTRUDA monotherapy are excluded.[1] †AEs graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, Version 4.0.[1] ‡Includes patients who discontinued pemetrexed, a platinum-based drug and KEYTRUDA or placebo because of an AE at any time, and patients who discontinued pemetrexed and KEYTRUDA or placebo for an AE after completing 4 cycles of a platinum-based drug.[1] §Regardless of attribution to trial drug by the investigator.[1] ¶All deaths were due to pneumonitis.[1]

AE, adverse event; pem, pemetrexed; plat, platinum.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092.

KEYNOTE-189: Summary of AEs in the as-treated population (updated analysis)*[1]

Median follow-up: 23.1 months.

AE, n (%)	KEYTRUDA–plat–pem (n=405)	Placebo–plat–pem (n=202)
All causes	404 (99.8)	200 (99.0)
Grade 3–5	291 (71.9)	135 (66.8)
Led to death†	29 (7.2)	14 (6.9)
Led to discontinuation of any treatment component	136 (33.6)	33 (16.3)
Immune-mediated	107 (26.4)	26 (12.9)
Grade 3–5	44 (10.9)	9 (4.5)

Adapted from Gadgeel S, *et al.* 2020.[1]

Data cut-off date: 21 September 2018.

*Median (range) duration of exposure to originally allocated study treatment was 7.2 months (0.03–30.4) in the KEYTRUDA + platinum + pemetrexed arm and 4.2 months (0.03–25.0) in the placebo + platinum + pemetrexed arm.[2] †8 (2.0%) of patients in the KEYTRUDA + platinum + pemetrexed arm and 2 (1.0%) in the placebo + platinum + pemetrexed arm died from AEs attributed to study treatment by the investigator.[1]

AE, adverse event; pem, pemetrexed; plat, platinum.

1. Gadgeel S, *et al. J Clin Oncol* 2020;38:1505–1517. **2.** Gadgeel S, *et al.* ASCO. 31 May – 4 June 2019. Chicago, USA.

KEYNOTE-189: Summary of AEs in the as-treated population (5-year update)[1,2]

Median follow-up: 64.6 months.

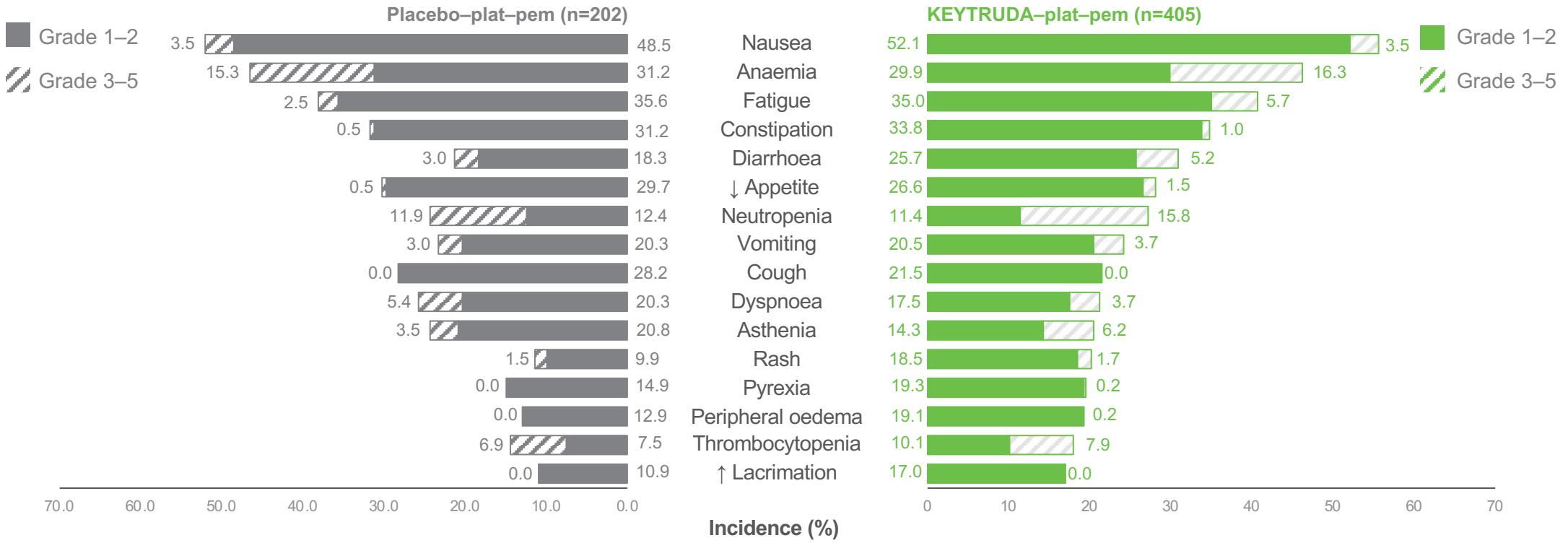
AE, n (%)	All treated patients		35 cycles of KEYTRUDA (n=57)
	KEYTRUDA–plat–pem (n=405)	Placebo–plat–pem (n=202)	
Any	404 (99.8)	200 (99.0)	57 (100)
Grade 3–5	295 (72.8)	136 (67.3)	38 (66.7)
Led to discontinuation of any treatment component	145 (35.8)	35 (17.3)	19 (33.3)
Led to death*	29 (7.2)	14 (6.9)	0
Treatment-related AE	377 (93.1)	183 (90.6)	56 (98.2)
Grade 3–5	212 (52.3)	85 (42.1)	27 (47.4)
Immune-mediated AEs and infusion reactions†	113 (27.9)	27 (13.4)	23 (40.4)
Grade 3–5	52 (12.8)	9 (4.5)	7 (12.3)

Adapted from Garassino MC, *et al*. 2023 & Garassino MC, *et al.* 2022.[1,2]

Data cut-off date: March 8 2022.
*All deaths were previously reported in Rodriguez-Abreu D *et al. Ann Oncol* 2021;32:881-895.[1] †Events considered regardless of attribution to treatment or immune relatedness by the investigator.[1]
AE, adverse event; pem, pemetrexed; plat, platinum.
1. Garassino MC, *et al. J Clin Oncol* 2023;41:1992–1998. **2.** Garassino MC, *et al.* ESMO. 9–13 September 2022. Paris, France.

KEYNOTE-189: All-cause AEs occurring in ≥15% of patients in the as-treated population (original analysis)*†[1]

Median follow-up: 10.5 months.



Adapted from Gandhi L, *et al.* 2018.[1]

Data cut-off date: 8 November 2017.

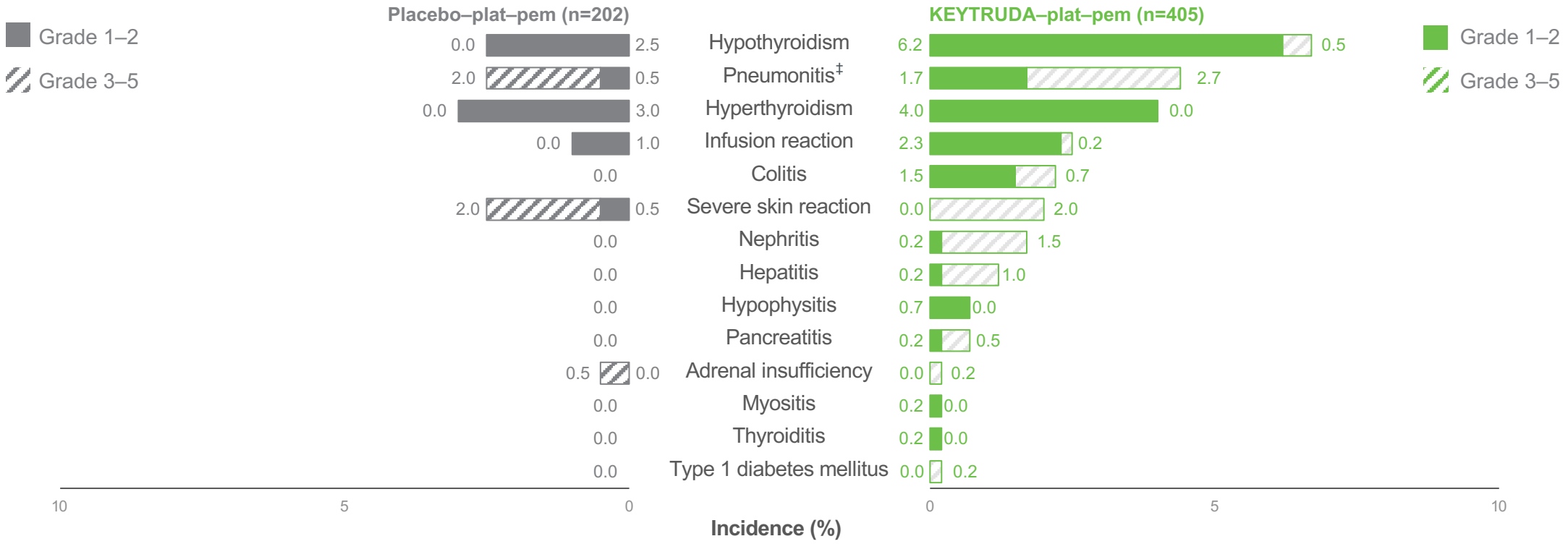
*AEs that occurred during crossover from the placebo-combination group to KEYTRUDA monotherapy are excluded.[1] †AEs were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, Version 4.0.[1]

AE, adverse event; pem, pemetrexed; plat, platinum.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092.

KEYNOTE-189: Immune-mediated AEs in the as-treated population (original analysis)*†[1]

Median follow-up: 10.5 months.



Adapted from Gandhi L, *et al.* 2018.[1]

Data cut-off date: 8 November 2017.

*Regardless of attribution to a trial drug by the investigator.[1] †AEs were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, Version 4.0.[1] ‡Includes three Grade 5 AEs in the KEYTRUDA group.[1]

AE, adverse event; pem, pemetrexed; plat, platinum.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092.

KEYNOTE-189: Renal events (original analysis)[1,2]

Median follow-up: 10.5 months.

Acute kidney injury

- Frequency: 5.2% (n=21) vs 0.5% (n=1) in the KEYTRUDA–plat–pem vs placebo–plat–pem arms, respectively
  - Grade 3–5 frequency:* 2.0% (n=8) vs 0%, respectively
  - Grade 5 frequency: 0.5% (n=2) with KEYTRUDA–plat–pem
- Grade ≤3 acute kidney injury had resolved or was resolving in 47% (9/19) of patients at the analysis cut-off date

Nephritis†‡

- Any-grade frequency: 1.7% (n=7) vs 0% in the KEYTRUDA–plat–pem vs placebo–plat–pem arms, respectively
  - Grade 3–5 frequency: 1.5% (n=6) vs 0%, respectively
  - Grade 5 frequency: 0%

Data cut-off date: 8 November 2017.

*Led to discontinuation of all trial therapy in all eight patients in the KEYTRUDA combination group.[1] †Includes preferred terms of autoimmune nephritis, nephritis and tubulointerstitial nephritis.[2] ‡Nephritis occurred in carboplatin-treated patients only.[1]

Pem, pemetrexed; plat, platinum.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092 (and supplementary appendix). **2.** Gandhi L, *et al.* AACR. 14–18 April 2018. Chicago, USA.

KEYNOTE-189: Post hoc analysis – evaluation of outcomes in patients with baseline brain and liver metastases*

Median follow-up: 18.7 months. No statistical conclusions can be drawn from this exploratory analysis.

- Extrapulmonary metastases to sites such as the liver and brain frequently occur in metastatic NSCLC and can be associated with a poor prognosis[1]
- Objective of current analysis: retrospectively evaluate outcomes among patients with baseline liver or brain metastases[2]
- Results were not controlled for multiplicity. The cut-off date for this analysis was 21 September 2018; median follow-up was 18.7 months (range: 0.2–30.9 months)[2]

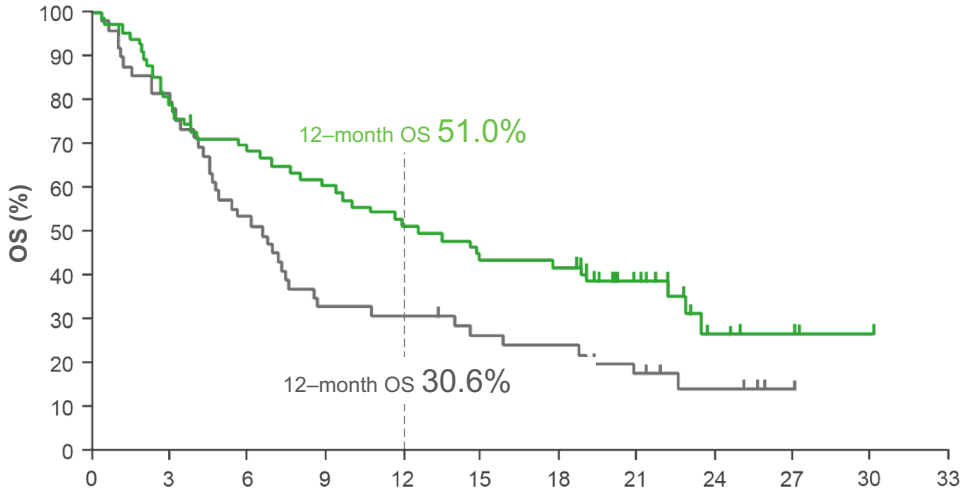
Data cut-off date: 21 September 2018.
*No other data was reported with this analysis.
NSCLC, non-small cell lung cancer.
1. Gibson AJW *et al. Med Oncol* 2018;35:117. **2.** Garassino MC, *et al.* AACR. 29 March – 18 April 2019. Atlanta, USA.

KEYNOTE-189: Post hoc analysis – OS in patients with liver metastases*†[1]

Median follow-up: 18.7 months. No statistical conclusions can be drawn from this exploratory analysis.

Patients with liver metastases

Treatment arm	Events, n (%)	Median, months (95% CI)	HR (95% CI)
KEYTRUDA–plat–pem	43 (65.2)	12.6 (8.1–19.1)	0.62 (0.39–0.98)
Placebo–plat–pem	41 (83.7)	6.6 (4.6–7.6)	–

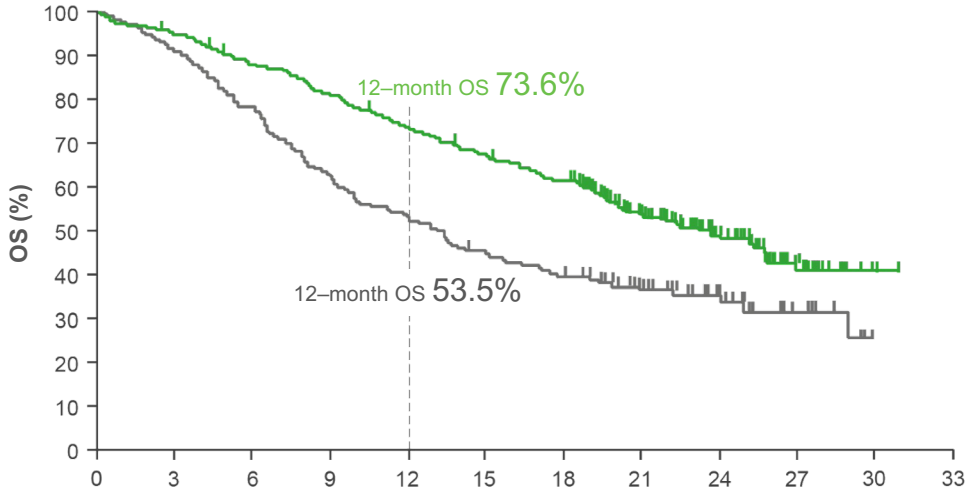


Number at risk

KEYTRUDA–plat–pem	66	52	45	39	33	28	27	16	5	2	1	0
Placebo–plat–pem	49	40	26	16	15	12	11	7	4	0	0	0

Patients without liver metastases

Treatment arm	Events, n (%)	Median, months (95% CI)	HR (95% CI)
KEYTRUDA–plat–pem	170 (49.4)	23.7 (20.1–25.9)	0.58 (0.45–0.74)
Placebo–plat–pem	103 (65.6)	13.2 (10.0–16.4)	–



Number at risk

KEYTRUDA–plat–pem	344	325	301	277	250	228	207	128	74	26	1	0
Placebo–plat–pem	157	143	123	99	84	70	61	38	22	10	0	0

Adapted from Garassino MC, *et al.* 2019.[1]

Data cut-off date: 21 September 2018.

