KEYTRUDA® (pembrolizumab) is the first immunotherapy to present 5-year data in three first-line metastatic NSCLC indications licensed in the UK[1–7]

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to MSD (Tel: 020 8154 8000).
By clicking the above link, you will leave the MSD website and be taken to the MHRA website.

UK prescribing information can be found here

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

GB-PDO-03873 | Date of preparation: May 2026

MSD Oncology

KEYNOTE-407

KEYTRUDA plus carboplatin-paclitaxel/ nab-paclitaxel for the first-line treatment of metastatic squamous NSCLC

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.[7]

KEYTRUDA in combination with nab-paclitaxel is not recommended for reimbursement in the UK by NICE or the SMC.[8,9]

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.

NSCLC, non-small cell lung cancer; SMC, Scottish Medicines Consortium.

1. Gandhi L, *et al. N Engl J Med* 2018;378:2078–2092. **2.** Garassino MC, *et al. J Clin Oncol* 2023;41:1992–1998. **3.** Paz-Ares L, *et al. N Engl J Med* 2018;379:2040–2051. **4.** Novello S, *et al. J Clin Oncol* 2023;41:1999–2006.**5.** Reck M, *et al. N Engl J Med* 2016;375:1823–1833. **6.** Reck M, *et al. J Clin Oncol* 2021;39:2339–2349. **7.** KEYTRUDA Summary of Product Characteristics. MSD. Available at: https://www.medicines.org.uk/emc/product/2498/smpc. Accessed: May 2026. **8.** 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guidance is prepared for the National Health Service in England, and is subject to regular review and may be updated or withdrawn.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 use of its content in this document to confirm that it accurately reflects the NICE publication from which it is taken. **9.** Scottish Medicines Consortium. SMC2187. Available at: https://scottishmedicines.org.uk/medicines-advice/pembrolizumab-keytruda-full-smc2187/. Accessed: May 2026.

KEYTRUDA® (pembrolizumab)

MSD

Links to external sites

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

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

2025 ESMO guidelines recommend KEYTRUDA in combination with chemotherapy for the first-line treatment of non-oncogene-addicted 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-407 received a curative (A) score, the AT criteria became applicable. With 29% treatment discontinuation, the KN-407 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 carboplatin and either paclitaxel or nab-paclitaxel, is indicated for the first-line treatment of metastatic, squamous NSCLC in adults**
- 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 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 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-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]

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

KEYNOTE-407: Definition of analyses

Analysis	Cut-off date	Slide symbol	Median follow-up (range) months
Original/second interim	3 April 2018	1	7.8 (0.1–19.1)[1]
Updated analysis	9 May 2019	2	14.3 (0.1–31.3)[2]
5-year follow-up	23 February 2022	3	56.9 (49.9–66.2)[3]

1. Paz-Ares L, *et al. N Engl J Med* 2018;379:2040–2051. **2.** Paz-Ares L, *et al. J Thorac Oncol* 2020;15:1657–1669. **3.** Novello S, *et al. J Clin Oncol* 2023;41:1999–2006.

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

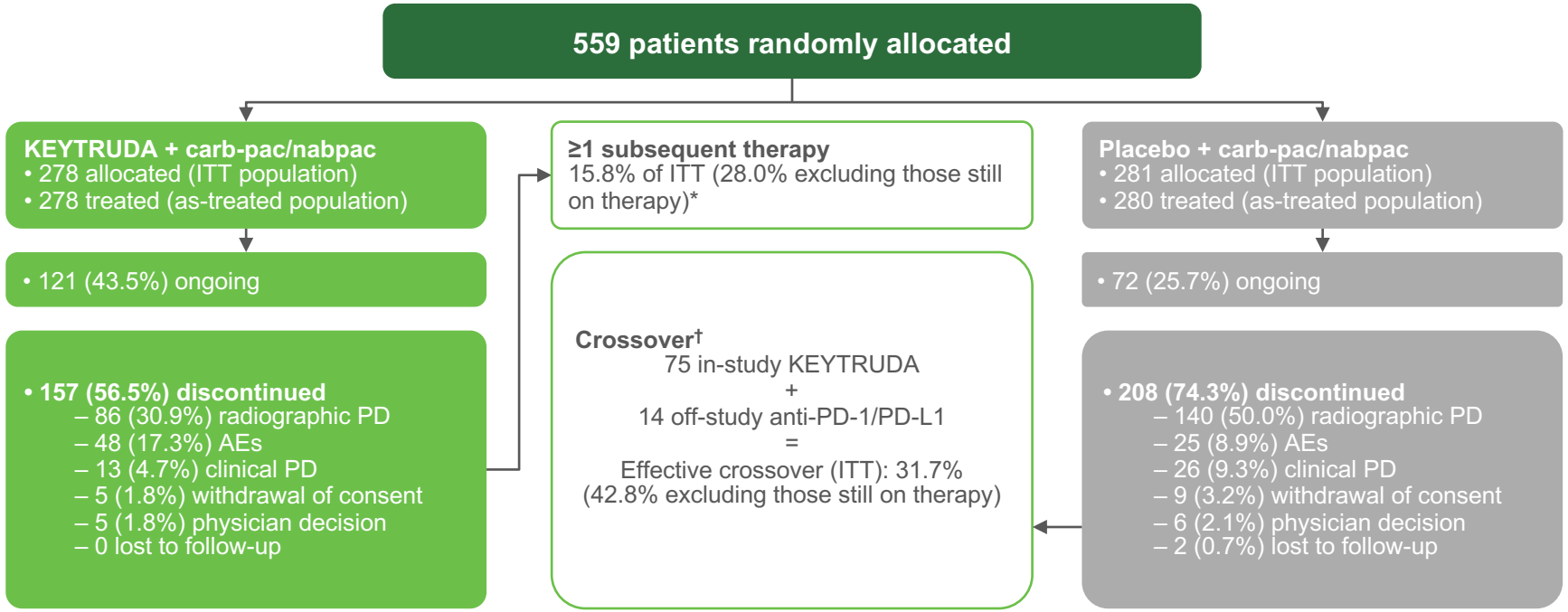
- Primary: OS, PFS†
- Secondary: ORR, DOR, safety†
- Exploratory: Effect of PD-L1 expression on efficacy, PROs

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: Disposition of study treatment – original/second interim analysis[1,2]

Median follow-up: 7.8 months.



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

Data cut-off date: 3 April 2018.[1]
*28.0%=44/157, where 157 is derived from the ITT population (278) minus the number of patients with ongoing treatment (121) and 44 is derived from subsequent treatment in 15.8% of the ITT population (278).[1]
†An additional 21 patients received other subsequent therapy (7.5% of the ITT population; 10.1% excluding those still on therapy).[2]
AE, adverse event; carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; ITT, intention-to-treat; PD, progressive disease; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1.
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: Baseline characteristics[1]

Median follow-up: 7.8 months.

Characteristic, n (%)*	KEYTRUDA + carb-pac/nabpac (n=278)	Placebo + carb-pac/nabpac (n=281)
Age, median (range), years	65 (29–87)	65 (36–88)
<65 years	127 (45.7)	127 (45.2)
Male sex	220 (79.1)	235 (83.6)
ECOG PS		
0	73 (26.3)	90 (32.0)
1	205 (73.7)	191 (68.0)
Brain metastases	20 (7.2)	24 (8.5)
Smoking status		
Former/current	256 (92.1)	262 (93.2)
Never	22 (7.9)	19 (6.8)
Region of enrolment		
East Asia	54 (19.4)	52 (18.5)
Rest of the world	224 (80.6)	229 (81.5)

Characteristic, n (%)*	KEYTRUDA + carb-pac/nabpac (n=278)	Placebo + carb-pac/nabpac (n=281)
PD-L1 TPS†		
<1%	95 (34.2)	99 (35.2)
≥1%	176 (63.3)	177 (63.0)
1–49%	103 (37.1)	104 (37.0)
≥50%	73 (26.3)	73 (26.0)
NE‡	7 (2.5)	5 (1.8)
Prior thoracic radiotherapy	17 (6.1)	22 (7.8)
Prior neoadjuvant or adjuvant therapy	5 (1.8)	8 (2.8)

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

Data cut-off date: 3 April 2018.

*Unless otherwise stated.[1] †PD-L1 TPS was defined as the percentage of tumour cells with membranous PD-L1 expression.[1]

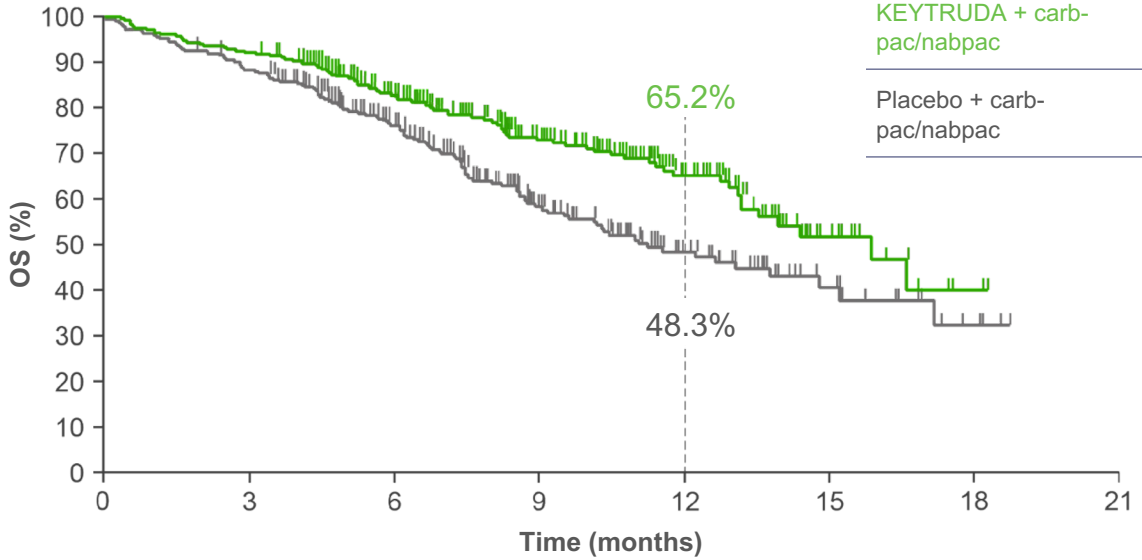
‡PD-L1 expression could not be evaluated because specimens had an inadequate number of tumour cells or no tumour cells. For stratification purposes, patients with PD-L1 expression that could not be evaluated were included in the subgroup with PD-L1 TPS <1%; these patients were excluded from analyses of efficacy according to PD-L1 TPS.[1]

carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; ECOG PS, Eastern Cooperative Oncology Group performance status; NE, not evaluated; PD-L1, programmed death-ligand 1; TPS, tumour proportion score.

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

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

Median follow-up: 7.8 months.



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

	Event, % (n/N)	Median, months (95% CI)	HR (95% CI)	P value
KEYTRUDA + carb-pac/nabpac	30.6	15.9 (13.2–NE)	0.64 (0.49–0.85)	<0.001
Placebo + carb-pac/nabpac	42.7	11.3 (9.5–14.8)	–	–

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]

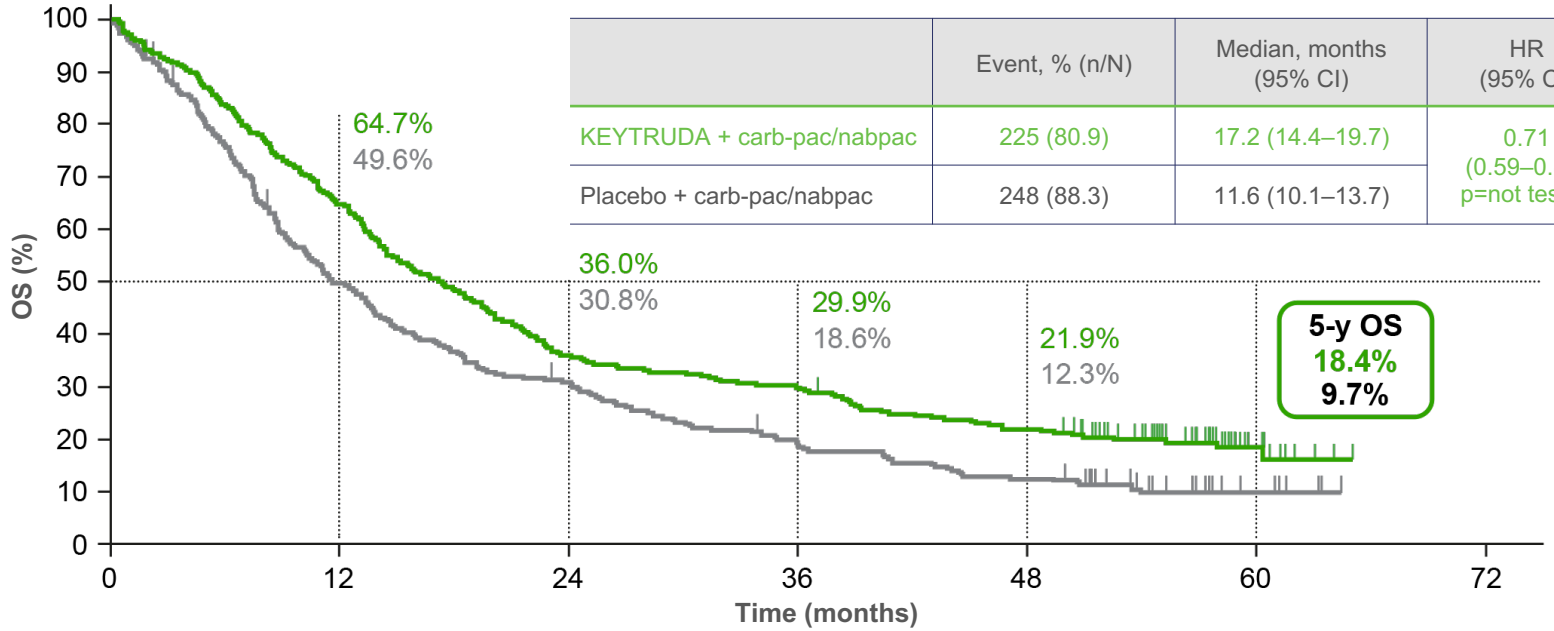
‡Overall alpha for study: strictly controlled at one-sided α=0.025, using the graphical method of Maurer and Bretz. Superiority threshold (one-sided) was 0.0029 for OS. Trial was determined to have 85% power for OS, with a target HR of 0.70 and critical alpha of 0.01.[1]

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

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



	Event, % (n/N)	Median, months (95% CI)	HR (95% CI)
KEYTRUDA + carb-pac/nabpac	225 (80.9)	17.2 (14.4–19.7)	0.71 (0.59–0.85) p=not tested
Placebo + carb-pac/nabpac	248 (88.3)	11.6 (10.1–13.7)	

Number at risk

KEYTRUDA + carb-pac/nabpac	278	180	100	83	60	10	0
Placebo + carb-pac/nabpac	281	137	84	50	33	7	0

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

Data cut-off date: 23 February 2022.[1]
*OS and PFS were both primary endpoints.[1]
†Kaplan-Meier estimate.[1]
‡Statistical significance was met for the primary endpoints in IA2 (2018).[1]
carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; CI, confidence interval; HR, hazard ratio; IA, interim analysis; ITT, intention-to-treat; OS, overall survival; PFS, progression-free survival.

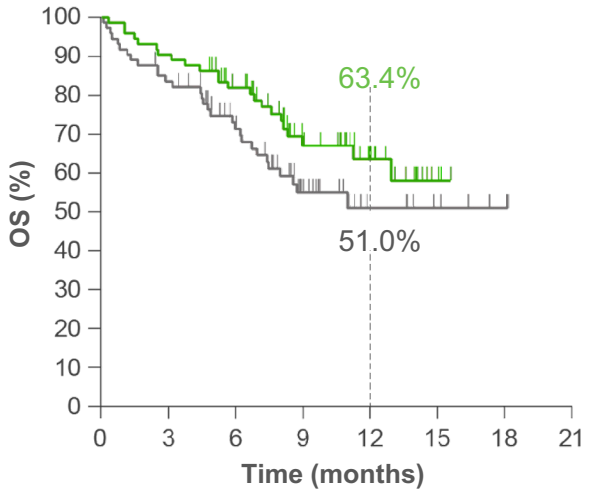
1. Novello S, *et al. J Clin Oncol* 2023;41:1999–2006.

KEYNOTE-407: Exploratory endpoint – OS by PD-L1 TPS (original analysis)*[1,2]

Median follow-up: 7.8 months. No statistical conclusions can be drawn from exploratory endpoints.

PD-L1 TPS ≥50%

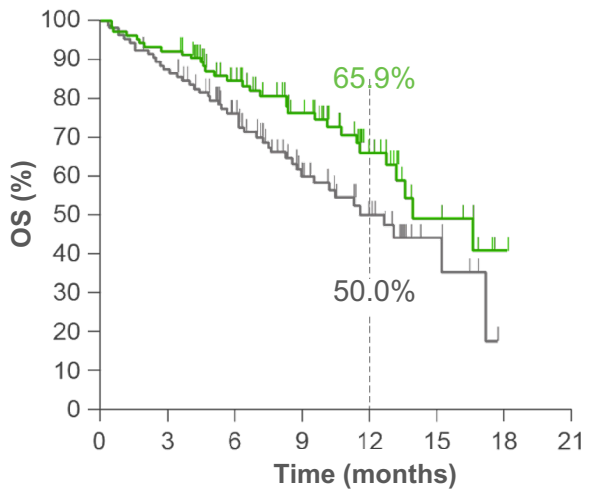
Treatment arm	Event, %	Median, months (95% CI)	HR (95% CI)
KEYTRUDA + carb-pac/nabpac	31.5	NR (11.3–NE)	0.64 (0.37–1.10)
Placebo + carb-pac/nabpac	41.1	NR (7.4–NE)	–



Number at risk								
KEYTRUDA + carb-pac/nabpac	73	66	53	28	15	3	0	0
Placebo + carb-pac/nabpac	73	60	42	21	9	5	2	0

PD-L1 TPS 1–49%

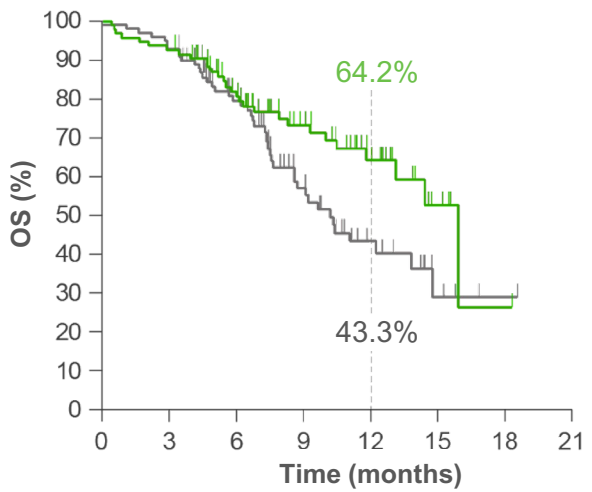
Treatment arm	Event, %	Median, months (95% CI)	HR (95% CI)
KEYTRUDA + carb-pac/nabpac	30.1	14.0 (12.8–NE)	0.57 (0.36–0.90)
Placebo + carb-pac/nabpac	43.3	11.6 (8.9–17.2)	–



KEYTRUDA + carb-pac/nabpac	103	95	68	50	25	9	1	0
Placebo + carb-pac/nabpac	104	90	66	37	21	6	0	0

PD-L1 TPS <1%

Treatment arm	Event, %	Median, months (95% CI)	HR (95% CI)
KEYTRUDA + carb-pac/nabpac	30.5	15.9 (13.1–NE)	0.61 (0.38–0.98)
Placebo + carb-pac/nabpac	44.4	10.2 (8.6–13.8)	–



KEYTRUDA + carb-pac/nabpac	95	88	62	41	20	5	1	0
Placebo + carb-pac/nabpac	99	92	63	32	14	4	1	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]

*Kaplan-Meier estimates.[1]

carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; CI, confidence interval; HR, hazard ratio; NE, not evaluable; NR, not reported; OS, overall survival; PD-L1, programmed death-ligand 1; TPS, tumour proportion score.