*No other data was reported with this analysis.[1] †Patients with liver metastases at baseline: 66 (16%) and 49 (24%) in the KEYTRUDA + platinum chemotherapy + pemetrexed and placebo + platinum chemotherapy + pemetrexed, respectively. 25 patients had both liver and brain metastases.[1]

CI, confidence interval; HR, hazard ratio; OS, overall survival; pem, pemetrexed; plat, platinum.

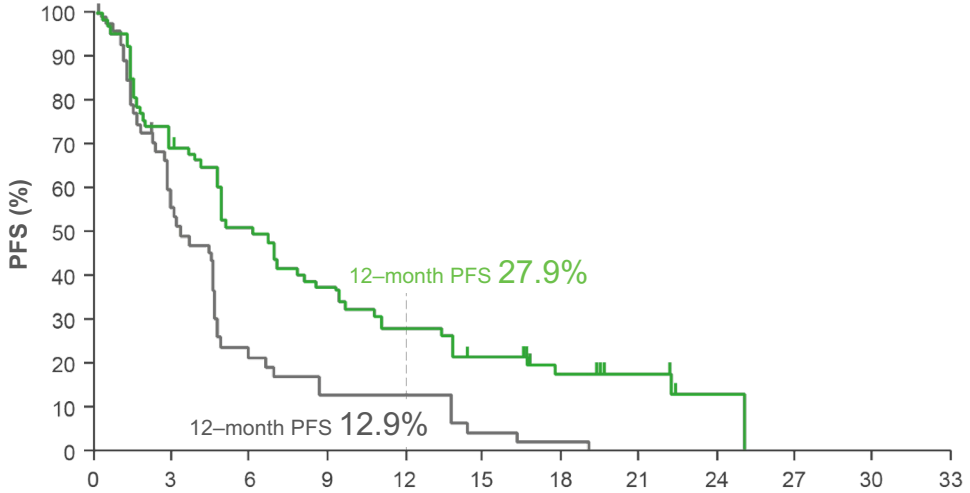
1. Garassino MC, *et al.* AACR. 29 March – 18 April 2019. Atlanta, USA.

KEYNOTE-189: Post hoc analysis – PFS in patients with liver metastases*†‡[1]

Median follow-up: 18.7 months. No statistical conclusions can be drawn from this exploratory analysis.

Patients with liver metastases

Treatment arm	Events, n (%)	Median, months (95% CI)	HR (95% CI)
KEYTRUDA–plat–pem	55 (83.3)	6.1 (4.7–8.5)	0.52 (0.34–0.81)
Placebo–plat–pem	47 (95.9)	3.4 (2.8–4.7)	–

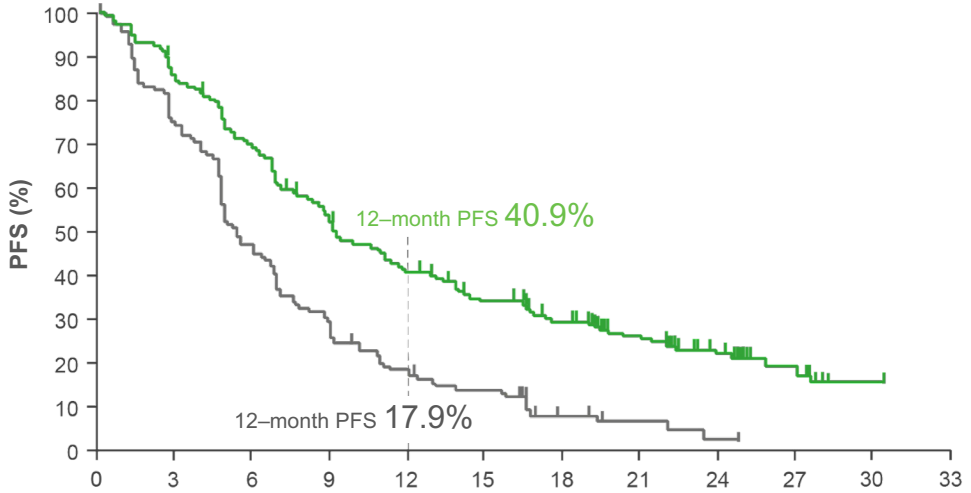


Number at risk

KEYTRUDA–plat–pem	66	45	33	24	18	13	9	5	1	0	0	0
Placebo–plat–pem	49	26	10	6	6	2	1	0	0	0	0	0

Patients without liver metastases

Treatment arm	Events, n (%)	Median, months (95% CI)	HR (95% CI)
KEYTRUDA–plat–pem	249 (72.4)	9.2 (8.8–11.0)	0.48 (0.39–0.59)
Placebo–plat–pem	143 (91.1)	5.4 (4.9–6.7)	–



Number at risk

KEYTRUDA–plat–pem	344	283	233	173	131	106	82	49	27	10	1	0
Placebo–plat–pem	157	116	71	44	25	18	7	3	1	0	0	0

Adapted from Garassino MC, *et al.* 2019.[1]

Data cut-off date: 21 September 2018.

*No other data was reported with this analysis.[1] †Assessed using RECIST by blinded, independent, central radiological review.[1] ‡Patients with liver metastases at baseline: 66 (16%) and 49 (24%) in the KEYTRUDA + platinum chemotherapy + pemetrexed and placebo + platinum chemotherapy + pemetrexed, respectively. 25 patients had both liver and brain metastases.[1]

CI, confidence interval; HR, hazard ratio; pem, pemetrexed; PFS, progression-free survival; plat, platinum; RECIST, Response Evaluation Criteria in Solid Tumours.

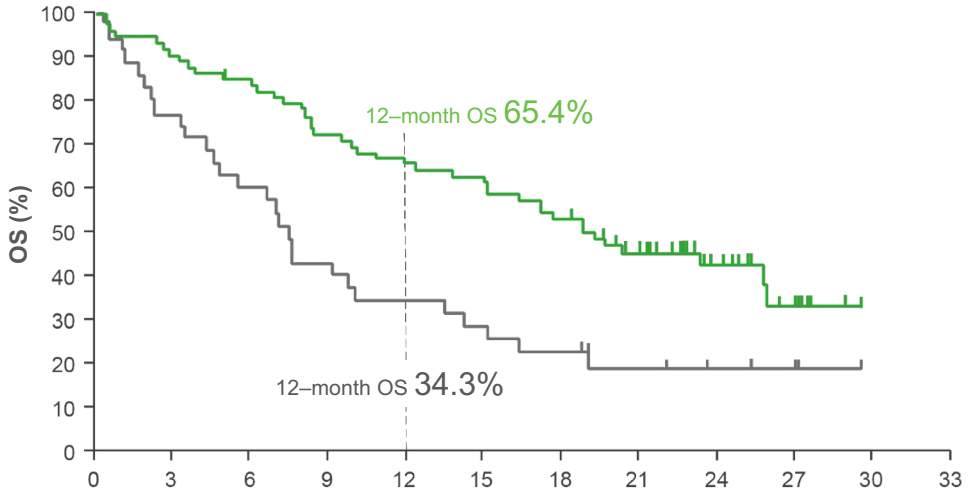
1. Garassino MC, *et al.* AACR. 29 March – 18 April 2019. Atlanta, USA.

KEYNOTE-189: Post hoc analysis – OS in patients with brain metastases*†[1]

Median follow-up: 18.7 months. No statistical conclusions can be drawn from this exploratory analysis.

Patients with brain metastases

Treatment arm	Events, n (%)	Median, months (95% CI)	HR (95% CI)
KEYTRUDA–plat–pem	42 (57.5)	19.2 (15.0–25.9)	0.41 (0.24–0.67)
Placebo–plat–pem	28 (80.0)	7.5 (4.6–10.0)	–

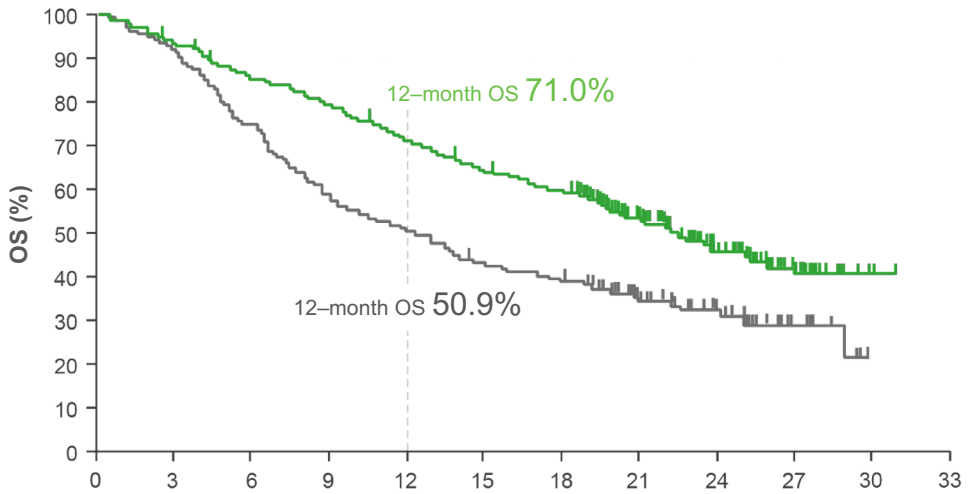


Number at risk

KEYTRUDA–plat–pem	73	66	61	52	47	45	38	25	14	5	0	0
Placebo–plat–pem	35	27	21	15	12	10	8	5	3	1	0	0

Patients without brain metastases

Treatment arm	Events, n (%)	Median, months (95% CI)	HR (95% CI)
KEYTRUDA–plat–pem	171 (50.7)	22.4 (19.7–25.4)	0.59 (0.46–0.75)
Placebo–plat–pem	116 (67.8)	12.1 (9.1–15.0)	–



Number at risk

KEYTRUDA–plat–pem	337	311	285	264	236	211	196	119	65	23	2	0
Placebo–plat–pem	171	156	128	100	87	72	64	40	23	9	0	0

Adapted from Garassino MC, *et al.* 2019.[1]

Data cut-off date: 21 September 2018.

*No other data was reported with this analysis.[1] †Patients with stable brain metastases at baseline: 73 (18%) and 35 (17%) in the KEYTRUDA + platinum chemotherapy + pemetrexed and placebo + platinum chemotherapy + pemetrexed, respectively. 25 patients had both liver and brain metastases.[1]

CI, confidence interval; HR, hazard ratio; OS, overall survival; pem, pemetrexed; plat, platinum.

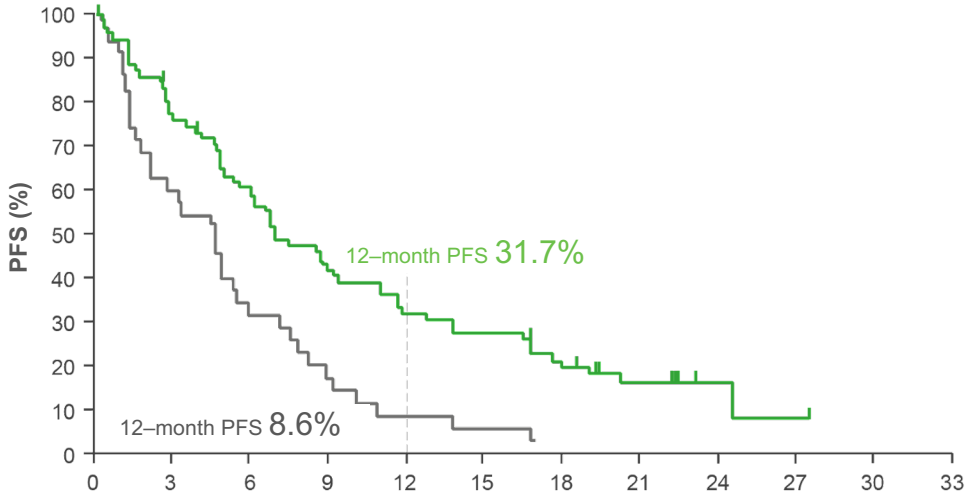
1. Garassino MC, *et al.* AACR. 29 March – 18 April 2019. Atlanta, USA.

KEYNOTE-189: Post hoc analysis – PFS in patients with brain metastases*†‡[1]

Median follow-up: 18.7 months. No statistical conclusions can be drawn from this exploratory analysis.

Patients with brain metastases

Treatment arm	Events, n (%)	Median, months (95% CI)	HR (95% CI)
KEYTRUDA–plat–pem	59 (80.8)	6.9 (5.4–11.0)	0.42 (0.27–0.67)
Placebo–plat–pem	34 (97.1)	4.7 (2.2–5.5)	–

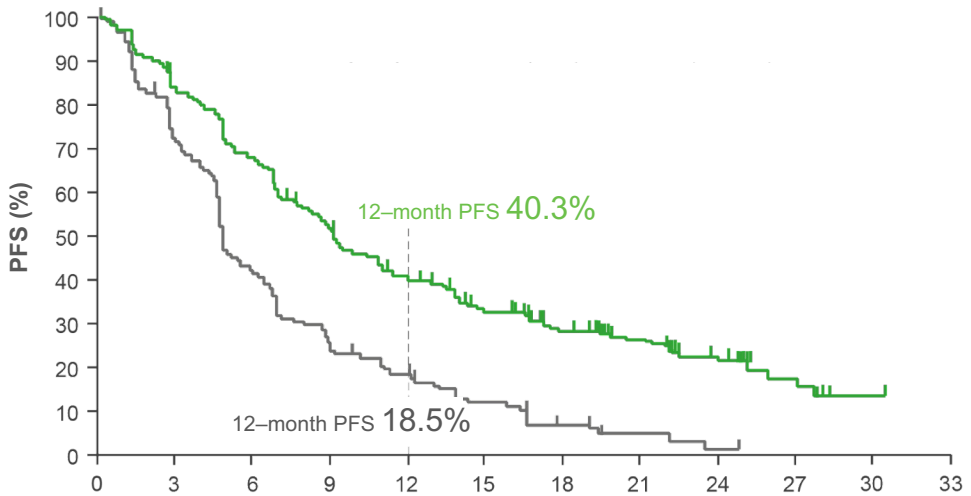


Number at risk

KEYTRUDA–plat–pem	73	55	42	29	22	19	14	7	2	1	0	0
Placebo–plat–pem	35	21	11	6	3	2	0	0	0	0	0	0

Patients without brain metastases

Treatment arm	Events, n (%)	Median, months (95% CI)	HR (95% CI)
KEYTRUDA–plat–pem	245 (72.7)	9.2 (8.3–10.9)	0.48 (0.39–0.59)
Placebo–plat–pem	156 (91.2)	4.9 (4.7–5.9)	–



Number at risk

KEYTRUDA–plat–pem	337	273	224	168	127	100	77	47	26	9	1	0
Placebo–plat–pem	171	121	70	44	28	18	8	3	1	0	0	0

Adapted from Garassino MC, *et al.* 2019.[1]

Data cut-off date: 21 September 2018.

*No other data was reported with this analysis.[1] †Assessed using RECIST by blinded, independent, central radiological review.[1] ‡Patients with stable brain metastases at baseline: 73 (18%) and 35 (17%) in the KEYTRUDA + platinum chemotherapy + pemetrexed and placebo + platinum chemotherapy + pemetrexed, respectively. 25 patients had both liver and brain metastases.[1]

CI, confidence interval; HR, hazard ratio; pem, pemetrexed; PFS, progression-free survival; plat, platinum; RECIST, Response Evaluation Criteria in Solid Tumours.

1. Garassino MC, *et al.* AACR. 29 March – 18 April 2019. Atlanta, USA.

KEYNOTE-189: Exploratory endpoint – QLQ-C30 completion and compliance rates*†[1]

Median follow-up: 10.5 months. No statistical conclusions can be drawn from exploratory endpoints.

		KEYTRUDA–plat–pem (n=402) n (%) or n/N (%)	Placebo–plat–pem (n=200) n (%) or n/N (%)
Baseline		359 (89%)	180 (90%)
Week 3	Completion Compliance	362 (90%) 362/389 (93%)	171 (86%) 171/186 (92%)
Week 6	Completion Compliance	342 (85%) 342/360 (95%)	154 (77%) 154/175 (88%)
Week 9	Completion Compliance	308 (77%) 308/342 (90%)	140 (70%) 140/156 (89%)
Week 12	Completion Compliance	319 (79%) 319/354 (90%)	149 (75%) 149/167 (89%)
Week 21	Completion Compliance	249 (62%) 249/326 (76%)	91 (46%) 91/143 (64%)
Week 30	Completion Compliance	210 (52%) 210/278 (76%)	63 (32%) 63/88 (72%)

Adapted from Garassino MC, *et al.* 2020.[1]

Data cut-off date: 8 November 2017.

*Completion was defined as completing at least one item among the total patient-reported outcome analysis population.[1] †Compliance was defined as completing at least one item at each timepoint, as listed in the numerator for each group, among patients who were expected to complete at each timepoint (e.g. among those who had not discontinued study treatment), as listed in the denominator for each group.[1]

Pem, pemetrexed; plat, platinum; QLQ-C30, Quality of Life Questionnaire Core 30.

1. Garassino MC, *et al. Lancet Oncol* 2020;21:387–397.

KEYNOTE-189: Exploratory endpoint – QLQ-LC13 completion and compliance rates*†[1]

Median follow-up: 10.5 months. No statistical conclusions can be drawn from exploratory endpoints.

		KEYTRUDA–plat–pem (n=402) n (%) or n/N (%)	Placebo–plat–pem (n=200) n (%) or n/N (%)
Baseline		357 (89%)	179 (90%)
Week 3	Completion Compliance	361 (90%) 361/389 (93%)	170 (85%) 170/186 (91%)
Week 6	Completion Compliance	341 (85%) 341/360 (95%)	153 (77%) 153/175 (87%)
Week 9	Completion Compliance	306 (76%) 306/341 (90%)	140 (70%) 140/158 (89%)
Week 12	Completion Compliance	317 (79%) 317/354 (90%)	148 (74%) 148/167 (89%)
Week 21	Completion Compliance	245 (61%) 245/326 (75%)	90 (45%) 90/143 (63%)
Week 30	Completion Compliance	211 (53%) 211/278 (76%)	63 (32%) 63/88 (72%)

Adapted from Garassino MC, *et al.* 2020.[1]

Data cut-off date: 8 November 2017.

*Completion was defined as completing at least one item among the total patient-reported outcome analysis population.[1] †Compliance was defined as completing at least one item at each timepoint, as listed in the numerator for each group, among patients who were expected to complete at each timepoint (e.g. among those who had not discontinued study treatment), as listed in the denominator for each group.[1]

Pem, pemetrexed; plat, platinum; QLQ-LC13, Quality of Life Questionnaire Lung Cancer 13.

1. Garassino MC, *et al. Lancet Oncol* 2020;21:387–397.

KEYNOTE-189: Exploratory endpoint – EORTC QLQ-C30 GHS[1]

Median follow-up: 10.5 months. No statistical conclusions can be drawn from exploratory endpoints.

	KEYTRUDA–plat–pem (n=402)	Placebo–plat–pem (n=200)
Baseline, mean (SD)	n=359* 62.0 (21.3)	n=180* 60.6 (21.4)
Week 12, mean (SD)	n=319* 63.8 (21.5)	n=150* 61.1 (20.8)
Change from baseline to Week 12, LS mean (95% CI)†	n=402‡ 1.0 (−1.3 to 3.2)	n=200‡ −2.6 (−5.8 to 0.5)
Difference in LS mean between treatment groups (95% CI)†	3.6 (−0.1 to 7.2) p=0.053	
Week 21, mean (SD)	n=248* 67.0 (19.4)	n=91* 62.6 (24.1)
Change from baseline to Week 21, LS mean (95% CI)†	n=402‡ 1.3 (−1.2 to 3.6)	n=200‡ −4.0 (−7.7 to −0.3)
Difference in LS mean between treatment groups (95% CI)	5.3 (1.1 to 9.5) p=0.014§	

Adapted from Garassino MC, *et al.* 2020.[1]

Data cut-off date: 8 November 2017.

*Number of patients who completed EORTC QLQ-C30 GHS/QoL at the noted timepoint.[1] †Based on cLDA model with EORTC QLQ-C30 GHS/QoL scores as response variable, treatment by study visit interaction and stratification factors for randomisation as covariates.[1] ‡Number of patients in analysis population.[1] §P values are 2-sided and nominal.[1]

CI, confidence interval; cLDA, constrained longitudinal data analysis; EORTC, European Organisation for Research and Treatment of Cancer; GHS, global health status; LS, least squares; pem, pemetrexed; plat, platinum; QLQ-C30, Quality of Life Questionnaire Core 30; QoL, quality of life; SD, standard deviation.

1. Garassino MC, *et al. Lancet Oncol* 2020;21:387–397.

KEYNOTE-189: Exploratory endpoint – QLQ-C30 GHS/QoL and functional and symptom subscales[1]

Median follow-up: 10.5 months. No statistical conclusions can be drawn from exploratory endpoints.

Mean QLQ-C30 GHS/QoL scores:

- Improved from baseline to Week 9 in both the KEYTRUDA–plat–pem and placebo–plat–pem groups
- Deteriorated in both groups from Week 9 onwards; however, scores in the KEYTRUDA–plat–pem group remained above baseline, whereas those in the placebo–plat–pem group did not

QLQ-C30 functional and symptom subscales:

- Were similar for both treatment groups across all domains at Week 12
- Mean score changes from baseline were generally better in the KEYTRUDA–plat–pem group than in the placebo–plat–pem group for most functional and symptom scales at Week 21
  - Symptom scale scores for dyspnoea and pain improved in the KEYTRUDA–plat–pem group and worsened/remained stable in the placebo–plat–pem group

Data cut-off date: 8 November 2017.

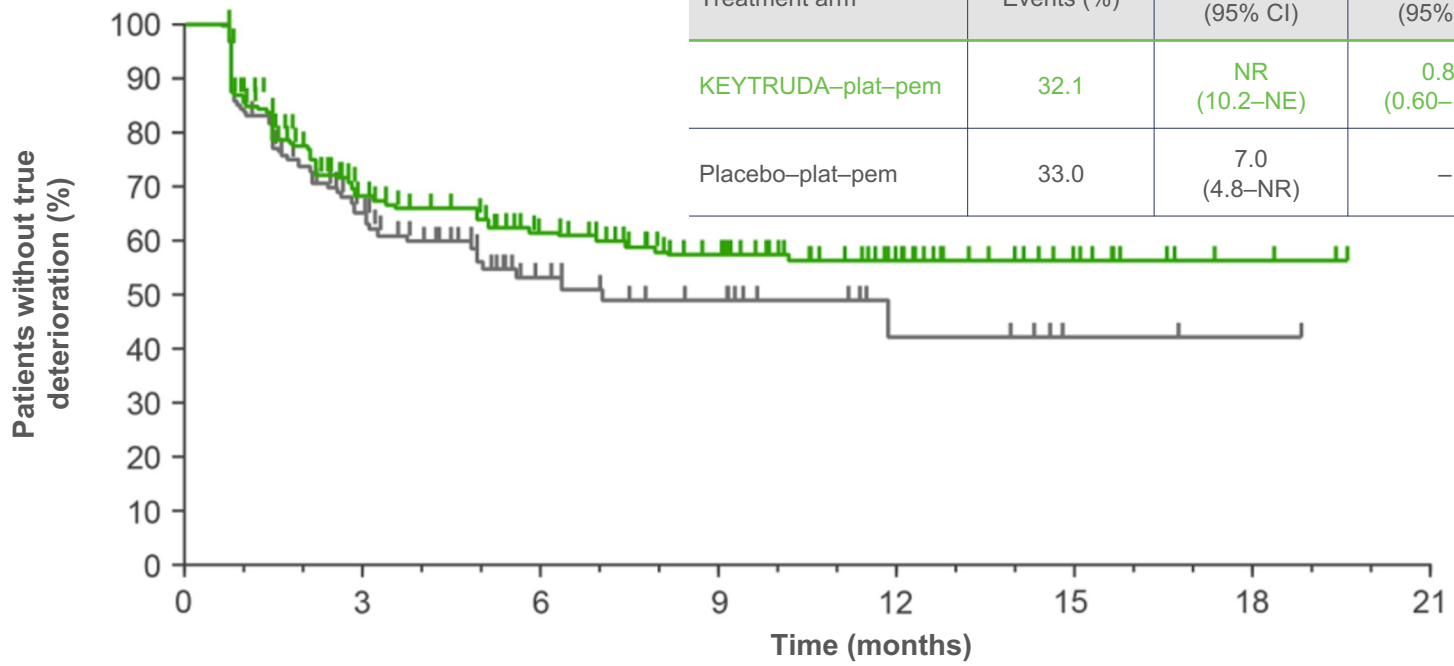
GHS, global health status; pem, pemetrexed; plat, platinum; QLQ-C30, Quality of Life Questionnaire Core 30.

1. Garassino MC, *et al. Lancet Oncol* 2020;21:387–397.

KEYNOTE-189: Exploratory endpoint – time to deterioration analysis
Composite endpoint of cough, chest pain and dyspnoea[1]

Median follow-up: 10.5 months. No statistical conclusions can be drawn from exploratory endpoints.

Treatment arm	Events (%)	Median, months (95% CI)	HR (95% CI)	P value
KEYTRUDA–plat–pem	32.1	NR (10.2–NE)	0.81 (0.60–1.09)	0.161
Placebo–plat–pem	33.0	7.0 (4.8–NR)	–	–



Number at risk								
KEYTRUDA–plat–pem	402	189	128	72	32	11	3	0
Placebo–plat–pem	200	68	29	17	6	2	1	0

Adapted from Garassino MC, *et al.* 2020.[1]

Data cut-off date: 8 November 2017.

*P value is 2-sided and nominal.[1] †Post-baseline assessments were not available for 56 patients in the KEYTRUDA–plat–pem group and for 33 patients in placebo–plat–pem group.[1]

CI, confidence interval; HR, hazard ratio; pem, pemetrexed; NE, not evaluable; NR, not reported; plat, platinum.

1. Garassino MC, *et al. Lancet Oncol* 2020;21:387–397.

KEYNOTE-189: Efficacy and safety summary

A key to more possibilities for appropriate patients with metastatic non-squamous NSCLC

Efficacy of KEYTRUDA in KEYNOTE-189[1,2]

- At IA1, KEYTRUDA + platinum chemotherapy + pemetrexed demonstrated a superior OS and PFS benefit vs placebo + platinum chemotherapy + pemetrexed (median follow-up: 10.5 months):[1]

51% reduced risk of death

HR: 0.49; 95% CI: 0.38–0.64; p<0.001 (dual primary endpoint, statistically significant)

48% reduced risk of progression

HR: 0.52; 95% CI: 0.43–0.64; p<0.001 (dual primary endpoint, statistically significant)

  - The treatment effect on OS was consistent across all PD-L1 subgroups, including PD-L1 TPS <1% and 1–49%*[1]
  - The treatment effect was consistent for OS and PFS in a post hoc analysis of patients with liver or brain metastases (median follow-up: 18.7 months)†[2]
  - Superior ORR (47.6% vs 18.9%, p<0.001) and improved DOR[1]

Safety profile of KEYTRUDA in KEYNOTE-189[1,2]

- At IA1, KEYTRUDA + platinum chemotherapy + pemetrexed displayed a generally manageable tolerability profile (median follow-up: 10.5 months)[1]
- The addition of KEYTRUDA did not appear to increase the frequency of AEs that are commonly associated with chemotherapy regimens involving pemetrexed and a platinum-based drug[1]
- The frequency of deaths due to pneumonitis in the KEYTRUDA + platinum chemotherapy + pemetrexed arm was consistent with the frequency previously observed with KEYTRUDA monotherapy in advanced NSCLC[1,4–6]
- No new safety signals were identified in the post hoc analysis for liver and brain metastases (median follow-up: 18.7 months)*[2]
- In the 5-year follow-up, toxicity was manageable, which was consistent with previous reports[3,7,8]

In the 5-year follow-up, treatment with KEYTRUDA + platinum chemotherapy + pemetrexed continued to demonstrate an OS and PFS benefit vs placebo + platinum chemotherapy + pemetrexed (median follow-up: 64.6 months; p not tested)[3]

- Benefits were observed despite an effective crossover rate of 57% from placebo + platinum chemotherapy + pemetrexed to subsequent anti-PD-L1 therapy during/outside study[3]
- OS and PFS benefits were seen irrespective of baseline PD-L1 expression[3]
- **Patients who received 35 cycles of KEYTRUDA (~2 years) had durable responses, with 72% patients alive at 3 years (~5 years from randomisation)**

*Exploratory endpoint – no statistical conclusions can be drawn.[1] †This analysis was post hoc and exploratory, and no statistical conclusions can be drawn.[2]

AE, adverse event; CI, confidence interval; DOR, duration of response; HR, hazard ratio; IA, interim analysis; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; TPS, tumour proportion score.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092. **2.** Garassino MC, *et al.* AACR. 29 March – 18 April 2019. Atlanta, USA. **3.** Garassino MC, *et al. J Clin Oncol* 2023;41:1992–1998. **4.** Reck M *et al. N Engl J Med* 2016;375:1823–1833. **5.** Herbst RS, *et al. Lancet* 2016;387:1540–1550. **6.** Garon EB *et al. N Engl J Med* 2015;372:2018–2028. **7.** Rodríguez-Abreu D, *et al. Ann Oncol* 2021;32:881–895. **8.** Gadgeel S, *et al. J Clin Oncol* 2020;38:1505–1517.

KEYNOTE-189: HRQoL summary

HRQoL was an exploratory endpoint. No statistical conclusions can be drawn.

HRQoL of KEYTRUDA in KEYNOTE-189[1]

- **At IA1,** KEYTRUDA + platinum chemotherapy + pemetrexed maintained or improved QoL (evaluated using the EORTC QLQ-C30) compared with placebo + platinum chemotherapy + pemetrexed in patients with previously untreated metastatic, non-squamous NSCLC without sensitising *EGFR* mutations or *ALK* translocations
  - At a median follow-up of 10.5 months, median time to true deterioration in the composite endpoint of increased cough, chest pain or dyspnoea was not reached among patients treated with KEYTRUDA + platinum chemotherapy + pemetrexed vs 7.0 months among those who received placebo + platinum chemotherapy + pemetrexed
  - These data complement the superior efficacy observed with KEYTRUDA + platinum chemotherapy + pemetrexed over placebo + platinum chemotherapy + pemetrexed in the KEYNOTE-189 study and support the use of KEYTRUDA + platinum chemotherapy + pemetrexed as first-line therapy for metastatic, non-squamous NSCLC

ALK, anaplastic lymphoma kinase; *EGFR*, epidermal growth factor receptor; EORTC, European Organisation for Research and Treatment of Cancer; HRQoL, health-related quality of life; IA, interim analysis; NSCLC, non-small cell lung cancer; QLQ-C30, Quality of Life Questionnaire Core 30; QoL, quality of life.

1. Garassino MC, *et al. Lancet Oncol* 2020;21:387–397.

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/smpc. Accessed: May 2026.

Post hoc exploratory pooled analysis (KEYNOTE-189, KEYNOTE-407)

5-year survival with KEYTRUDA plus chemotherapy for mNSCLC with PD-L1 TPS <1%[1]

mNSCLC, metastatic non-small cell lung cancer; PD-L1, programmed death-ligand 1; TPS, tumour proportion score.

1. Gadgeel S, *et al.* 5-year survival of pembrolizumab plus chemotherapy for metastatic NSCLC with PD-L1 tumor proportion score <1%. WCLC. 9–12 September 2023. Singapore.