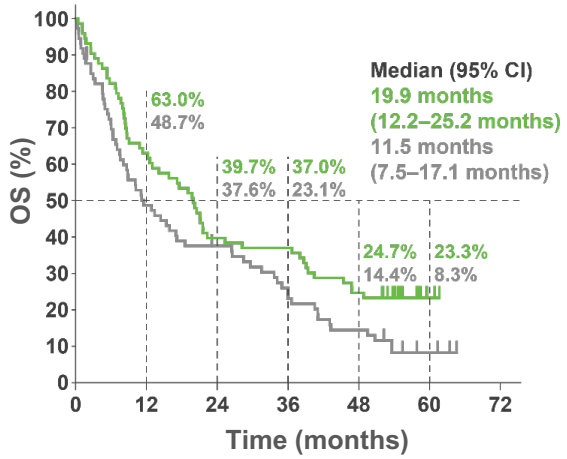
1. Paz-Ares L, *et al. N Engl J Med* 2018;379:2040–2051 (and supplementary appendix). **2.** Paz-Ares L, *et al.* ASCO. 1–5 June 2018. Chicago, USA. Oral presentation.

KEYNOTE-407: Exploratory analysis – OS by PD-L1 TPS (5-year update)*[1]

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

PD-L1 TPS ≥50%

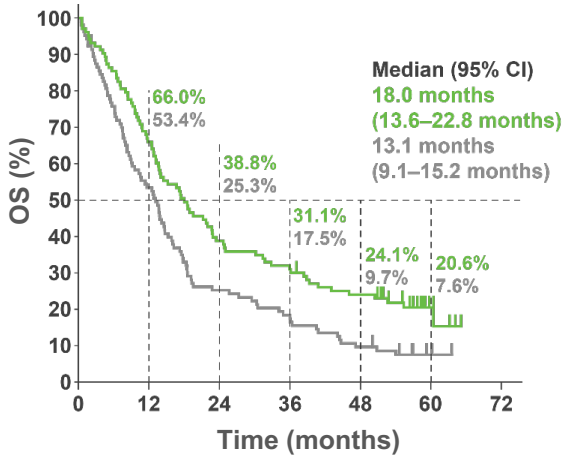
Treatment arm	Events, %	HR (95% CI)	5-year OS rate, % (95% CI)
KEYTRUDA + carb-pac/nabpac	56 (76.7)	0.68 (0.47–0.97)	23.3 (14.4–33.5)
Placebo + carb-pac/nabpac	65 (89.0)		8.3 (3.2–16.4)



Number at risk							
KEYTRUDA + carb-pac/nabpac	3	46	29	27	18	2	0
Placebo + carb-pac/nabpac	3	35	26	16	10	3	0

PD-L1 TPS 1–49%

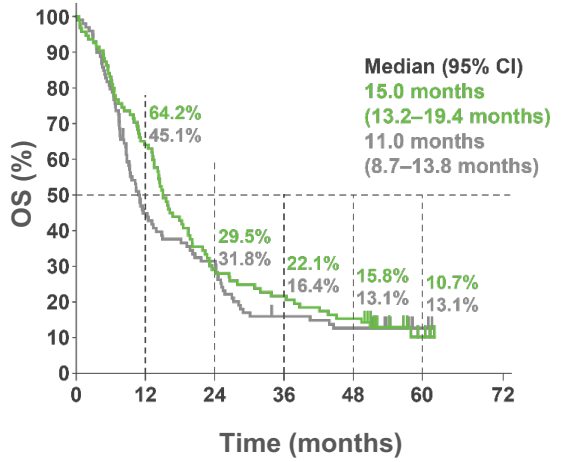
Treatment arm	Events, %	HR (95% CI)	5-year OS rate, % (95% CI)
KEYTRUDA + carb-pac/nabpac	82 (79.6)	0.61 (0.45–0.83)	20.6 (13.2–29.0)
Placebo + carb-pac/nabpac	95 (91.3)		7.6 (3.5–13.8)



KEYTRUDA + carb-pac/nabpac	103	68	40	32	24	5	0
Placebo + carb-pac/nabpac	104	55	26	18	10	1	0

PD-L1 TPS <1%

Treatment arm	Events, %	HR (95% CI)	5-year OS rate, % (95% CI)
KEYTRUDA + carb-pac/nabpac	83 (87.4)	0.83 (0.61–1.13)	10.7 (4.8–19.2)
Placebo + carb-pac/nabpac	85 (85.9)		13.1 (7.3–20.7)



KEYTRUDA + carb-pac/nabpac	95	61	28	21	15	3	0
Placebo + carb-pac/nabpac	99	44	31	15	12	3	0

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

Data cut-off date: 23 February 2022.[1]

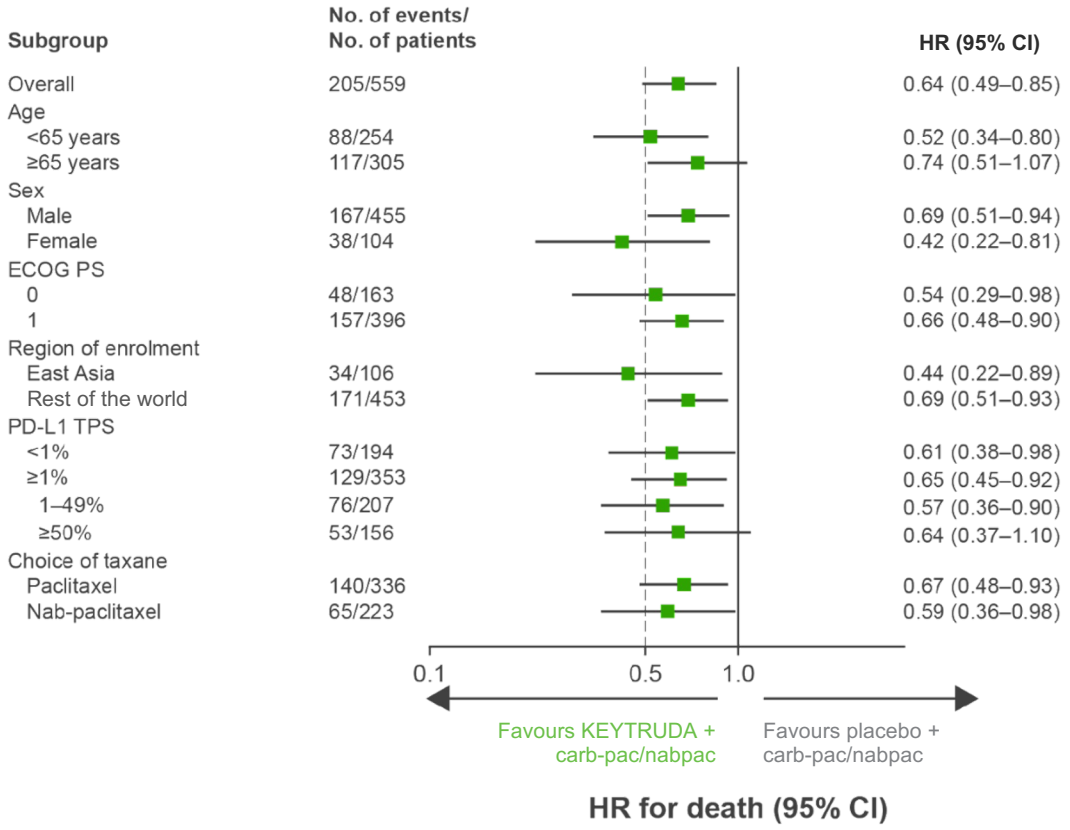
*Kaplan-Meier estimates.[1]

carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; CI, confidence interval; HR, hazard ratio; OS, overall survival; PD-L1, programmed death-ligand 1; TPS, tumour proportion score.

1. Novello S, *et al. J Clin Oncol* 2023;41:1999–2006.

KEYNOTE-407: Exploratory endpoint – OS in key subgroups (original analysis)[1]

Median follow-up: 7.8 months. No statistical conclusions can be drawn from exploratory endpoints.