KEYNOTE-189: KEYTRUDA

plus chemotherapy for the first-line treatment of metastatic, non-squamous, *EGFR/ALK*-wild-type NSCLC[1]

Skip ahead to KEYNOTE-407 ▶

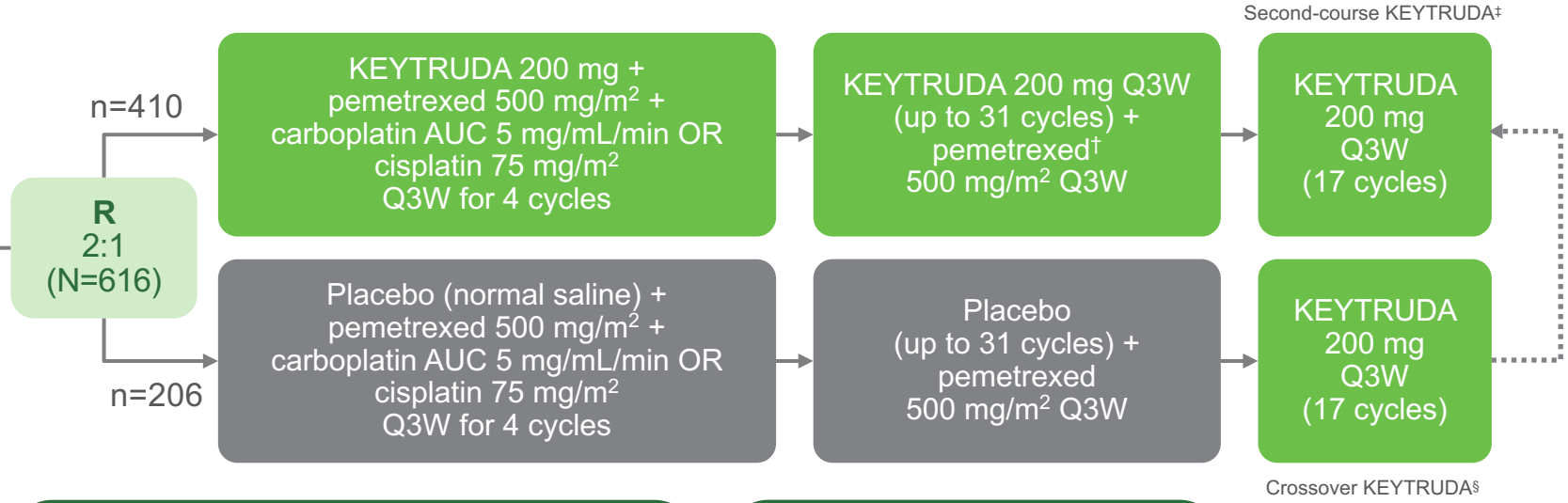
ALK, anaplastic lymphoma kinase; *EGFR*, epidermal growth factor receptor; NSCLC, non-small cell lung cancer.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092 (and supplementary appendix).

KEYNOTE-189 study design: Multicentre, randomised active-controlled, double-blind, Phase III trial[1–3]

Key eligibility criteria

- Untreated metastatic, non-squamous NSCLC
- No sensitising *EGFR* or *ALK* mutations
- ECOG PS 0 or 1
- Provision of a sample for PD-L1 assessment
- No symptomatic CNS metastases*
- No history of non-infectious pneumonitis requiring use of glucocorticoids, no active autoimmune disease and no systemic immunosuppressive treatment
- <30 Gy of RT to the lung in the previous 6 months



Stratification factors

- PD-L1 expression (TPS¶ ≥1% vs <1%)
- Platinum-based chemotherapy (cisplatin vs carboplatin)
- Smoking history (never vs former/current)

Endpoints

- Primary: OS, PFS‖
- Secondary: ORR, ‖ DOR, ‖ safety#
- Exploratory: Effect of PD-L1 expression on efficacy, PFS2, PROs

Adapted from Gandhi L, *et al.* 2018 & Gray JE, *et al.* 2020.[1,3]

*Patients were permitted to enrol if their brain lesions were previously treated, clinically stable for ≥2 weeks without evidence of new or enlarging lesions, and steroid-free for ≥3 days prior to receiving study treatment.[1] †Efficacy assessed in the ITT population.[1] ‡Patients who had SD or better after completing 35 cycles of KEYTRUDA or had stopped trial treatment after achieving CR and received ≥8 cycles of treatment, but then experienced PD, could receive second-course KEYTRUDA for 17 cycles if they had received no new anti-cancer treatment since the last dose of KEYTRUDA.[1] §To be eligible for crossover to KEYTRUDA monotherapy, PD had to have been verified by blinded, independent, central radiological review and all safety criteria had to have been met.[1] ¶Percentage of tumour cells with membrane PD-L1 staining, as assessed using the PD-L1 IHC 22C3 pharmDx assay.[1] ‖Assessed by blinded, independent central review per RECIST 1.1.[1] #Assessed in all patients who received ≥1 dose of study medication.[1]

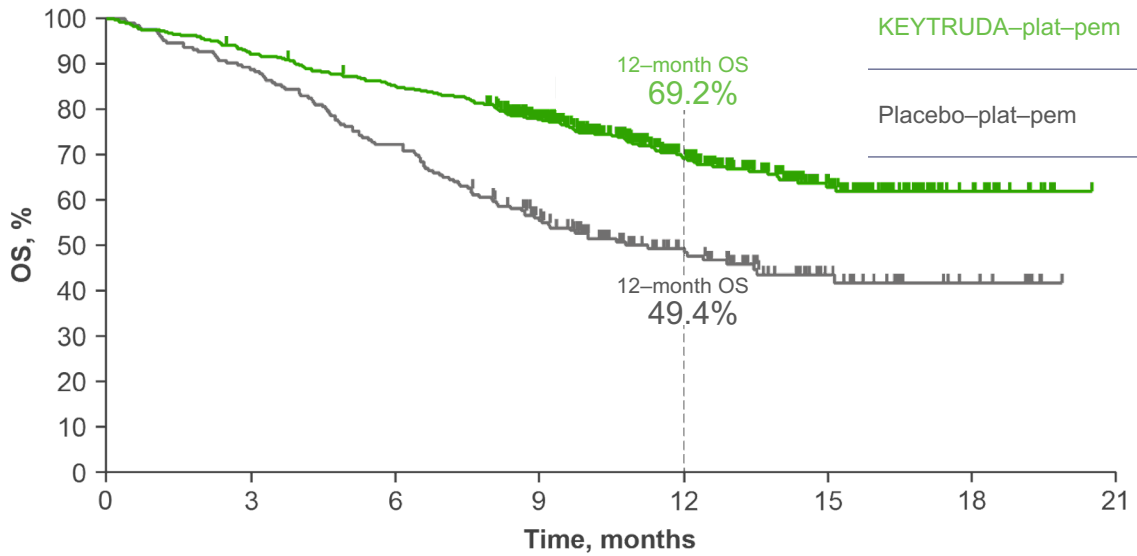
ALK, anaplastic lymphoma kinase; AUC, area under the curve; CNS; central nervous system; CR, complete response; DOR, duration of response; ECOG PS; Eastern Cooperative Oncology Group performance status; *EGFR,* epidermal growth factor receptor; IHC, immunohistochemistry; ITT, intention-to-treat; NSCLC, non-small cell lung carcinoma; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PFS2, progression after second-line therapy; PRO, patient-reported outcome; Q3W, every 3 weeks; R, randomisation; RECIST, (Response Evaluation Criteria in Solid Tumours; RT, radiotherapy; SD, stable disease; TPS, tumour proportion score.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092 (and protocol). **2.** Gandhi L, *et al.* AACR. 14–18 April 2018. Chicago, USA. **3.** Gray JE, *et al.* WCLC. 28–31 January 2021. Virtual.

KEYNOTE-189: 1-year landmark OS in the ITT population (original analysis)*†‡[1,2]

Median follow-up: 10.5 months.

	Events (%)	Median, months (95% CI)	HR (95% CI)	P value
KEYTRUDA–plat–pem	31.0	NR (NE–NE)	0.49 (0.38–0.64)	<0.001
Placebo–plat–pem	52.4	11.3 (8.7–15.1)	–	–



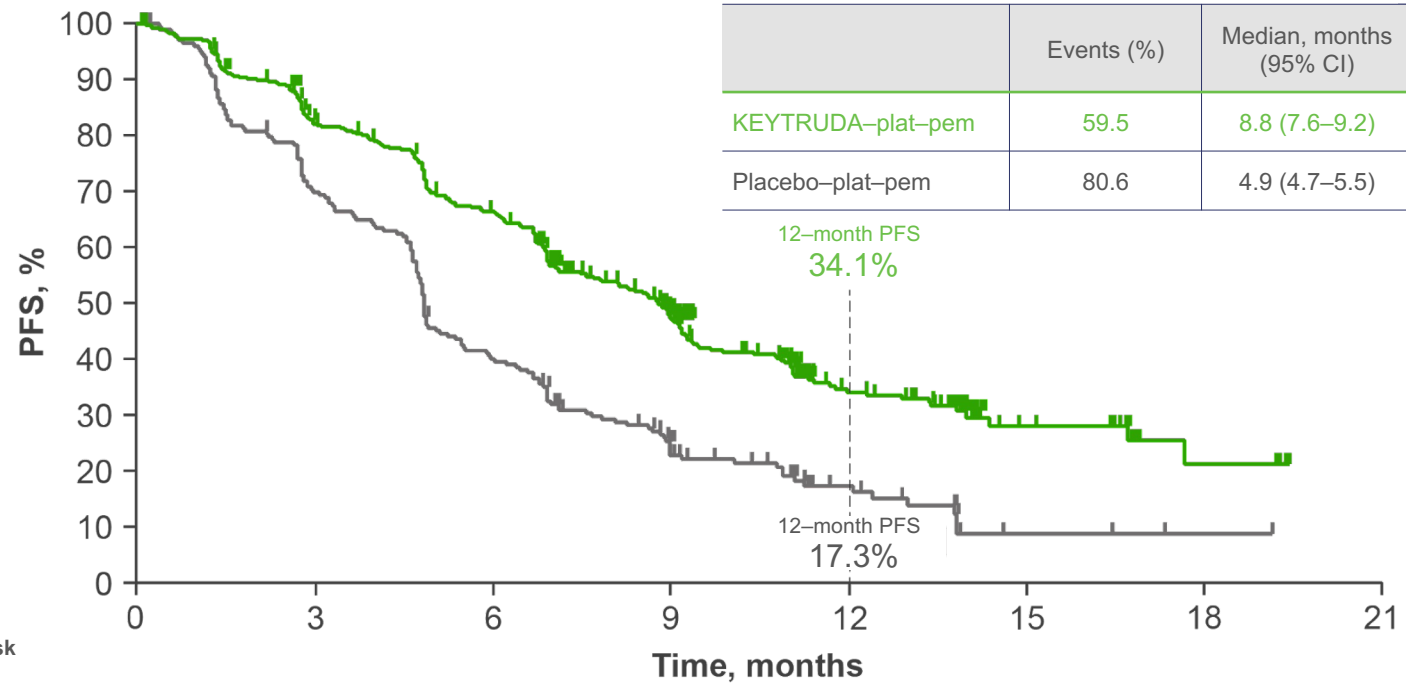
Adapted from Gandhi L, *et al.* 2018 & Gandhi L, *et al.* 2018.[1,2]

Data cut-off date: 8 November 2017.
*OS and PFS were both primary endpoints.[1] †Kaplan-Meier estimate.[1] ‡Overall alpha for study: strictly controlled at one-sided α=0.025, using the graphical method of Maurer and Bretz. The study had 90% power to show an HR of 0.70 for OS at one-sided α=0.0155 (based on 416 deaths) for the comparison between the KEYTRUDA and placebo combination groups. At IA1: one-sided α=0.00128 for OS.[1]
CI, confidence interval; HR, hazard ratio; IA, interim analysis; ITT, intent-to-treat; NE, not evaluable; NR, not reported; OS, overall survival; pem, pemetrexed; PFS, progression-free survival; plat, platinum.
1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092. **2.** Gandhi L, *et al.* AACR. 14–18 April 2018. Chicago, USA.

KEYNOTE-189: 1-year landmark PFS in the ITT population (original analysis)*†‡[1,2]

Median follow-up: 10.5 months.

	Events (%)	Median, months (95% CI)	HR (95% CI)	P value
KEYTRUDA–plat–pem	59.5	8.8 (7.6–9.2)	0.52 (0.43–0.64)	<0.001
Placebo–plat–pem	80.6	4.9 (4.7–5.5)	–	–



Adapted from Gandhi L, *et al.* 2018 & Gandhi L, *et al.* 2018.[1,2]

Data cut-off date: 8 November 2017.

*OS and PFS were both primary endpoints.[1] †Kaplan-Meier estimate.[1] ‡Assessed using RECIST by blinded, independent, central radiological review.[1] §Overall alpha for study: strictly controlled at one-sided α=0.025, using the graphical method of Maurer and Bretz. The study had 90% power to show an HR of 0.70 for PFS at one-sided α=0.0095 (based on 468 deaths) for the comparison between the KEYTRUDA and placebo combination groups. At IA1: one-sided α=0.00559 for PFS.[1]

CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; OS, overall survival; PD-L1, programmed death-ligand 1; pem, pemetrexed; PFS, progression-free survival; plat, platinum; RECIST, Response Evaluation Criteria in Solid Tumours; TPS, tumour proportion score.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092. **2.** Gandhi L, *et al.* AACR. 14–18 April 2018. Chicago, USA.

KEYNOTE-189: Summary of AEs in the as-treated population (original analysis)*[1]

Median follow-up: 10.5 months.

AE, n (%)	KEYTRUDA–plat–pem (n=405)	Placebo–plat–pem (n=202)
All causes	404 (99.8)	200 (99.0)
Grade 3–5†	272 (67.2)	133 (65.8)
Led to death	27 (6.7)	12 (5.9)
Led to discontinuation		
All treatment‡	56 (13.8)	16 (7.9)
Any treatment component	112 (27.7)	30 (14.9)
Immune-mediated§	92 (22.7)	24 (11.9)
Grade 3–5†	36 (8.9)	9 (4.5)
Led to death	3 (0.7)¶	0

Adapted from Gandhi L, *et al.* 2018.[1]

Data cut-off date: 8 November 2017.

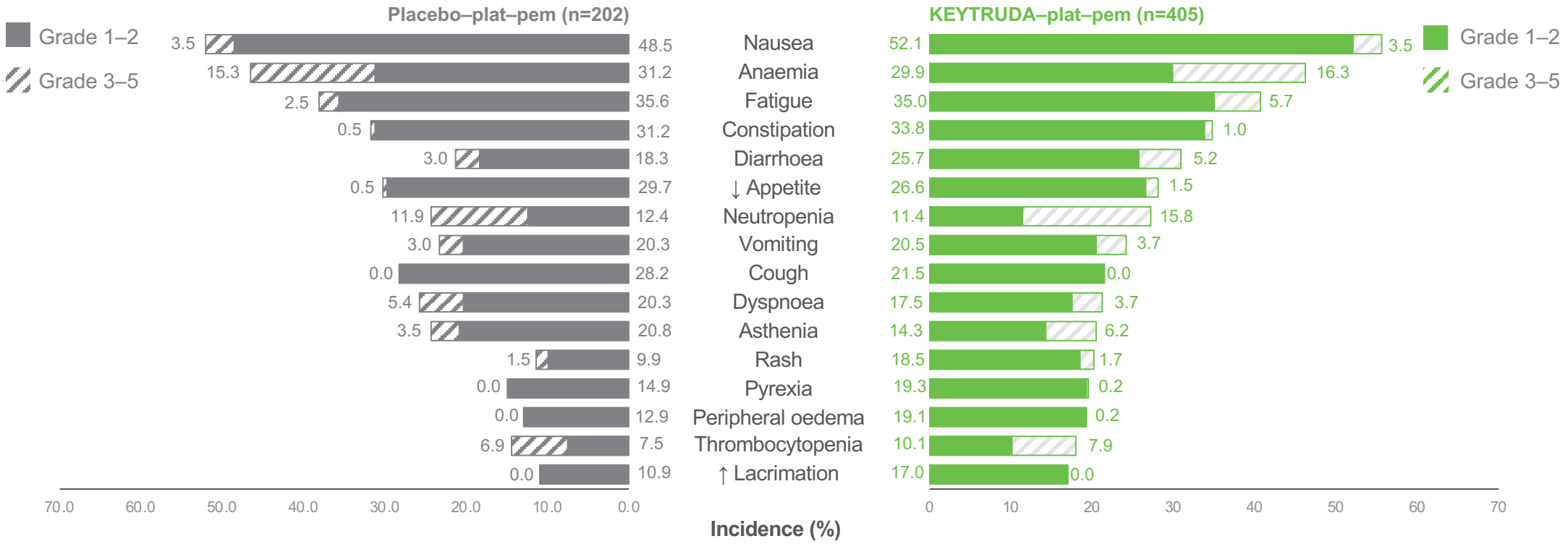
*All patients who had undergone randomisation and received ≥1 dose of the assigned combination therapy. AEs that occurred during crossover from the placebo-combination group to KEYTRUDA monotherapy are excluded.[1] †AEs graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, Version 4.0.[1] ‡Includes patients who discontinued pemetrexed, a platinum-based drug and KEYTRUDA or placebo because of an AE at any time, and patients who discontinued pemetrexed and pembrolizumab or placebo for an AE after completing 4 cycles of a platinum-based drug.[1] §Regardless of attribution to trial drug by the investigator.[1] ¶All deaths were due to pneumonitis.[1]

AE, adverse event; pem, pemetrexed; plat, platinum.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092.