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

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

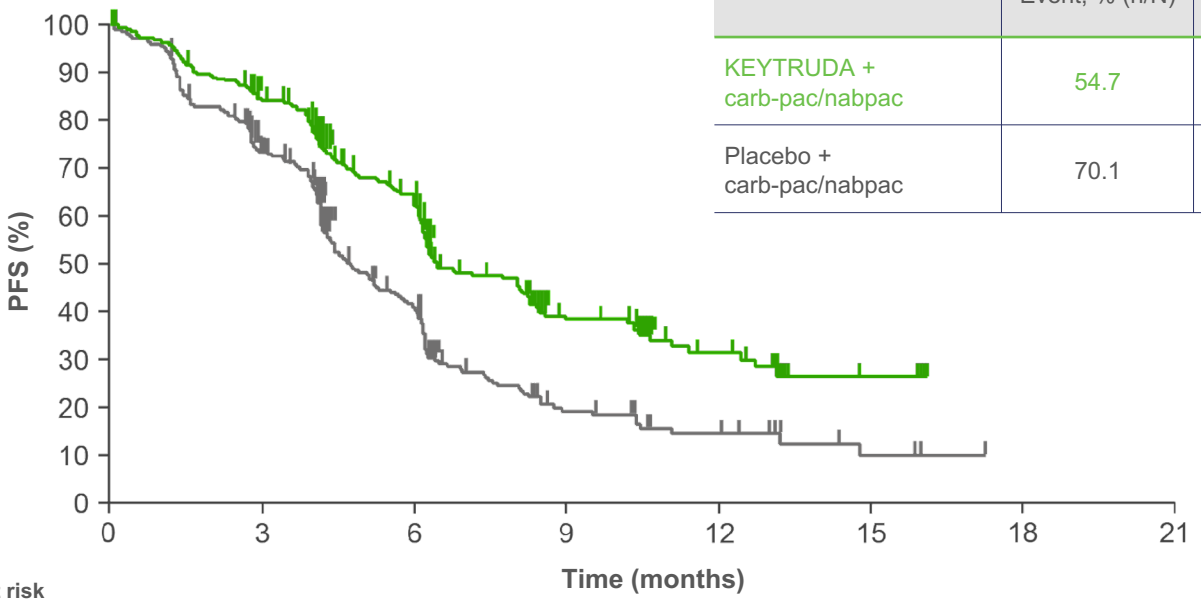
carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; OS, overall survival; PD-L1; programmed death-ligand 1; TPS, tumour proportion score.

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

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

Median follow-up: 7.8 months.

	Event, % (n/N)	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)	–	–



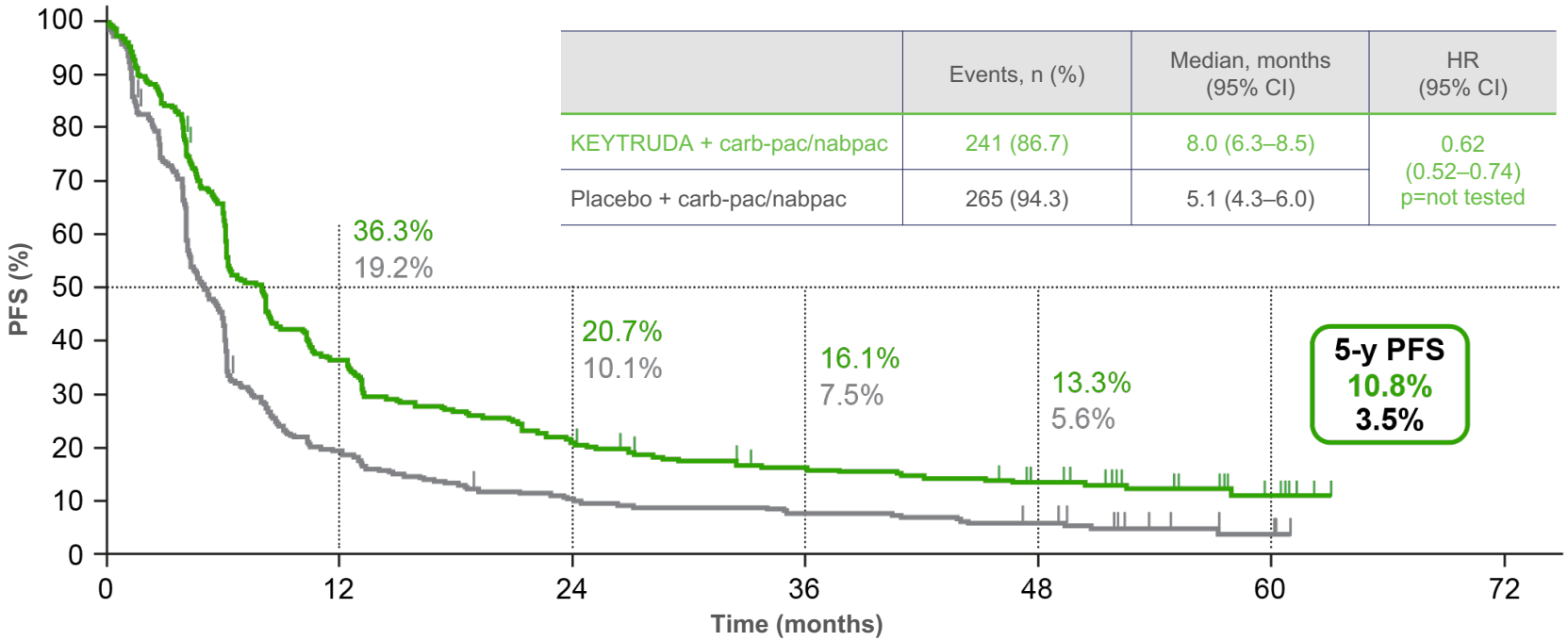
Number at risk								
KEYTRUDA + carb-pac/nabpac	278	223	142	57	23	5	0	0
Placebo + carb-pac/nabpac	281	190	90	26	12	4	0	0

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 v1.1 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: 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 + carb-pac/nabpac	241 (86.7)	8.0 (6.3–8.5)	0.62 (0.52–0.74) p=not tested
Placebo + carb-pac/nabpac	265 (94.3)	5.1 (4.3–6.0)	

Number at risk							
KEYTRUDA + carb-pac/nabpac	278	100	56	40	30	7	0
Placebo + carb-pac/nabpac	281	53	27	20	14	1	0

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

Data cut-off date: 23 February 2022.[1]
*Kaplan-Meier estimate.[1]
†Assessed using RECIST v1.1 by blinded, independent, central review.[1]
carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours.

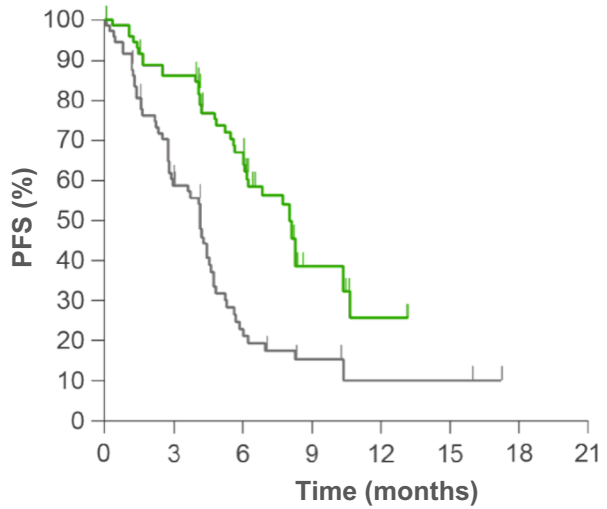
1. Novello S, *et al. J Clin Oncol* 2023;41:1999–2006.

KEYNOTE-407: Exploratory endpoint – PFS by PD-L1 TPS (original analysis)*†[1,2]

Median follow-up: 7.8 months. No statistical conclusions can be drawn from exploratory endpoints.

PD-L1 TPS ≥50%

Treatment group	Events, %	Median, months (95% CI)	5-year PFS rate, % (95% CI)
KEYTRUDA + carb-pac/nabpac	53.4	8.0 (6.1–10.3)	0.37 (0.24–0.58)
Placebo + carb-pac/nabpac	75.3	4.2 (2.8–4.6)	–

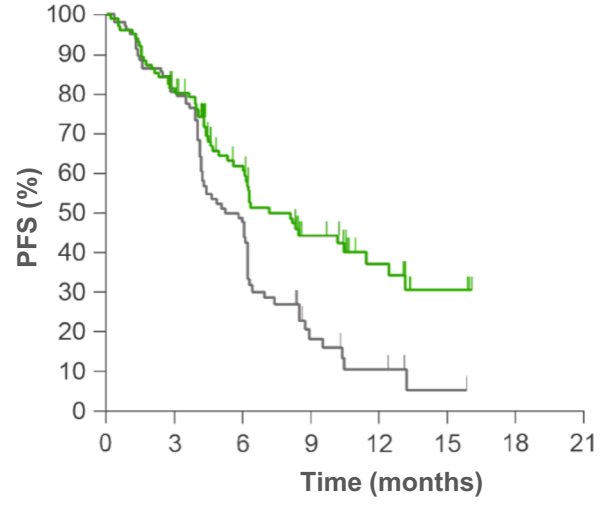


Number at risk

KEYTRUDA + carb-pac/nabpac	73	60	41	12	4	0	0	0
Placebo + carb-pac/nabpac	73	38	13	5	2	2	0	0

PD-L1 TPS 1–49%

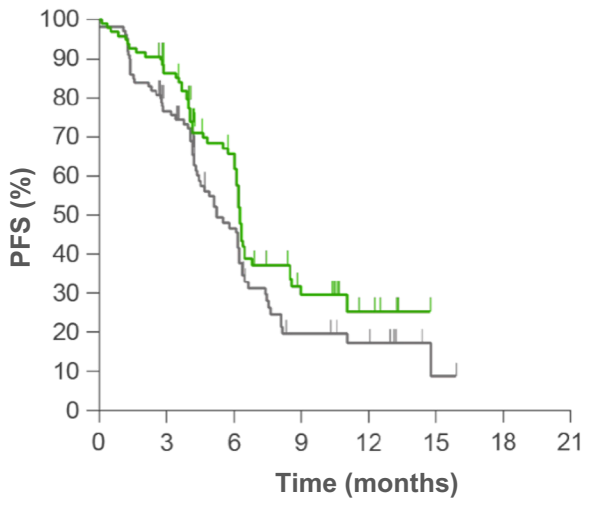
Treatment arm	Events, %	Median, months (95% CI)	HR (95% CI)
KEYTRUDA + carb-pac/nabpac	52.4	7.2 (6.0–11.4)	0.56 (0.39–0.80)
Placebo + carb-pac/nabpac	70.2	5.2 (4.2–6.2)	–



KEYTRUDA + carb-pac/nabpac	103	79	49	26	13	5	0	0
Placebo + carb-pac/nabpac	104	79	40	8	4	1	0	0

PD-L1 TPS <1%

Treatment arm	Events, %	Median, months (95% CI)	HR (95% CI)
KEYTRUDA + carb-pac/nabpac	57.9	6.3 (6.16.5)	0.68 (0.47–0.98)
Placebo + carb-pac/nabpac	67.7	5.3 (4.4–6.2)	–



KEYTRUDA + carb-pac/nabpac	95	78	48	16	5	0	0	0
Placebo + carb-pac/nabpac	99	71	35	11	6	1	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]

*Assessed using RECIST v1.1 by blinded, independent, central radiological review.[1]

†Kaplan-Meier estimates.[1]

carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; CI, confidence interval; HR, hazard ratio; PD-L1, programmed death-ligand 1; PFS, progression-free survival; 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 supplementary appendix). **2.** Paz-Ares L, *et al.* KEYNOTE-407: Phase 3 study of carboplatin-paclitaxel/nab-paclitaxel with or without pembrolizumab for metastatic squamous NSCLC. ASCO. 1–5 June 2018. Chicago, USA. Oral presentation.

KEYNOTE-407: Exploratory analysis – PFS by PD-L1 TPS (5-year update)*†[1]

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

PD-L1 TPS ≥50%

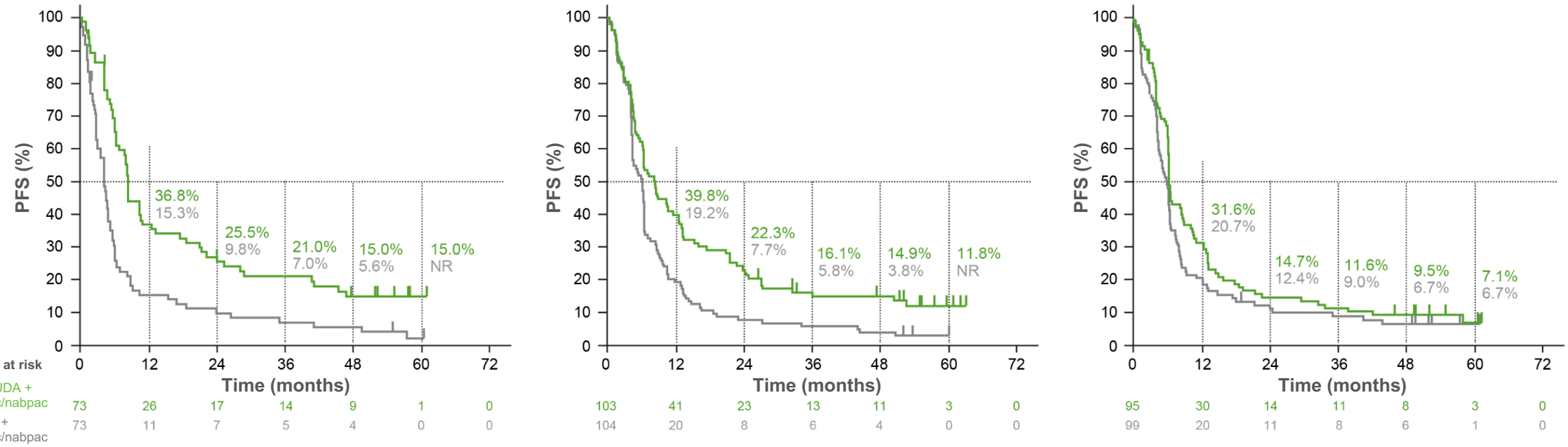
Treatment group	Events, %	Median, months (95% CI)	HR (95% CI)	5-year PFS rate, % (95% CI)†
KEYTRUDA + carb-pac/nabpac	60 (82.2)	8.3 (6.2–10.7)	0.48 (0.33–0.69)	15.0 (7.8–24.4)
Placebo + carb-pac/nabpac	70 (95.9)	4.2 (2.9–4.8)		NR

PD-L1 TPS 1–49%

Events, %	Median, months (95% CI)	HR (95% CI)	5-year PFS rate, % (95% CI)†
89 (86.4)	8.2 (6.2–11.4)	0.60 (0.45–0.81)	11.8 (6.1–19.6)
101 (97.1)	6.0 (4.2–6.2)		NR

PD-L1 TPS <1%

Events, %	Median, months (95% CI)	HR (95% CI)	5-year PFS rate, % (95% CI)†
87 (91.6)	6.3 (6.1–8.5)	0.70 (0.52–0.95)	7.1 (2.6–14.6)
91 (91.9)	5.9 (4.4–6.2)		6.7 (2.8–13.1)



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

Data cut-off date: 23 February 2022.[1]

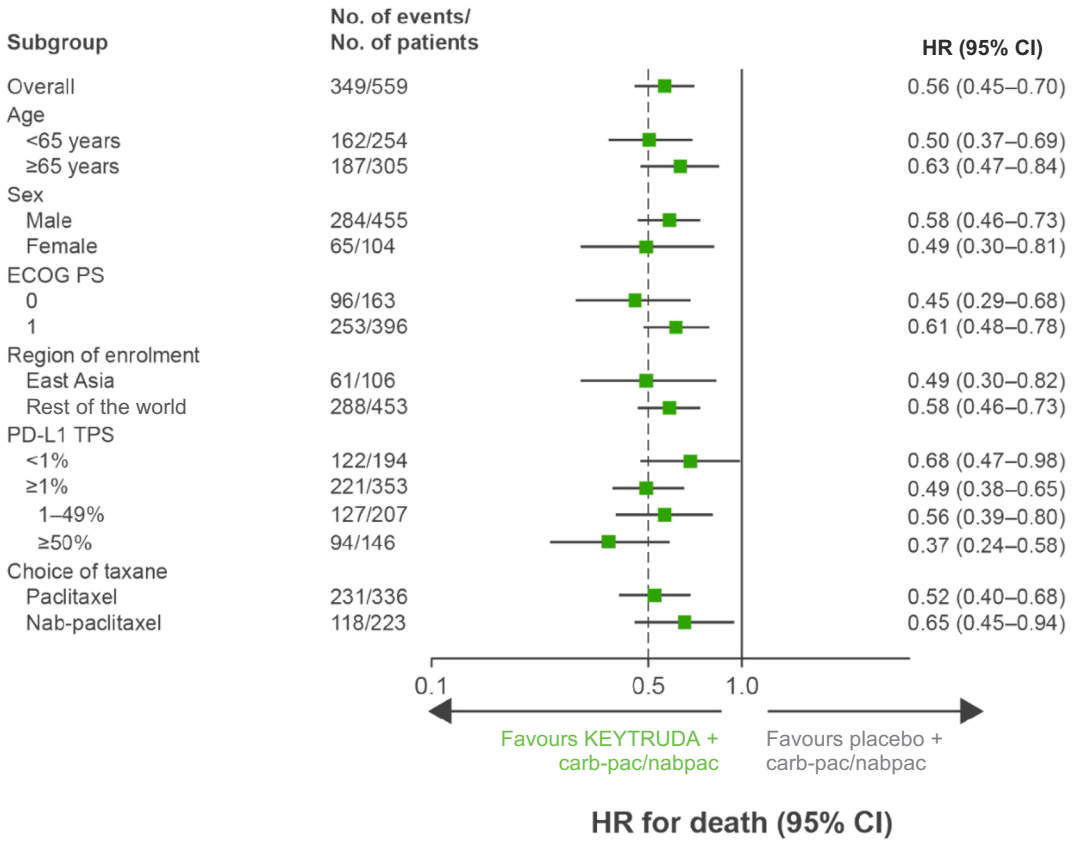
*Kaplan-Meier estimates.[1] †Assessed using RECIST v1.1 by blinded, independent, central review.[1]

carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; CI, confidence interval; HR, hazard ratio; NR, not reported; PD-L1, programmed death-ligand 1; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours; TPS, tumour proportion score.

1. Novello S, *et al. J Clin Oncol* 2023;41:1999–2006.

KEYNOTE-407: Exploratory endpoint – PFS in key subgroups (original analysis)*[1]

Median follow-up: 7.8 months. No statistical conclusions can be drawn from exploratory endpoints.