KEYNOTE-189: All-cause AEs occurring in ≥15% of patients in the as-treated population (original analysis)*†[1]

Median follow-up: 10.5 months.



Adapted from Gandhi L, *et al.* 2018.[1]

Data cut-off date: 8 November 2017.

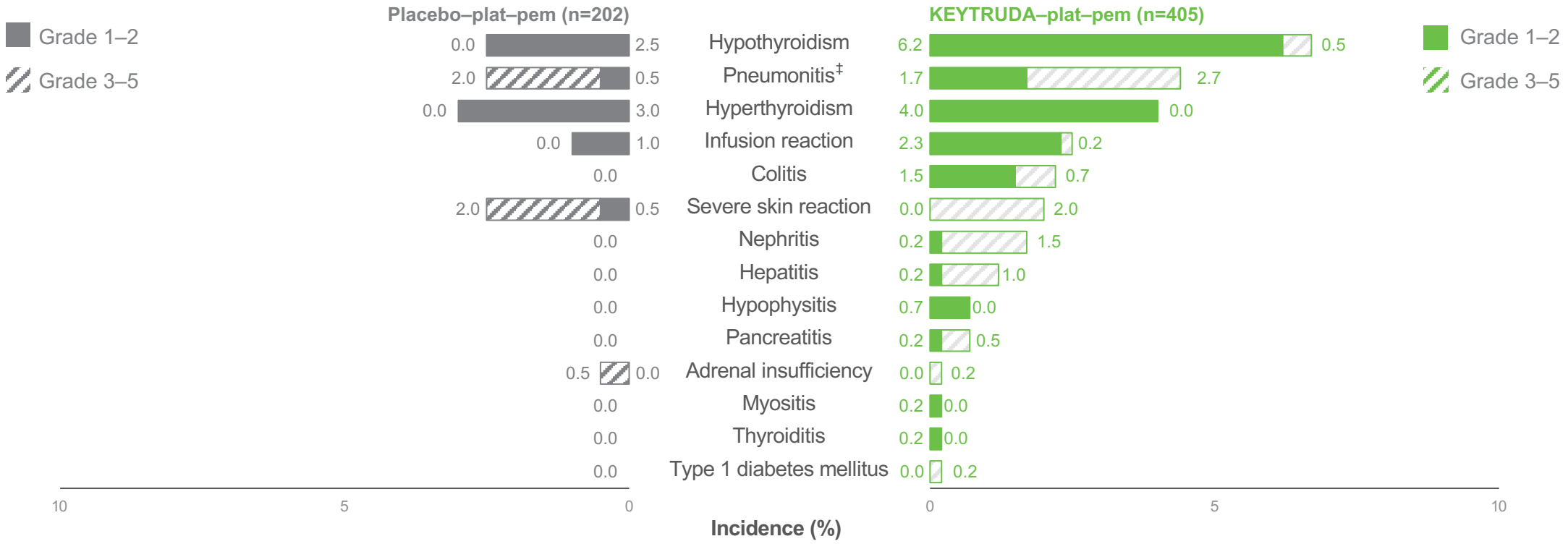
*AEs that occurred during crossover from the placebo-combination group to KEYTRUDA monotherapy are excluded.[1] †AEs were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, Version 4.0.[1]

AE, adverse event; pem, pemetrexed; plat, platinum.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092.

KEYNOTE-189: Immune-mediated AEs in the as-treated population (original analysis)*†[1]

Median follow-up: 10.5 months.



Adapted from Gandhi L, *et al.* 2018.[1]

Data cut-off date: 8 November 2017.

*Regardless of attribution to a trial drug by the investigator.[1] †AEs were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, Version 4.0.[1] ‡Includes three Grade 5 AEs in the KEYTRUDA group.[1]

AE, adverse event; pem, pemetrexed; plat, platinum.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092.

KEYNOTE-407 indication:

KEYTRUDA, in combination with carboplatin and either paclitaxel or nab-paclitaxel, is indicated for the first-line treatment of metastatic squamous non-small cell lung carcinoma in adults*[1]

*KEYTRUDA in combination with nab-paclitaxel is not recommended for reimbursement in the UK by NICE or the SMC.[2,3]

1. KEYTRUDA Summary of Product Characteristics. MSD. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed: May 2026. **2.** National Institute for Health and Care Excellence. TA770. Available at: https://www.nice.org.uk/guidance/ta770/chapter/1-Recommendations. Accessed: May 2026. NICE guidance is prepared for the National Health Service in England, and is subject to regular review and may be updated or withdrawn. NICE has not checked the user of its content in this document to confirm that it accurately reflects the NICE publication from which it is taken. **3.** Scottish Medicines Consortium. SMC2187. Available at: https://scottishmedicines.org.uk/medicines-advice/pembrolizumab-keytruda-full-smc2187/. Accessed: May 2026.

KEYNOTE-407 study design: Randomised, double-blind, Phase III trial[1,2]

Key eligibility criteria

- Untreated Stage IV NSCLC with squamous histology
- ECOG PS 0 or 1
- Provision of a sample for PD-L1 assessment
- No symptomatic CNS metastases
- No history of non-infectious pneumonitis requiring use of glucocorticoids, no active autoimmune disease and no systemic immunosuppressive treatment

R
1:1
(N=559)

n=278

KEYTRUDA 200 mg Q3W + **carboplatin** AUC 6 mg/mL/min Q3W + **paclitaxel** 200 mg/m^2 Q3W OR **nab-paclitaxel** 100 mg/m^2 Q1W for 4 cycles Q3W

KEYTRUDA 200 mg Q3W (up to 31 cycles)

n=281

Placebo (normal saline) Q3W + **carboplatin** AUC 6 mg/ml/min Q3W + **paclitaxel** 200 mg/m^2 Q3W OR **nab-paclitaxel** 100 mg/m^2 Q1W for 4 cycles Q3W

Placebo (normal saline) Q3W (up to 31 cycles)

PD‡

Optional crossover:‡ **KEYTRUDA** 200 mg Q3W (up to 35 cycles)

Stratification factors

- PD-L1 expression (TPS* <1% vs ≥1%)
- Choice of taxane (paclitaxel vs nab-paclitaxel)
- Geographic region (East Asia vs rest of world)

Endpoints

- Primary: OS, PFS†
- Secondary: ORR, DOR, safety†
- Exploratory: Effect of PD-L1 expression on efficacy, PROs

Adapted from Paz-Ares L, *et al*. 2018 & Paz-Ares L, *et al*. 2018.[1,2]

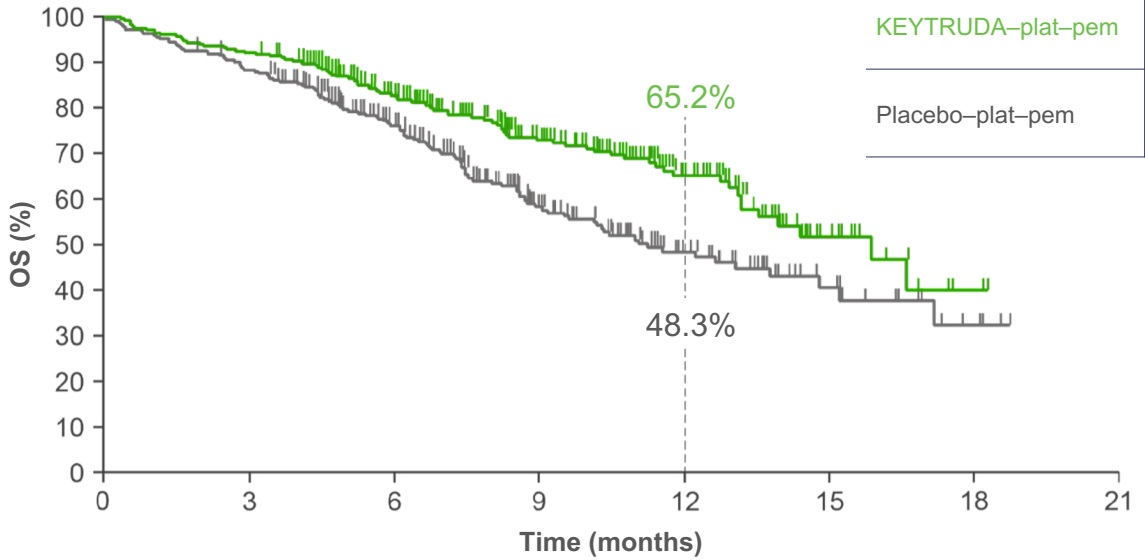
*Percentage of tumour cells with membrane PD-L1 staining, as assessed using the PD-L1 IHC 22C3 pharmDx assay.[1]
†Assessed by blinded, independent central review per RECIST v1.1.[1]
‡Patients in the placebo arm could cross over to KEYTRUDA 200mg Q3W during the induction or maintenance phase. To be eligible for crossover, PD must have been verified by blinded, independent, central radiological review and all safety criteria had to have been met.[1]
AUC, area under the curve; CNS; central nervous system; DOR, duration of response; ECOG PS; Eastern Cooperative Oncology Group performance status; IHC, immunohistochemistry; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PRO, patient-reported outcome; Q1W, every 1 week; Q3W, every 3 weeks; R, randomisation; RECIST, Response Evaluation Criteria in Solid Tumours; TPS, tumour proportion score.

1. Paz-Ares L, *et al. N Engl J Med* 2018;379:2040–2051 (and protocol). **2.** Paz-Ares L, *et al.* ASCO. 1–5 June 2018. Chicago, USA. Oral presentation.

KEYNOTE-407: OS in the ITT population (original analysis)*†‡[1,2]

Median follow-up: 7.8 months

	Events (%)	Median, months (95% CI)	HR (95% CI)	P value
KEYTRUDA–plat–pem	30.6	15.9 (13.2–NE)	0.64 (0.49–0.85)	<0.001
Placebo–plat–pem	42.7	11.3 (9.5–14.8)	–	–



Number at risk								
KEYTRUDA + carb-pac/nabpac	278	256	188	124	62	17	2	0
Placebo + carb-pac/nabpac	281	246	175	93	45	16	4	0

Adapted from Paz-Ares L, *et al*. 2018 & Paz-Ares L, *et al*. 2018.[1,2]

Data cut-off date: 3 April 2018.

*OS and PFS were both primary endpoints.[1] †Kaplan-Meier estimate.[1] ‡Overall alpha for study: strictly controlled at one-sided α=0.025, using the graphical method of Maurer and Bretz. Superiority threshold (one-sided) was 0.0029 for OS. Trial was determined to have 85% power for OS, with a target HR of 0.70 and critical alpha of 0.01.[1]

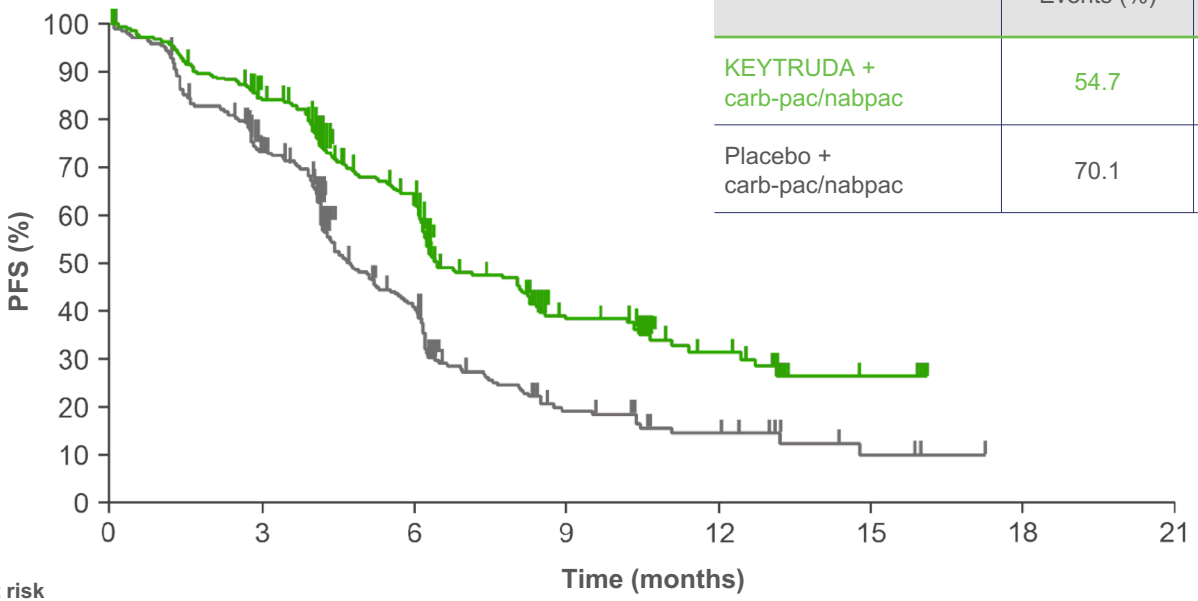
carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; NE, not evaluable; OS, overall survival; PFS, progression-free survival.

1. Paz-Ares L, *et al. N Engl J Med* 2018;379:2040–2051 (and supplementary appendix). **2.** Paz-Ares L, *et al.* ASCO. 1–5 June 2018. Chicago, USA. Oral presentation.

KEYNOTE-407: PFS in the ITT population (original analysis)*†‡§[1,2]

Median follow-up: 7.8 months

	Events (%)	Median, months (95% CI)	HR (95% CI)	P value
KEYTRUDA + carb-pac/nabpac	54.7	6.4 (6.2–8.3)	0.56 (0.45–0.70)	<0.001
Placebo + carb-pac/nabpac	70.1	4.8 (4.3–5.7)	–	–



Number at risk

KEYTRUDA + carb-pac/nabpac	278	223	142	57	23	5	0	0
Placebo + carb-pac/nabpac	281	190	90	26	12	4	0	0

Adapted from Paz-Ares L, *et al*. 2018 & Paz-Ares L, *et al*. 2018.[1,2]

Data cut-off date: 3 April 2018.[1]

*OS and PFS were both primary endpoints.[1] †Kaplan-Meier estimate.[1] ‡Assessed using RECIST by blinded, independent, central radiological review.[1] §Overall alpha for study: strictly controlled at one-sided α=0.025, using the graphical method of Maurer and Bretz. Superiority threshold (one-sided) was 0.008 for PFS. Trial was determined to have 90% power for PFS, with a target HR of 0.70 and critical alpha of 0.01.[1]

carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours.

1. Paz-Ares L, *et al. N Engl J Med* 2018;379:2040–2051 (and supplementary appendix). **2.** Paz-Ares L, *et al.* ASCO. 1–5 June 2018. Chicago, USA. Oral presentation.