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

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

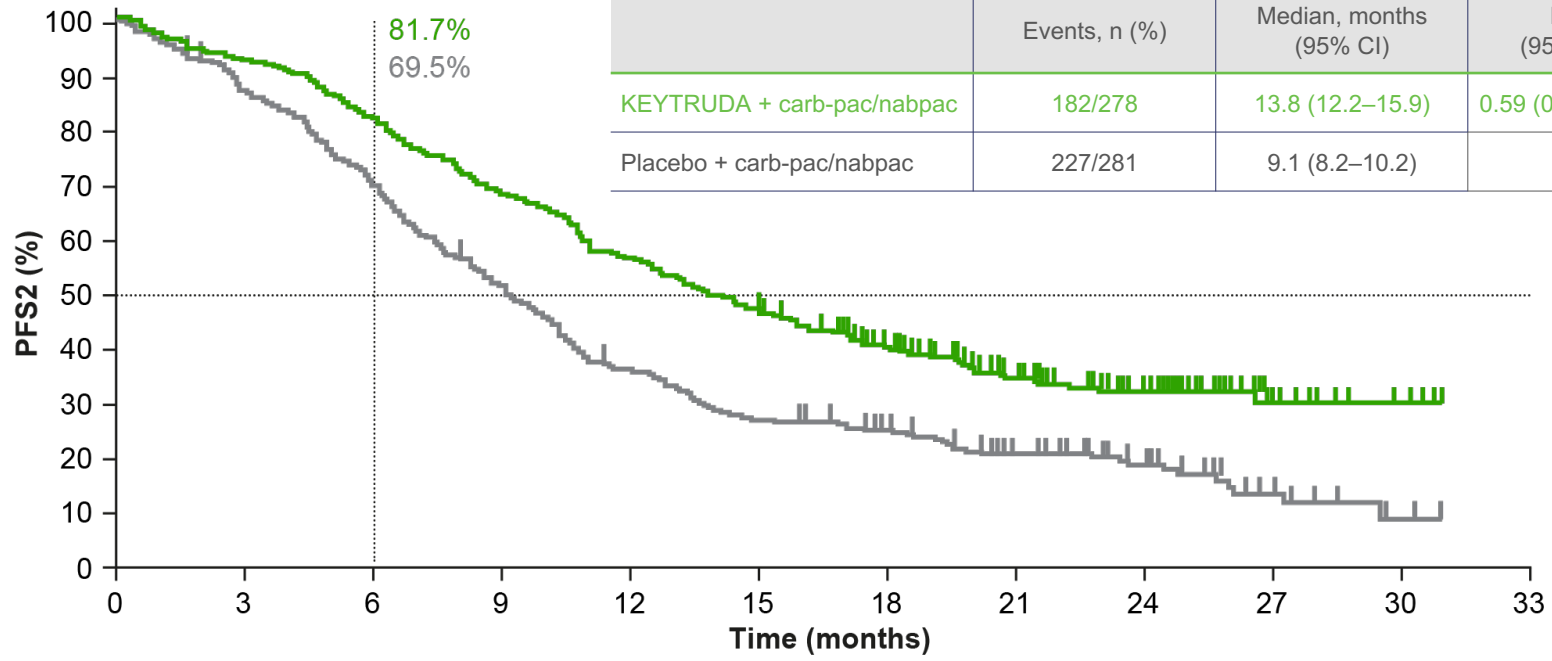
*Assessed using RECIST v1.1 by blinded, independent, central radiological review.[1]

carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; PD-L1, programmed death-ligand 1; PFS, progression-free survival; 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.

KEYNOTE-407: Exploratory analysis – PFS2 (updated analysis)*†‡[1,2]

Median follow-up: 14.3 months. No statistical conclusions can be drawn from this analysis.



	Events, n (%)	Median, months (95% CI)	HR (95% CI)
KEYTRUDA + carb-pac/nabpac	182/278	13.8 (12.2–15.9)	0.59 (0.49–0.72)
Placebo + carb-pac/nabpac	227/281	9.1 (8.2–10.2)	–

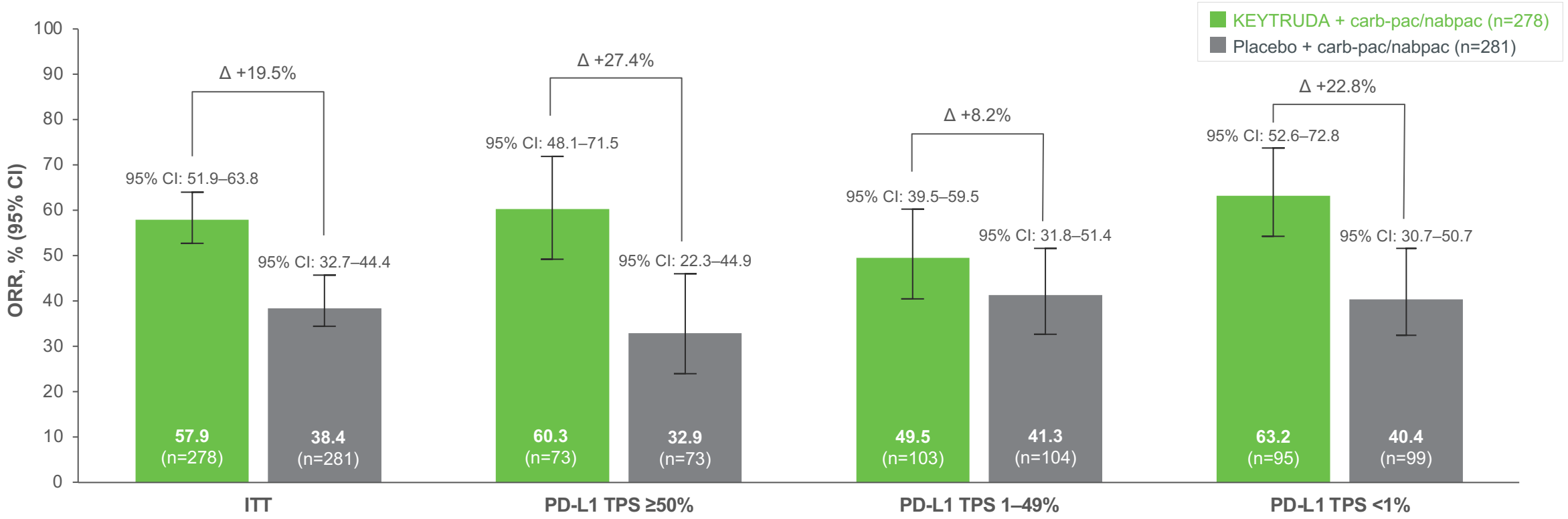
Number at risk												
KEYTRUDA + carb-pac/nabpac	278	256	227	189	157	127	98	67	39	10	4	0
Placebo + carb-pac/nabpac	281	241	193	142	99	74	62	42	24	9	2	0

Adapted from Paz-Ares L, *et al*. 2020 & Paz-Ares L, *et al.* 2019.[1,2]

Data cut-off date: 9 May 2019.[1]
*Assessed using RECIST v1.1 by investigator review.[1]
†Kaplan-Meier estimate.[1]
‡Defined as the time from randomisation to second or subsequent tumour progression on next line of treatment or death.[1]
carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; CI, confidence interval; HR, hazard ratio; PFS2; progression after second-line therapy; RECIST, Response Evaluation Criteria in Solid Tumours.
1. Paz-Ares L, *et al. J Thorac Onco* 2020;15:1657–1669. **2.** Paz-Ares L, *et al.* Pembrolizumab Plus Platinum-Based Chemotherapy for Metastatic NSCLC: Tissue TMB (tTMB) and Outcomes in KEYNOTE-021, 189, and 407 ESMO. 27 September – 1 October 2019. Barcelona, Spain. Oral presentation.

KEYNOTE-407: ORR in the ITT population and exploratory endpoint of ORR by PD-L1 TPS (original analysis)*†[1]

Median follow-up: 7.8 months. ORR was not subject to statistical testing at IA2 – no statistical conclusions can be drawn.



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

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

*At the first interim analysis (cut-off date: 27 October 2017), the response rate was formally tested and shown to be significantly higher in the KEYTRUDA + carb-pac/nabpac group of 101 patients (58.4% [95% CI: 48.2–68.1%]) than in the placebo + carb-pac/nabpac group of 103 patients (35.0% [95% CI: 25.8–45.0%]), p<0.001.[1]

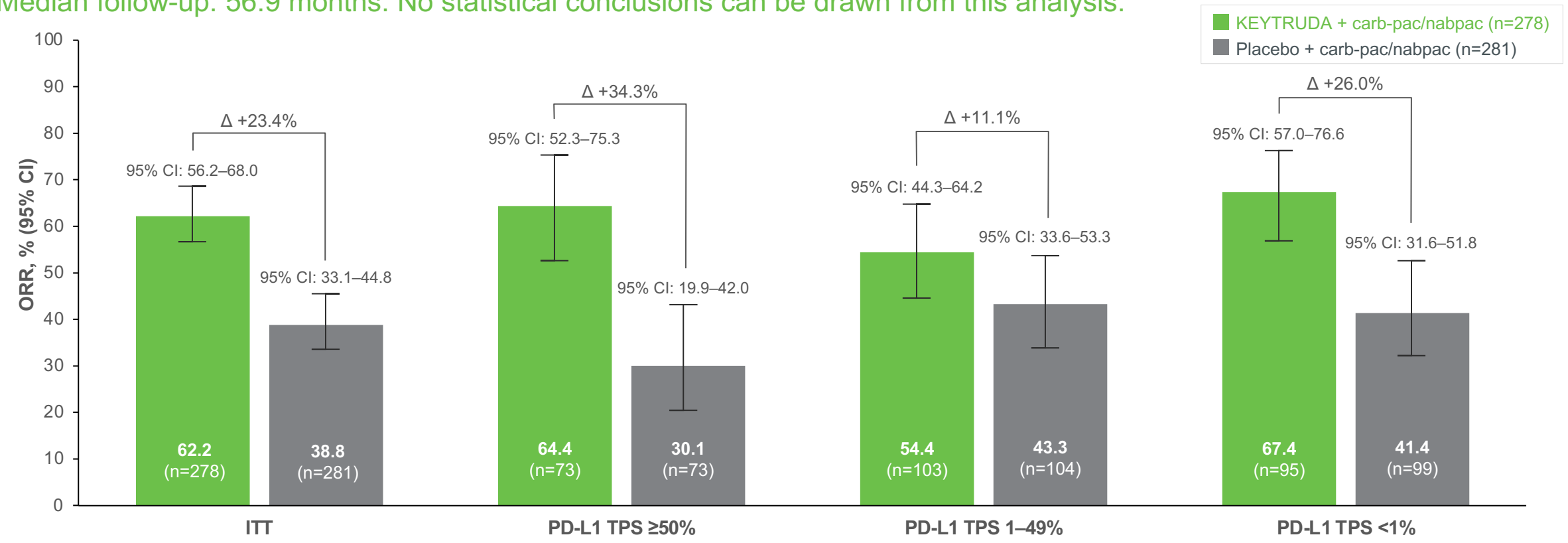
†Assessed using RECIST v1.1 by blinded, independent, central radiological review.[1]

carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; CI, confidence interval; IA, interim analysis; ITT, intention-to-treat; ORR, objective response rate; PD-L1, programmed death-ligand 1; 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 supplementary appendix).