KEYNOTE-407: Summary of AEs in the as-treated population (original analysis)*[1]

Median follow-up: 7.8 months

n (%)	KEYTRUDA + carb-pac/nabpac (n=278)	Placebo + carb-pac/nabpac (n=280)
All-cause AEs	273 (98.2)	274 (97.9)
Grade 3–5	194 (69.8)	191 (68.2)
Led to death	23 (8.3)	18 (6.4)
Treatment related	10 (3.6)	6 (2.1)
Led to discontinuation		
All treatment†	37 (13.3)	18 (6.4)
Any treatment‡	65 (23.4)	33 (11.8)
Immune-mediated AEs and infusion reactions	80 (28.8)	24 (8.6)
Grade 3–5	30 (10.8)	9 (3.2)
Led to death§	1 (0.4)	1 (0.4)

Adapted from Paz-Ares L, *et al.* 2018.[1]

Data cut-off date: 3 April 2018.[1]

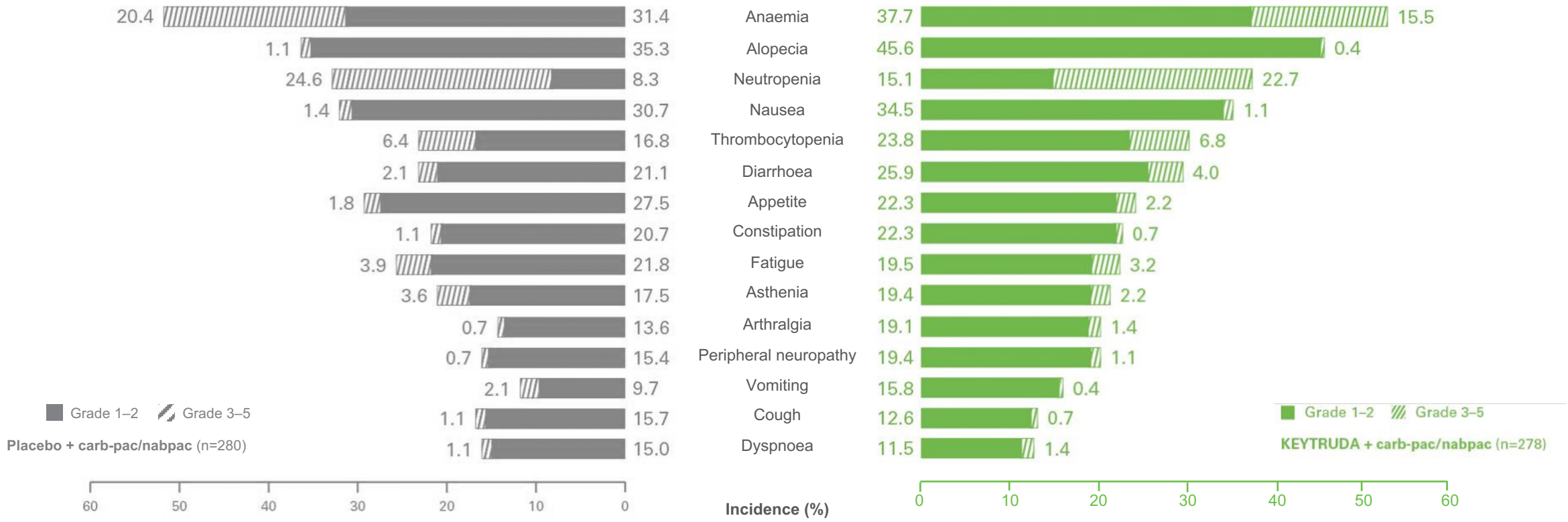
*All patients who had undergone randomisation and received ≥1 dose of the assigned combination therapy.[1] AEs that occurred during crossover from the placebo-combination group to KEYTRUDA monotherapy are excluded.[1] †Includes patients who discontinued KEYTRUDA or placebo, carboplatin and taxane for an AE at any time, and patients who discontinued KEYTRUDA or placebo for an AE after completing 4 cycles of carboplatin and taxane.[1] ‡Patients could have discontinued one, two, or all agents for a given adverse event.[1] §Both deaths were due to pneumonitis.[1]

AE, adverse event; carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel.

1. Paz-Ares L, *et al. N Engl J Med* 2018;379:2040–2051.

KEYNOTE-407: All-cause AEs occurring in ≥15% of patients in the as-treated population (original analysis)*†[1]

Median follow-up: 7.8 months



Adapted from Paz-Ares L, *et al.* 2018.[1]

Data cut-off date: 3 April 2018.

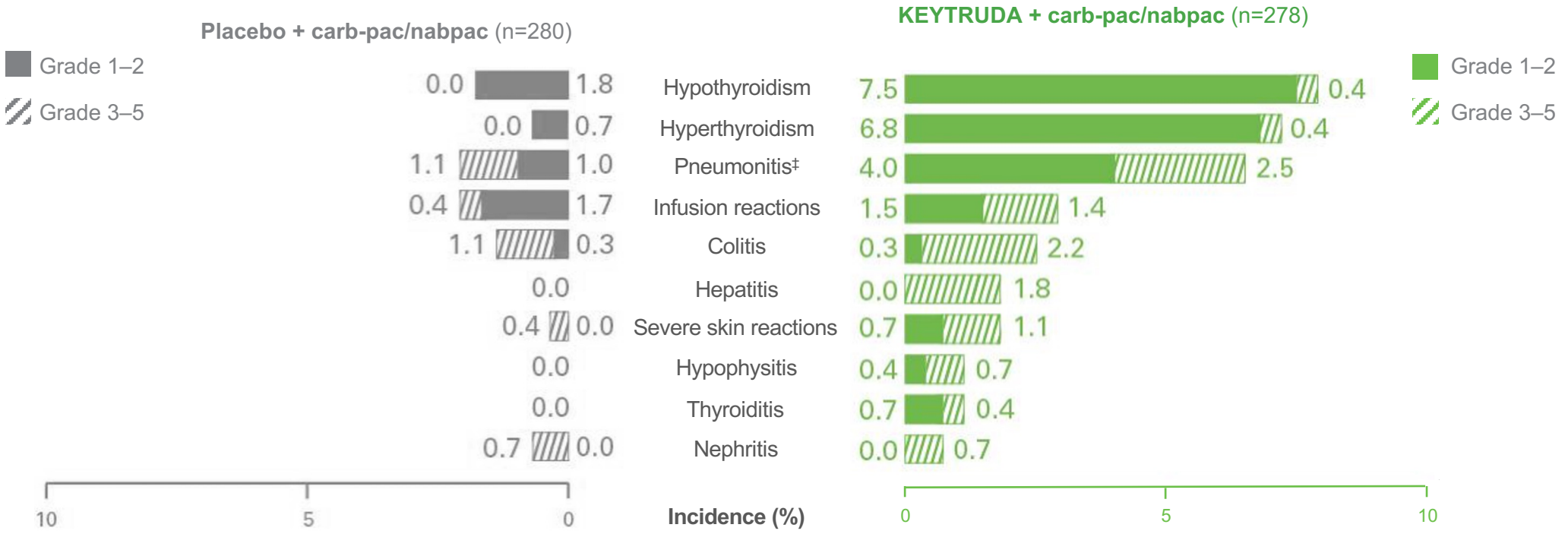
*AEs that occurred during crossover from the placebo–plat–pem group to KEYTRUDA monotherapy were excluded.[1] †AEs were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, Version 4.0.[1]

AE, adverse event; carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel.

1. Paz-Ares L, *et al. N Engl J Med* 2018;379:2040–2051.

KEYNOTE-407: Immune-mediated AEs and infusion reactions in the as-treated population (original analysis)*†[1]

Median follow-up: 7.8 months



Adapted from Paz-Ares L, *et al.* 2018.[1]

Data cut-off date: 3 April 2018.[1]

*Regardless of attribution to a trial drug by the investigator.[1] †AEs were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, Version 4.0.[1] ‡Includes one patient in each trial arm who had Grade 5 pneumonitis.[1]

AE, adverse event; carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel.

1. Paz-Ares L, *et al. N Engl J Med* 2018;379:2040–2051.

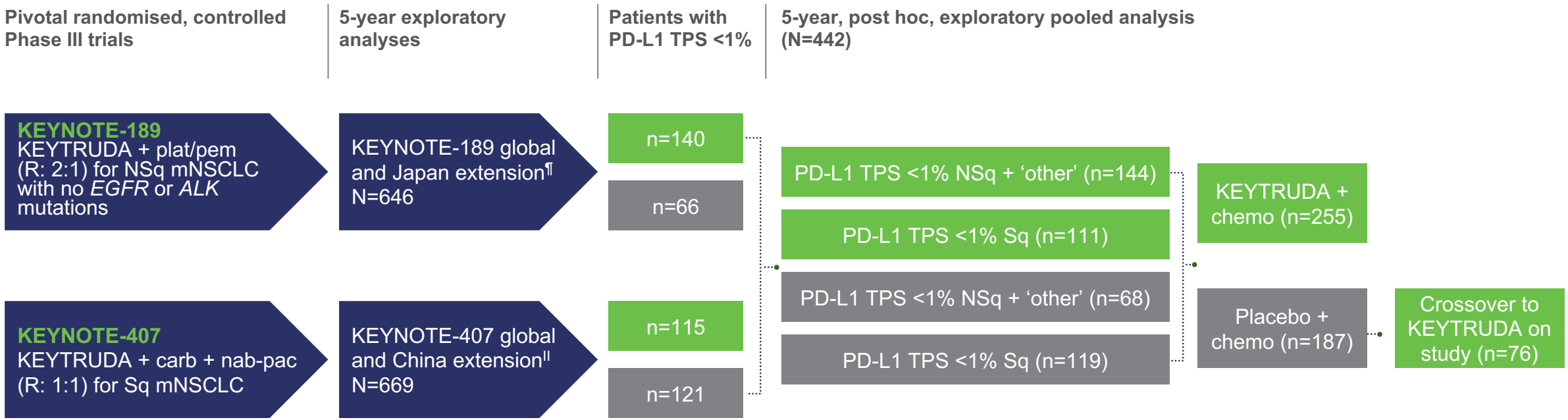
Post hoc exploratory pooled analysis (KEYNOTE-189, KEYNOTE-407)

5-year survival with KEYTRUDA plus chemotherapy for mNSCLC with PD-L1 TPS <1%[1]

mNSCLC, metastatic non-small cell lung cancer; PD-L1, programmed death-ligand 1; TPS, tumour proportion score.

1. Gadgeel S, *et al.* 5-year survival of pembrolizumab plus chemotherapy for metastatic NSCLC with PD-L1 tumor proportion score <1%. WCLC. 9-12 September 2023. Singapore.

KEYNOTE-189 & KEYNOTE-407: Post hoc exploratory pooled analysis – PD-L1 non-expresser subgroups (5-year update)*†‡§[1–4]



Adapted from Gadgeel S, *et al.* 2024.[1]

The exploratory pooled analysis included patient data from KEYNOTE-189 global (data cut-off 8 March 2022) and Japan extension (data cut-off 7 February 2023) and the KEYNOTE-407 global (data cut-off 23 February 2022) and China extension (data cut-off 10 February 2023).[1]

*All 442 patients had PD-L1 TPS <1% (negative).[1] †PD-L1 expression was centrally assessed using PD-L1 IHC 22C3 pharmDX (Agilent Technologies, Carpinteria, CA).[1] ‡Tumour response was assessed per RECIST by blinded independent central review.[1] §Efficacy was evaluated in the intention-to-treat population and safety in the as-treated population.[1] ¶Included 40 patients from the Japan extension.[5] ‖Included 125 patients from the China extension.[6]

ALK, anaplastic lymphoma kinase; carb, carboplatin; chemo, chemotherapy; *EGFR*, epidermal growth factor receptor; mNSCLC, metastatic non-small cell lung cancer; nab-pac, nab-paclitaxel; NSq, non-squamous; PD-L1, programmed death-ligand 1; pem, pemetrexed; plat, platinum; R, randomisation; RECIST, Response Evaluation Criteria in Solid Tumours; Sq, squamous; TPS, tumour proportion score.

1. Gadgeel S, *et al. J Thorac Oncol* 2024;19:1228–1241. **2.** Garassino MC, *et al. J Clin Oncol* 2023;41:1992–1998. **3.** Novello S, *et al. J Clin Oncol* 2023;41:1999–2006. **4.** Gadgeel S, *et al.* 5-year survival of pembrolizumab plus chemotherapy for metastatic NSCLC with PD-L1 tumor proportion score <1%. WCLC. 9–12 September 2023. Singapore. **5.** Horinouchi H, *et al. Cancer Sci* 2021;112::3255–3265. **6.** Cheng Y, *et al. J Thorac Oncol* 2021;2:100225.

KEYNOTE-189 & KEYNOTE-407: Post hoc exploratory pooled analysis – baseline disease characteristics (5-year update)*[1]

Median follow-up: 60.7 months.

	KEYTRUDA + chemo (n=255)	Placebo + chemo (n=187)	Completed 35 cycles of KEYTRUDA (n=27)
Age, median (range), years	65 (31–87)	64 (43–82)	63 (31–74)
Men	181 (71.0)	148 (79.1)	24 (88.9)
ECOG PS 1	165 (64.7)	123 (65.8)	17 (63.0)
Squamous histology	111 (43.5)	119 (63.6)	18 (66.7)
Current or former smoker	225 (88.2)	175 (93.6)	26 (96.3)
Brain metastases	40 (15.7)	26 (13.9)	2 (7.4)
Liver metastases	35 (13.7)	40 (21.4)	3 (11.1)
Prior neoadjuvant therapy	4 (1.6)	4 (2.1)	0
Prior adjuvant therapy	14 (5.5)	8 (4.3)	1 (3.7)
Prior radiotherapy	47 (18.4)	34 (18.2)	1 (3.7)

Adapted from Gadgeel S, *et al.* 2024.[1]

The exploratory pooled analysis included patient data from KEYNOTE-189 global (data cut-off 8 March 2022) and Japan extension (data cut-off 7 February 2023) and the KEYNOTE-407 global (data cut-off 23 February 2022) and China extension (data cut-off 10 February 2023).

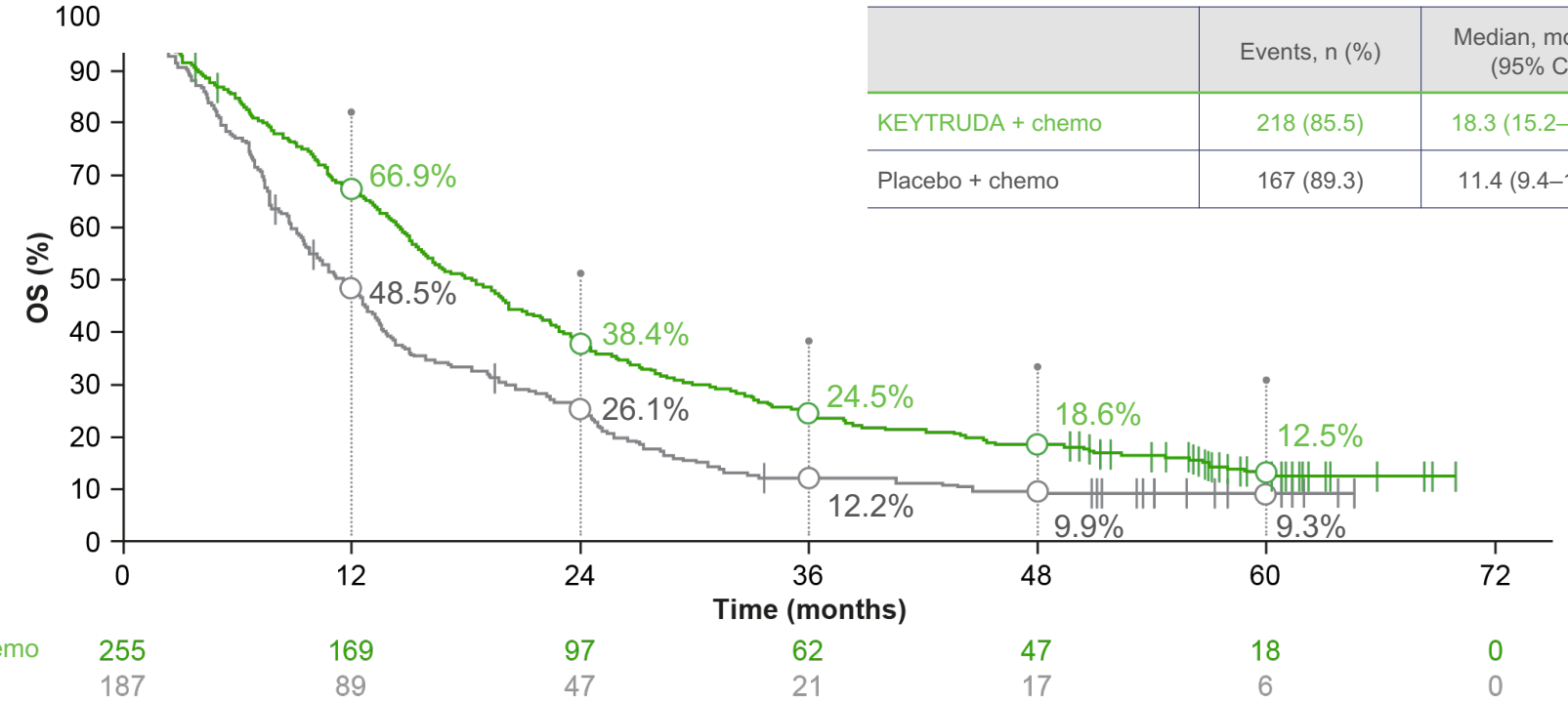
*Values are n (%) unless noted otherwise.[1]

chemo, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status.