KEYNOTE-407: Exploratory analysis – ORR in the ITT population and exploratory endpoint ORR by PD-L1 TPS (5-year update)*[1]

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



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

Data cut-off date: 23 February 2022.[1]

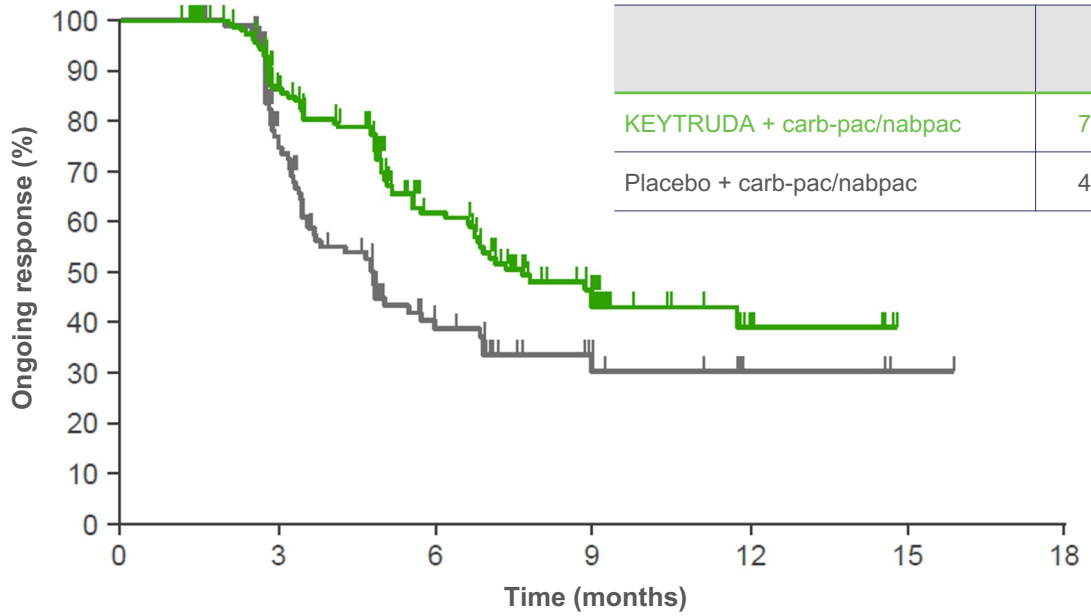
*Assessed using RECIST v1.1 by blinded, independent, central review.[1]

T carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; CI, confidence interval; ITT, intention-to-treat; ORR, objective response rate; PD-L1, programmed death-ligand 1; RECIST, Response Evaluation Criteria in Solid Tumours; TPS, tumour proportion score.

1. Novello S, *et al. J Clin Oncol* 2023;41:1999–2006.

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

Median follow-up: 7.8 months. No statistical conclusions can be drawn from this analysis.



	Median, months (95% CI)
KEYTRUDA + carb-pac/nabpac	7.7 (1.1+ to 14.7+)
Placebo + carb-pac/nabpac	4.8 (1.3+ to 15.8+)

Number at risk

KEYTRUDA + carb-pac/nabpac	161	120	65	27	5	0	0
Placebo + carb-pac/nabpac	108	69	25	10	3	1	0

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

Data cut-off date: 3 April 2018.[1]
*Kaplan-Meier estimate.[1]
†+ denotes a response that was ongoing at the analysis cut-off date.[1]
‡Assessed using RECIST v1.1 by blinded, independent, central review.[1]
carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; CI, confidence interval; DOR, duration of response; ITT, intention-to-treat; RECIST, Response Evaluation Criteria in Solid Tumours.

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

KEYNOTE-407: Exploratory analysis – DOR in the ITT population and exploratory endpoint of DOR by PD-L1 TPS (5-year update)*†[1]

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

	ITT		PD-L1 TPS ≥50%		PD-L1 TPS 1–49%		PD-L1 TPS <1%	
	KEYTRUDA + carb-pac/nabpac	Placebo + carb-pac/nabpac	KEYTRUDA + carb-pac/nabpac	Placebo + carb-pac/nabpac	KEYTRUDA + carb-pac/nabpac	Placebo + carb-pac/nabpac	KEYTRUDA + carb-pac/nabpac	Placebo + carb-pac/nabpac
DOR Median, months (95% CI)	9.0 (1.3+ to 61.5+)	4.9 (1.3+ to 58.6+)	10.4 (2.7 to 59.4+)	4.6 (1.3+ to 58.6+)	11.1 (1.3+ to 61.5+)	4.8 (2.0 to 58.6+)	6.9 (1.4+ to 58.9+)	5.7 (1.4+ to 55.8+)

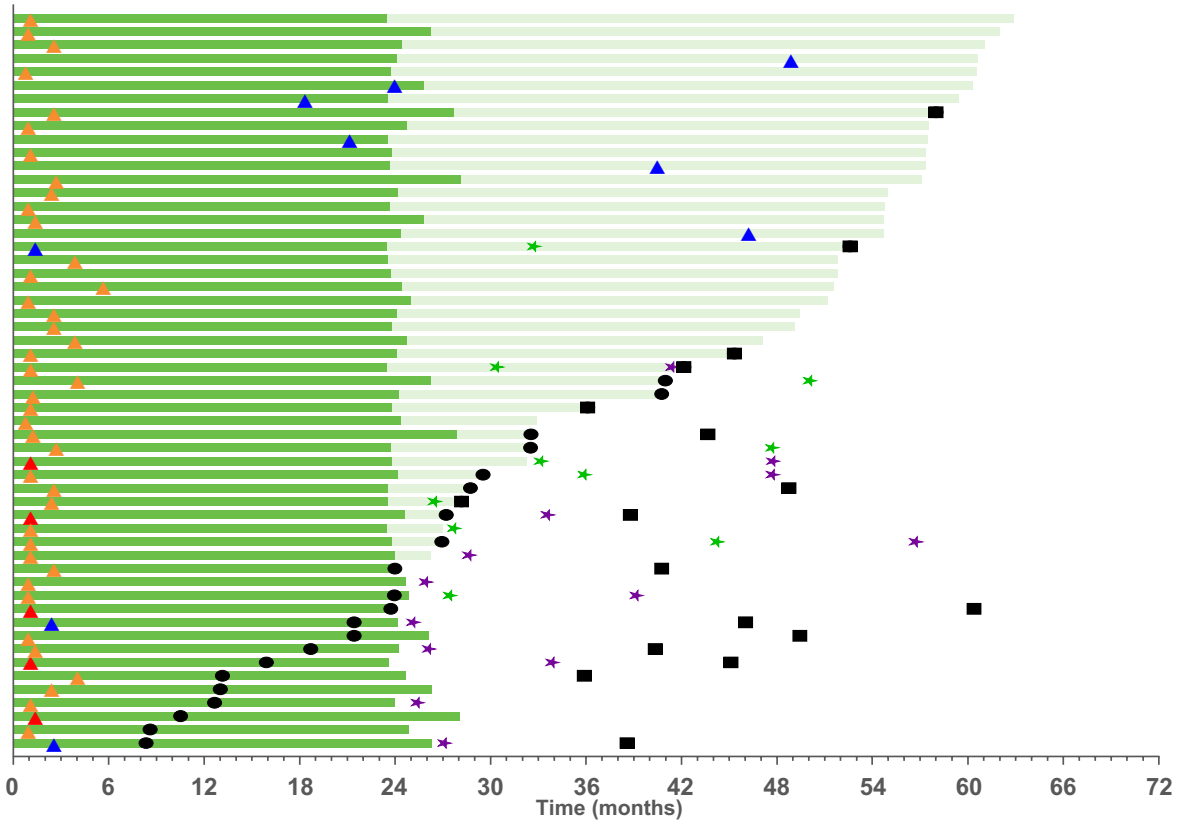
Adapted from Novello S, *et al.* 2023.[1]

Data cut-off date: 23 February 2022.[1]
*Assessed using RECIST v1.1 by blinded, independent, central review.[1]
†Kaplan-Meier estimates.[1]
carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; CI, confidence interval; DOR, duration of response; ITT, intention-to-treat; PD-L1, programmed death-ligand 1; RECIST, Response Evaluation Criteria in Solid Tumours; TPS, tumour proportion score.

1. Novello S, *et al. J Clin Oncol* 2023;41:1999–2006.

KEYNOTE-407: 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=55)
ORR (95% CI),* %	90.9 (80.0–97.0)
Best overall response, n (%)	
CR	9 (16.4)
PR	41 (74.5)
Median DOR (range),† mo	NR (7.1 to 61.5+)
3-year OS rate after completing 35 cycles‡	69.5%
Alive without PD or subsequent therapy, n (%)	24 (43.6)

Adapted from Novello S, *et al.* 2023 & Novello S, *et al.* 2022.[1,2]

Data cut-off date: 23 February 2022.[1]
*Assessed using RECIST v1.1 by blinded, independent, central review.[2]
†Kaplan-Meier estimates.[1] ‡Approximately 5 years after randomisation.[2]
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. Novello S, *et al. J Clin Oncol* 2023;41:1999–2006. **2.** Novello S, *et al.* 5-Year Update From KEYNOTE-407: Pembrolizumab Plus Chemotherapy in Squamous Non–Small-Cell Lung Cancer. ESMO. 9–13 September 2022. Paris, France. Oral presentation.