1. Gadgeel S, *et al. J Thorac Oncol* 2024;19:1228–1241.

KEYNOTE-189 & KEYNOTE-407: Post hoc exploratory pooled analysis – OS for PD-L1 non-expresser patients (5-year update)*[1]

Median follow-up: 60.7 months. No statistical conclusions can be drawn from this exploratory analysis.



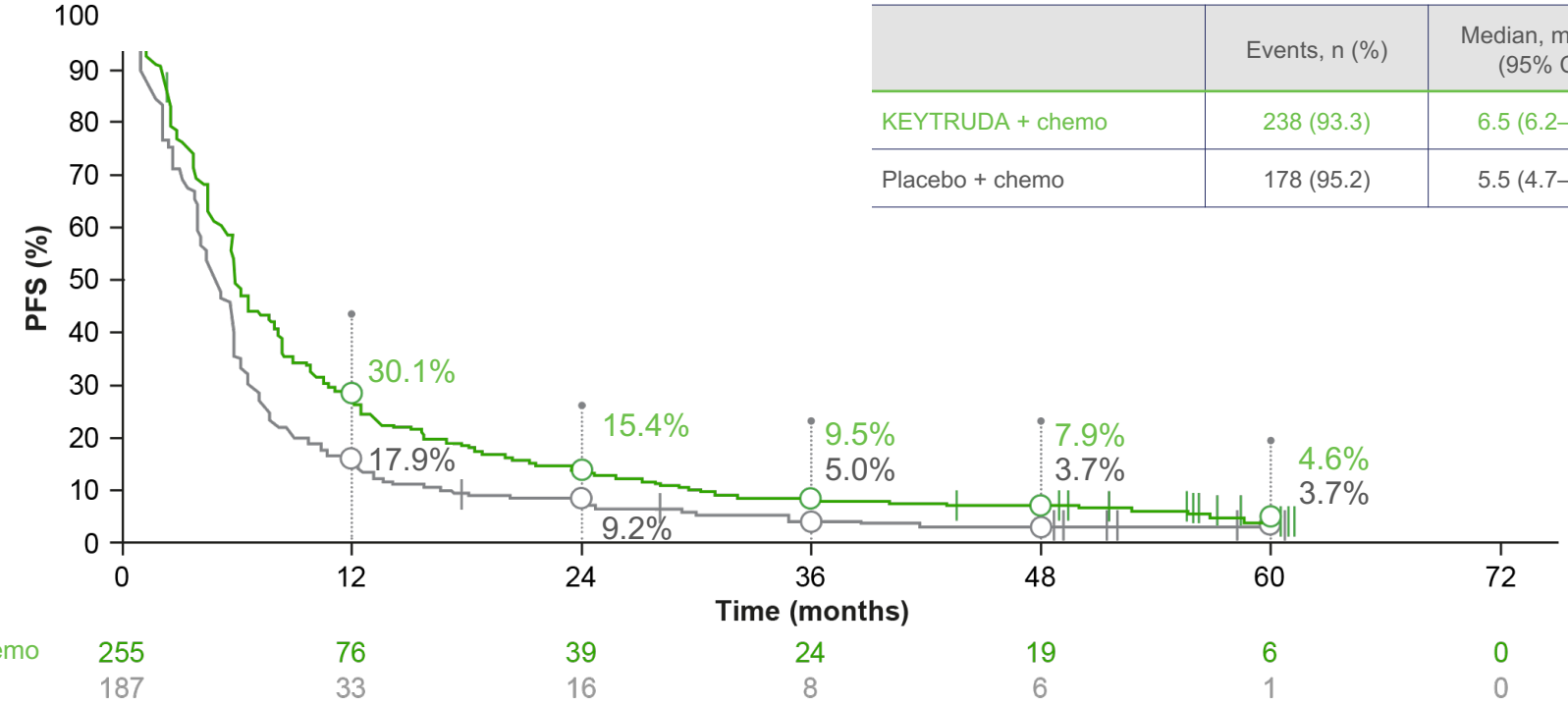
	Events, n (%)	Median, months (95% CI)	HR (95% CI)
KEYTRUDA + chemo	218 (85.5)	18.3 (15.2–20.9)	0.64 (0.51–0.79)
Placebo + chemo	167 (89.3)	11.4 (9.4–13.2)	–

Adapted from Gadgeel S, *et al.* 2024.[1]

The exploratory pooled analysis included patient data from KEYNOTE-189 global (data cut-off 8 March 2022) and Japan extension (data cut-off 7 February 2023) and the KEYNOTE-407 global (data cut-off 23 February 2022) and China extension (data cut-off 10 February 2023).
*Kaplan-Meier estimate.[1]
chemo, chemotherapy; CI, confidence interval; HR, hazard ratio; OS, overall survival; PD-L1, programmed death-ligand 1.
1. Gadgeel S, *et al. J Thorac Oncol* 2024;19:1228–1241.

KEYNOTE-189 & KEYNOTE-407: Post hoc exploratory pooled analysis – PFS for PD-L1 non-expresser patients (5-year update)*†[1]

Median follow-up: 60.7 months. No statistical conclusions can be drawn from this exploratory analysis.



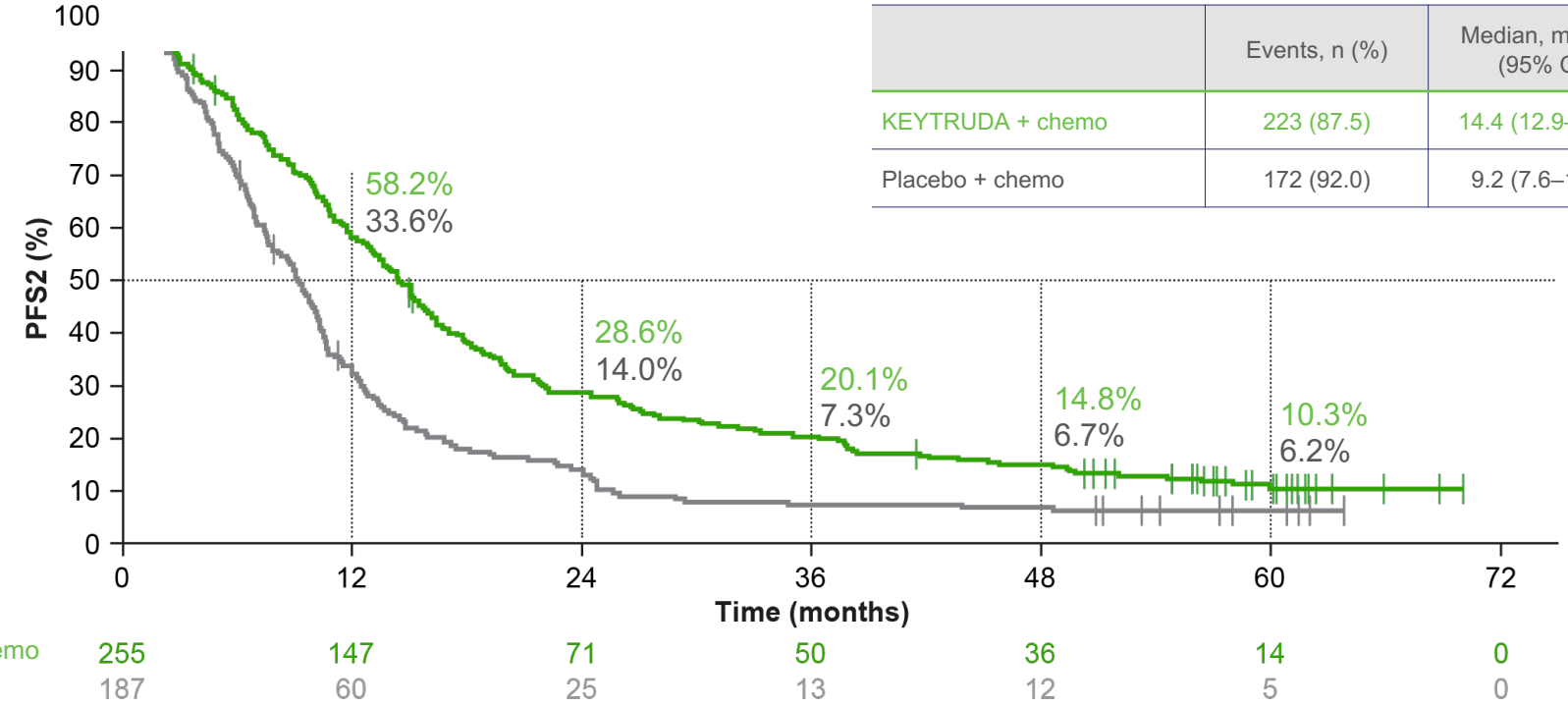
	Events, n (%)	Median, months (95% CI)	HR (95% CI)
KEYTRUDA + chemo	238 (93.3)	6.5 (6.2–8.4)	0.66 (0.54–0.81)
Placebo + chemo	178 (95.2)	5.5 (4.7–6.2)	–

Adapted from Gadgeel S, *et al.* 2024.[1]

The exploratory pooled analysis included patient data from KEYNOTE-189 global (data cut-off 8 March 2022) and Japan extension (data cut-off 7 February 2023) and the KEYNOTE-407 global (data cut-off 23 February 2022) and China extension (data cut-off 10 February 2023).
*Assessed using RECIST-v1.1 by blinded independent central review.[1] †Kaplan-Meier estimate.[1]
chemo, chemotherapy; CI, confidence interval; HR, hazard ratio; PD-L1, programmed death-ligand 1; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours.
1. Gadgeel S, *et al. J Thorac Oncol* 2024;19:1228–1241.

KEYNOTE-189 & KEYNOTE-407: Post hoc exploratory pooled analysis – PFS2 for PD-L1 non-expresser patients (5-year update)*†‡[1]

Median follow-up: 60.7 months. No statistical conclusions can be drawn from this exploratory analysis.



	Events, n (%)	Median, months (95% CI)	HR (95% CI)
KEYTRUDA + chemo	223 (87.5)	14.4 (12.9–15.9)	0.55 (0.44–0.68)
Placebo + chemo	172 (92.0)	9.2 (7.6–10.2)	–

Adapted from Gadgeel S, *et al.* 2024.[1]

The exploratory pooled analysis included patient data from KEYNOTE-189 global (data cut-off 8 March 2022) and Japan extension (data cut-off 7 February 2023) and the KEYNOTE-407 global (data cut-off 23 February 2022) and China extension (data cut-off 10 February 2023).

*Defined as the time from randomisation to second or subsequent tumour progression on next line of treatment or death.[1] †Assessed using RECIST-v1.1 by investigator review.[1] ‡Kaplan-Meier estimate.
chemo, chemotherapy; CI, confidence interval; HR, hazard ratio; PD-L1, programmed death-ligand 1; PFS2, progression-free survival 2; RECIST, Response Evaluation Criteria in Solid Tumours.

1. Gadgeel S, *et al. J Thorac Oncol* 2024;19:1228–1241.

KEYNOTE-189 & KEYNOTE-407: Post hoc exploratory pooled analysis – anti-tumour activity and DOR for PD-L1 non-expresser patients (5-year update)*[1]

Median follow-up: 60.7 months. No statistical conclusions can be drawn from this exploratory analysis.

	KEYTRUDA + chemo (n=255)	Placebo + chemo (n=187)
ORR (95% CI), %	50.6 (44.3–56.9)	33.2 (26.5–40.4)
Best overall response, n (%)		
Complete response	4 (1.6)	5 (2.7)
Partial response	125 (49.0)	57 (30.5)
Stable disease†	88 (34.5)	79 (42.2)
Progressive disease	20 (7.8)	31 (16.6)
Not evaluable‡	11 (4.3)	6 (3.2)
No assessment§	7 (2.7)	9 (4.8)
Median DOR (range), months	7.6 (1.1+ to 59.4+)	5.5 (1.4+ to 55.8+)

Adapted from Gadgeel S, *et al.* 2024.[1]

The exploratory pooled analysis included patient data from KEYNOTE-189 global (data cut-off 8 March 2022) and Japan extension (data cut-off 7 February 2023) and the KEYNOTE-407 global (data cut-off 23 February 2022) and China extension (data cut-off 10 February 2023).

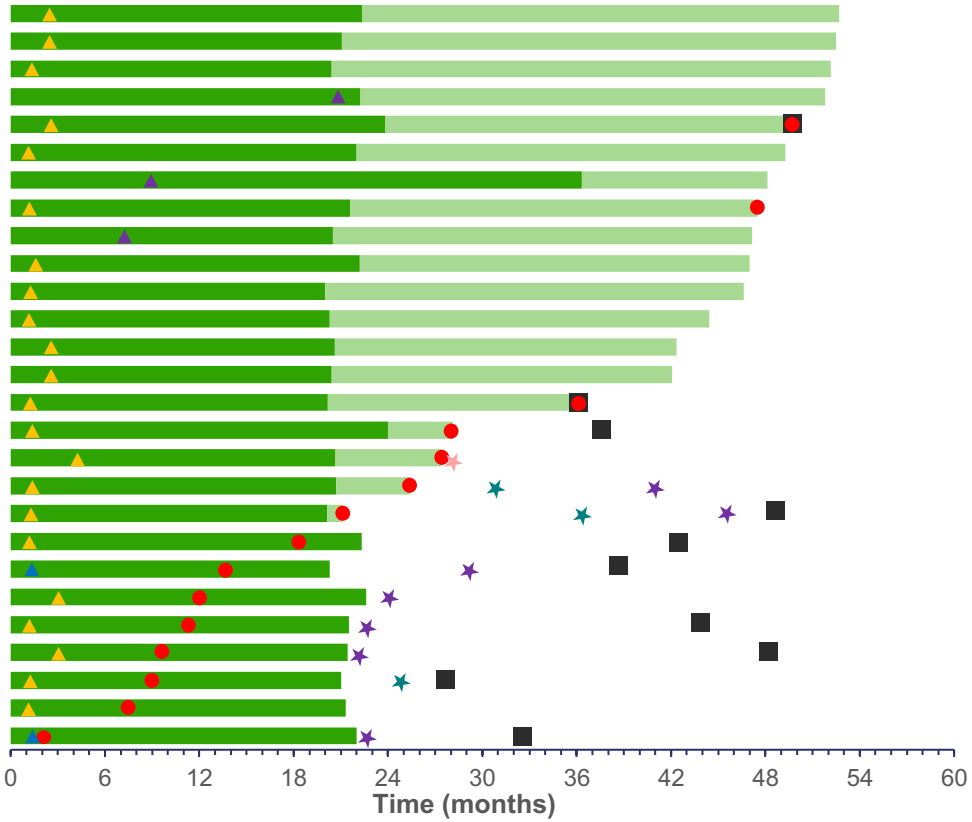
*Assessed using RECIST-v1.1 by blinded independent central review.[1] †Includes SD and non-CR/non-PD.[1] ‡Post-baseline assessment(s) available but not evaluable or CR/PR/SD <6 weeks from randomisation. §No post-baseline assessment available for response evaluation.[1]

chemo, chemotherapy; CI, confidence interval; CR, complete response; DOR, duration of response; ORR, objective response rate; PD, progressive disease; PD-L1, programmed death-ligand 1; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours; SD, stable disease.

1. Gadgeel S, *et al.* 5-year survival of pembrolizumab plus chemotherapy for metastatic NSCLC with PD-L1 tumor proportion score <1%. WCLC. 9–12 September 2023. Singapore.

KEYNOTE-189 & KEYNOTE-407: Post hoc exploratory pooled analysis – outcomes in patients who completed 35 cycles (5-year update)[1,2]

Median follow-up: 60.7 months. No statistical conclusions can be drawn from this exploratory analysis.



Outcome	Patients who completed 35 cycles* n=27
ORR† (95% CI), %	92.6 (75.7–99.1)
Best overall response, n (%)	
Complete response	3 (11.1)
Partial response	22 (81.5)
Stable disease‡	2 (7.4)
Median DOR (range), months	55.1 (7.4–59.3+)
3-year OS rate after completing 35 cycles, %	56.7
Alive without PD or subsequent therapy, n (%)	12 (44.4)

- BOR CR
- BOR PR
- BOR SD
- PD
- First course treatment
- First course follow-up
- Second-course KEYTRUDA
- Subsequent anti-cancer therapy
- Subsequent radiation therapy
- Death

Adapted from Gadgeel S, *et al.* 2023.[1]

The exploratory pooled analysis included patient data from KEYNOTE-189 global (data cut-off 8 March 2022) and Japan extension (data cut-off 7 February 2023) and the KEYNOTE-407 global (data cut-off 23 February 2022) and China extension (data cut-off 10 February 2023).

*Patients with PD-L1 TPS <1%.[1] †Response assessed per RECIST per blinded independent central review.[1] ‡Includes SD and non-CR/non-PD.[1]

BOR, best overall response; CI, confidence interval; CR, complete response; DOR, duration of response; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-L1, programmed death-ligand 1; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours; SD, stable disease; TPS, tumour proportion score.

1. Gadgeel S, *et al. J Thorac Oncol* 2024;19:1228–1241. **2.** Gadgeel S, *et al.* 5-year survival of pembrolizumab plus chemotherapy for metastatic NSCLC with PD-L1 tumor proportion score <1%. WCLC. 9-12 September 2023. Singapore.

KEYNOTE-189 & KEYNOTE-407: Post hoc exploratory pooled analysis – summary of safety data (5-year update)[1]

Median follow-up: 60.7 months.

AEs, n (%)	KEYTRUDA + chemo (n=254)	Placebo + chemo n=186
Treatment-related AEs	245 (96.5)	175 (94.1)
Grade 3–5	150 (59.1)	114 (61.3)
Led to discontinuation	72 (28.3)	17 (9.1)
Led to death*	14 (5.5)	1 (0.5)
Immune-mediated AEs and infusion reactions	78 (30.7)	20 (10.8)
Grade 3–5	32 (12.6)	6 (3.2)
Led to death	2 (0.8)	0

Adapted from Gadgeel S, *et al.* 2024.[1]

The exploratory pooled analysis included patient data from KEYNOTE-189 global (data cut-off 8 March 2022) and Japan extension (data cut-off 7 February 2023) and the KEYNOTE-407 global (data cut-off 23 February 2022) and China extension (data cut-off 10 February 2023).

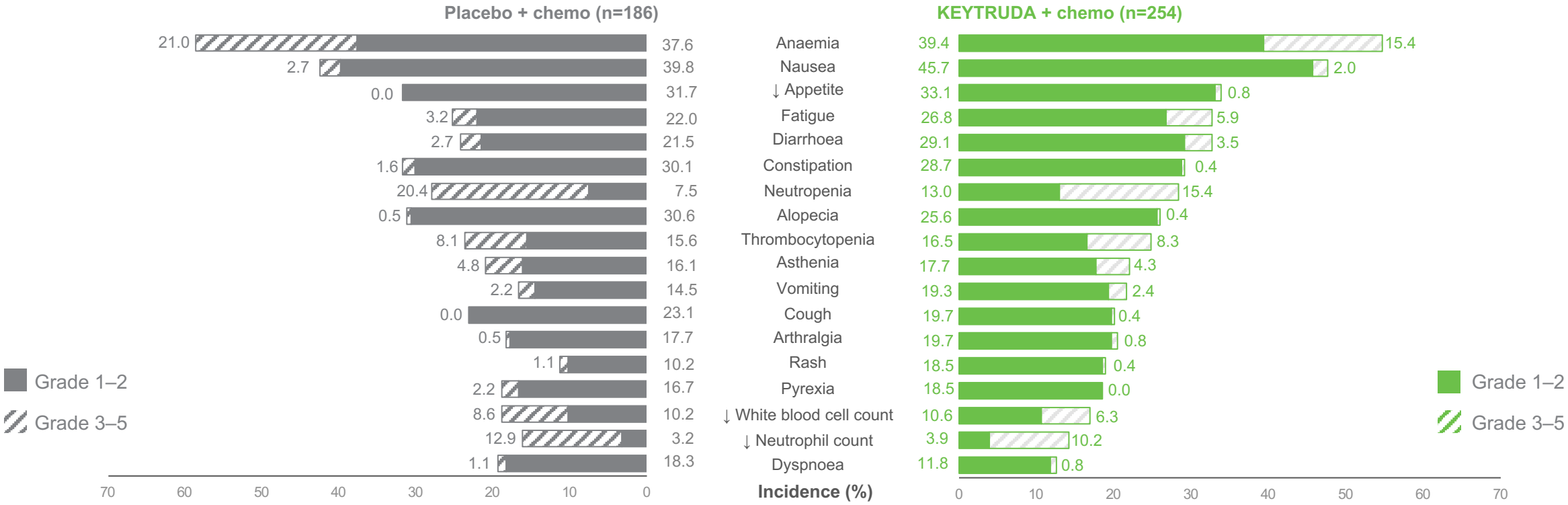
*Treatment-related AEs that led to death were: death, pneumonia and pneumonitis (each n=2); acute kidney injury, cardiac arrest, cardiac failure, encephalopathy, hepatic failure, neutropenic sepsis, pulmonary haemorrhage, respiratory failure and septic shock (each n=1) in the KEYTRUDA plus chemotherapy group; and septic shock (n=1) in the placebo plus chemotherapy group.[1]

AE, adverse event; chemo, chemotherapy.

1. Gadgeel S, *et al. J Thorac Oncol* 2024;19:1228–1241.

KEYNOTE-189 & KEYNOTE-407: Post hoc exploratory pooled analysis – AEs occurring in ≥15% of patients in either treatment group (5-year update)*[1]

Median follow-up: 60.7 months.



Adapted from Gadgeel S, *et al.* 2024.[1]

The exploratory pooled analysis included patient data from KEYNOTE-189 global (data cut-off 8 March 2022) and Japan extension (data cut-off 7 February 2023) and the KEYNOTE-407 global (data cut-off 23 February 2022) and China extension (data cut-off 10 February 2023).

*Treatment-related AEs that led to death were: death, pneumonia and pneumonitis (each n=2); acute kidney injury, cardiac arrest, cardiac failure, encephalopathy, hepatic failure, neutropenic sepsis, pulmonary haemorrhage, respiratory failure and septic shock (each n=1) in the KEYTRUDA plus chemotherapy group; and septic shock (n=1) in the placebo plus chemotherapy group.[1]

AE, adverse event; chemo, chemotherapy.

1. Gadgeel S, *et al. J Thorac Oncol* 2024;19:1228–1241.

KEYNOTE-189 & KEYNOTE-407: Post hoc exploratory pooled analysis – AEs occurring in ≥15% of patients in either treatment group (5-year update)*[1]

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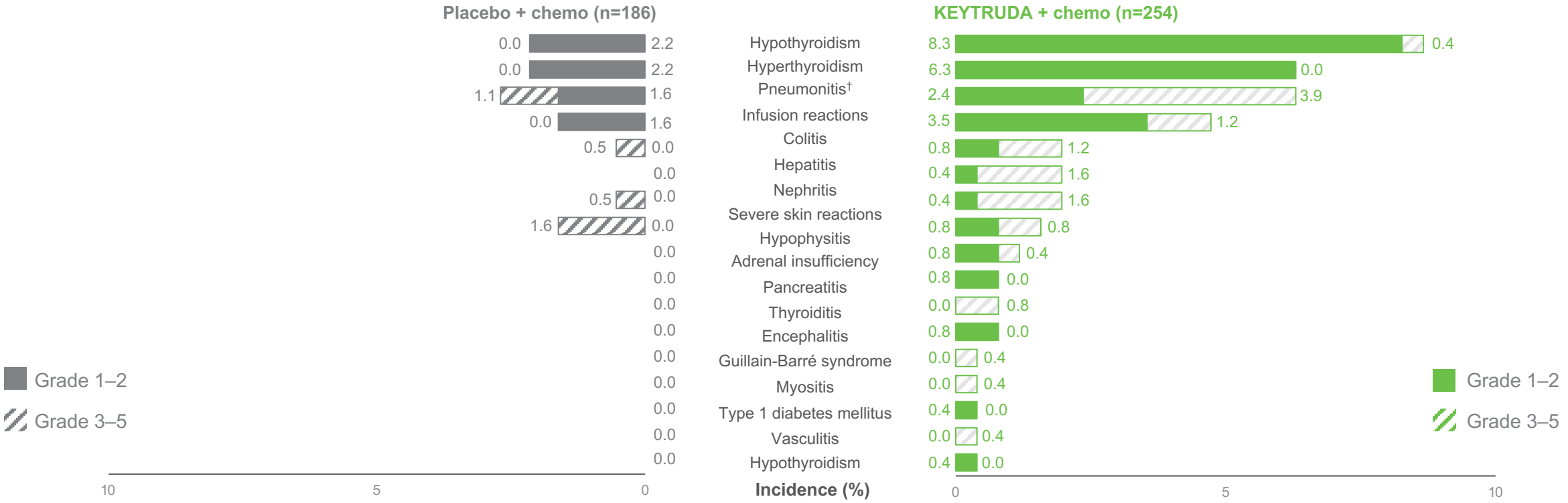


Adapted from Gadgeel S, *et al.* 2024.[1]

The exploratory pooled analysis included patient data from KEYNOTE-189 global (data cut-off 8 March 2022) and Japan extension (data cut-off 7 February 2023) and the KEYNOTE-407 global (data cut-off 23 February 2022) and China extension (data cut-off 10 February 2023).

*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] †Two patients experienced Grade 5 pneumonitis.[1]

AE, adverse event; chemo, chemotherapy.

1. Gadgeel S, *et al. J Thorac Oncol* 2024;19:1228–1241.

KEYNOTE-189 & KEYNOTE-407: Post hoc exploratory pooled analysis – summary of efficacy and safety data at 5-year follow-up[1]

- The 5-year pooled analysis data shows KEYTRUDA plus chemotherapy demonstrated numerical improvements in OS, PFS and ORR compared with chemotherapy alone in this exploratory analysis of with patients with previously untreated mNSCLC PD-L1 TPS <1% without *EGFR/ALK* alterations enrolled in KEYNOTE-189 and KEYNOTE-407
- KEYTRUDA plus chemotherapy had a manageable toxicity profile
- Patients in this subgroup who completed 35 cycles (~2 years) of KEYTRUDA experienced durable responses and 57% were alive 3 years after completion of 35 cycles (~5 years after randomisation)
- These results continue to support KEYTRUDA plus chemotherapy as a standard-of-care, first-line therapy for mNSCLC patients with PD-L1 TPS <1%

ALK, anaplastic lymphoma kinase; *EGFR*, epidermal growth factor receptor; mNSCLC, metastatic non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; TPS, tumour proportion score.

1. Gadgeel S, *et al. J Thorac Oncol* 2024;19:1228–1241.

Appendices

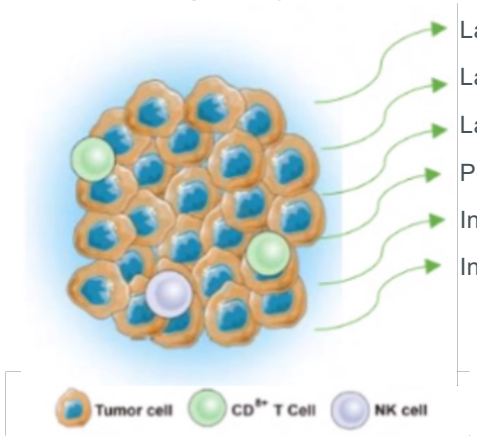
Immune checkpoint inhibitors, in combination with chemotherapy, can help improve outcomes, harnessing the patient's immune system against cancer[1]

This is a hypothesis based on experimental models.

Some NSCLCs are cold tumours that lack activated tumour-specific T cells[2] → Absence of tumour-specific T cells is a mechanism of primary resistance to ICBs[2] → Effective combination therapy can turn cold tumours into hot tumours that are sensitive to ICBs[2]

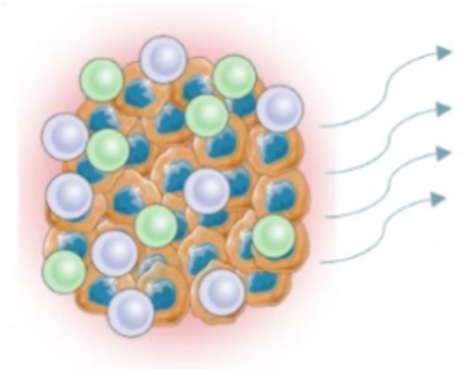
Chemotherapy, through its induction of immunogenic cell death (ICD), can turn a cold tumour into a hot tumour:
Converting a cold tumour microenvironment into a hot tumour can enable increased expression of PD-L1 and sensitise the tumour to PD-1 blockade[3,4]

Cold tumours are characterised by decreased immunogenicity and an immunosuppressive TME[5]



- Lack of CD8 cytotoxic T cells[5,6]
- Lack of PD-L1 expression[7,8]
- Lack of immunoregulatory genes[5]
- Poor antigen presentation[8]
- Increased MDSCs[5]
- Increased Tregs[5]

Hot tumours are characterised by an inflammatory profile and an immunosuppressive TME[5,8]



- Prominent CD8 cytotoxic T-cell infiltration[5,8]
- PD-L1 expression[7,8]
- Suppression of immunosuppressive cells[5]
- Increased pro-inflammatory cytokines[8]

Adapted from Ren X, *et al.* 2022.[8]

CD8, cluster of differentiation 8; ICB, immune checkpoint blocker; MDSC, myeloid-derived suppressor cell; NK, natural killer; NSCLC, non-small cell lung cancer; PD-L1, programmed death-ligand 1; TME, tumour microenvironment.

1. Kersten K, *et al. Front Immunol* 2015;6:516. **2.** Wu M, *et al. J Hematol Oncol* 2022;15:24. **3.** Liu YT, *et al. Theranostics* 2021;11:5365–5386. **4.** Ledys F, *et al. Cancers* (Basel) 2021;13:5999. **5.** Chen Q, *et al. Nanomicro Lett* 2021;13:92. **6.** Holmen Olofsson G, *et al. Int J Mol Sci* 2020;21:3816. **7.** Leonetti A, *et al. Drug Resist Updat* 2019;46:100644. **8.** Ren X, *et al. Front Immunol* 2022;13:790113.

Data dive

KEYNOTE-189

OS	PFS	ORR/DOR	Safety	Liver Mets	Brain Mets	HRQoL
ITT	ITT	ORR (ITT + PDL-1 TPS)	AEs	OS	OS	QLQ-C30
PD-L1 TPS	PD-L1 TPS	DOR/DCR (ITT (original analysis))	All-cause AEs	PFS	PFS	QLQ-LC13
Key subgroups	Key subgroups	DOR (ITT + PD-L1 TPS [5-year])	Immune-mediated AEs			Time to deterioration
	PFS2		Renal AEs			

KEYNOTE-189 & KEYNOTE-407 pooled analysis

AE, adverse event; DCR, disease control rate; DOR, duration of response; HRQoL, health-related quality of life; ITT, intent-to-treat; Mets, metastases; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PFS2, progression-free survival 2; QLQ-C30, Quality of Life Questionnaire Core 30; QLQ-LC13, Quality of Life Questionnaire Lung Cancer 13; TPS, tumour proportion score.