KEYNOTE-407: Exposure to study treatment (original analysis)[1]

Median follow-up: 7.8 months.

n (%)*	KEYTRUDA + carb-pac/nabpac (n=278)	Placebo + carb-pac/nabpac (n=280)
Treatment duration, months, mean (SD)	6.3 (4.1)	4.7 (3.5)
Treatment cycles		
Mean (SD)	9.3 (5.8)	7.3 (5.0)
Median (range)	8 (1–27)	6 (1–27)
4 doses of carboplatin	219 (78.8)	205 (73.2)
4 doses of paclitaxel	133/169 (78.7)	119/167 (71.3)
5–11 doses of nab-paclitaxel	72/109 (66.1)	73/113 (64.6)
12 doses of nab-paclitaxel	25/109 (22.9)	24/113 (21.2)
≥5 doses of KEYTRUDA or placebo	214 (77.0)	189 (67.5)

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

Data cut-off date: 3 April 2018.[1]
*Unless otherwise stated.[1]
carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; SD, standard deviation.
1. 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. 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: Summary of AEs in all treated patients (5-year update)[1,2]

Median follow-up: 56.9 months.

Adverse event, n (%)	All treated patients: KEYTRUDA + carb-pac/nabpac (n=278)	All treated patients: Placebo + carb-pac/nabpac (n=280)	35 cycles of KEYTRUDA (n=55)
Any	274 (98.6)	275 (98.2)	55 (100)
Grade 3–5	208 (74.8)	196 (70.0)	35 (63.6)
Led to treatment discontinuation*			
Any treatment	80 (28.8)	37 (13.2)	3 (5.5)
All treatments	48 (17.3)	21 (7.5)	0
Led to death	32 (11.5)	20 (7.1)	0
Immune-mediated AEs and infusion reactions†	99 (35.6)	26 (9.3)	21 (38.2)
Grade 3–5	37 (13.3)	9 (3.2)	1 (1.8)‡

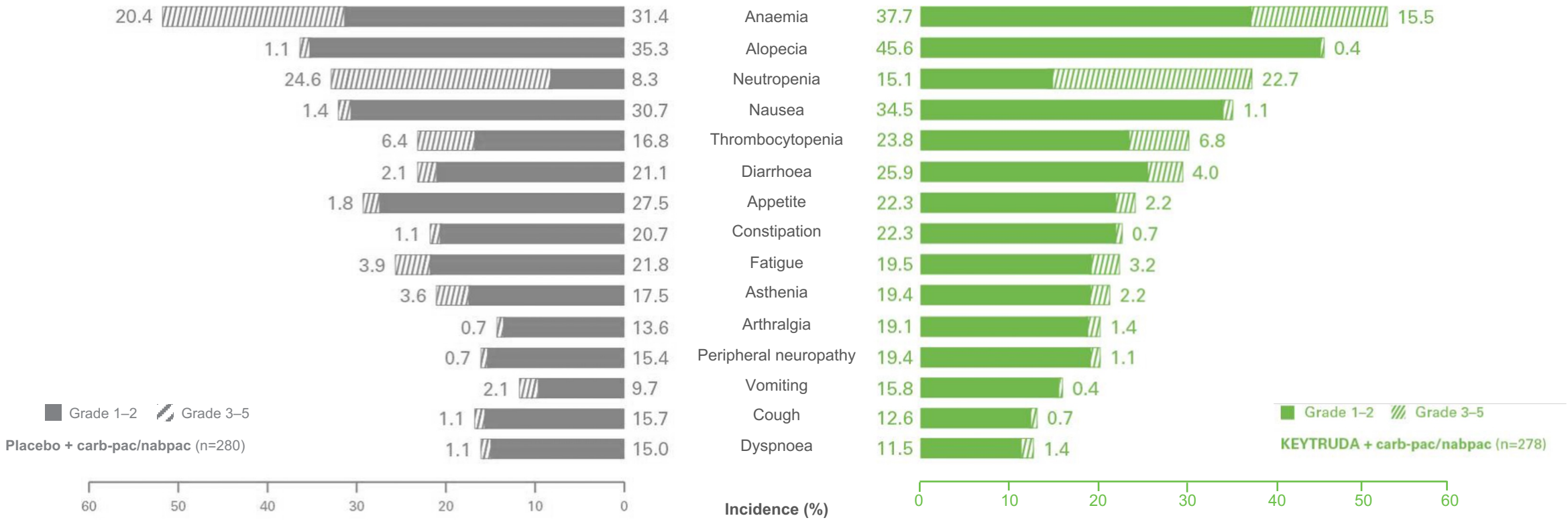
Adapted from Novello S, *et al.* 2023 & Novello S, *et al.* 2022.[1,2]

Data cut-off date: 23 February 2022.[1]
*Includes patients who discontinued KEYTRUDA or placebo, carboplatin and taxane owing to an AE at any time, and patients who discontinued KEYTRUDA or placebo owing to an AE after completing four 3-week cycles of carboplatin and taxane.[1]
†Events considered regardless of attribution to treatment or immune relatedness by the investigator.[1]
‡There was one Grade 3 event of colitis; there were no Grade 4 or Grade 5 immune-mediated AEs or infusion reactions among patients who completed 35 cycles of KEYTRUDA.[1]
AE, adverse event; carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel.

1. Novello S, *et al. J Clin Oncol* 2023;41:1999–2006. **2.** Novello S, *et al.* 5-Year Update From KEYNOTE-407: Pembrolizumab Plus Chemotherapy in Squamous Non–Small-Cell Lung Cancer. ESMO. 9–13 September 2022. Paris, France. Oral presentation.

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

Median follow-up: 7.8 months.



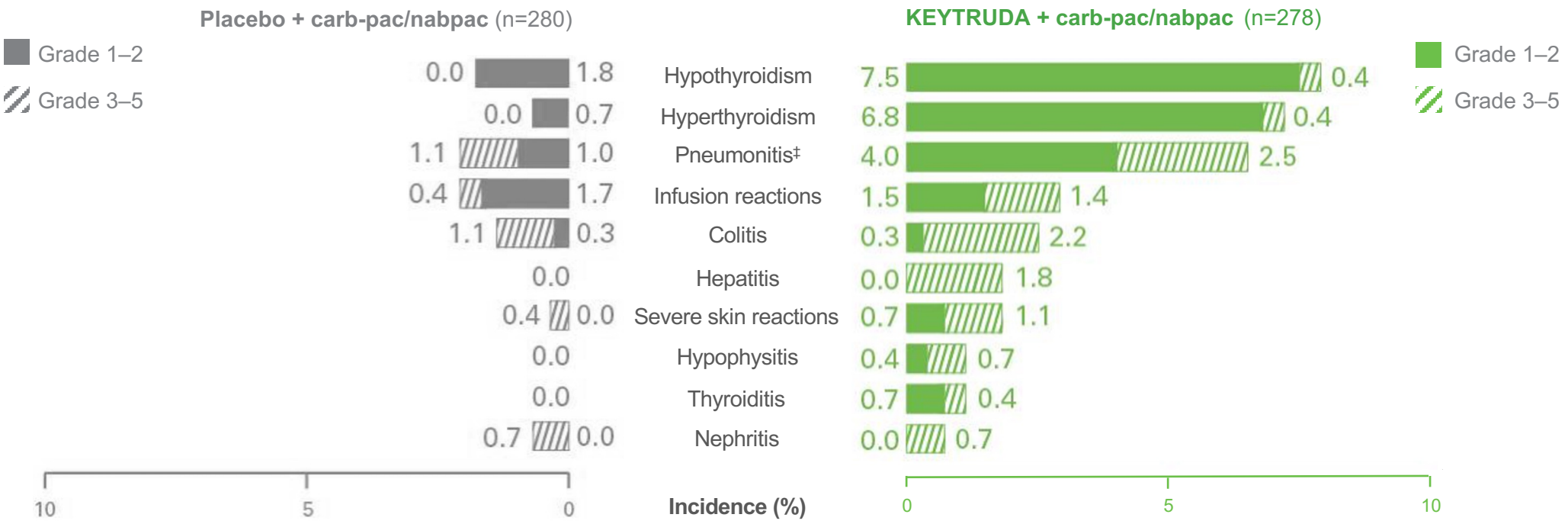
Adapted from Paz-Ares L, *et al.* 2018.[1]

Data cut-off date: 3 April 2018.
*AEs that occurred during crossover from the placebo + carb-pac/nabpac 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.

KEYNOTE-407: Exploratory endpoint – QLQ-C30 completion and compliance rates*†[1]

Median follow-up: 7.8 months. No statistical conclusions can be drawn from exploratory endpoints.

		KEYTRUDA + carb-pac/nabpac (n=276), n (%)	Placebo + carb-pac/nabpac (n=278), n (%)
Baseline		254 (92.0)	264 (95.0)
Week 3	Completion	228 (82.6)	237 (85.3)
	Compliance	228/265 (86.0)	237/266 (89.1)
Week 6	Completion	226 (81.9)	204 (73.4)
	Compliance	226/253 (89.3)	204/251 (81.3)
Week 9	Completion	187 (67.8)	199 (71.6)
	Compliance	187/233 (80.3)	199/225 (88.4)
Week 12	Completion	194 (70.3)	177 (63.7)
	Compliance	194/227 (85.5)	177/224 (79.0)
Week 15	Completion	191 (69.2)	165 (59.4)
	Compliance	191/224 (85.3)	165/201 (82.1)
Week 18	Completion	191 (69.2)	162 (58.3)
	Compliance	191/217 (88.0)	162/187 (86.6)

Adapted from Mazieres J, *et al.* 2020.[1]

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

*Completion rate was defined as the proportion of patients in the analysis population at each time point who completed ≥ one assessment.[1] †Compliance rate was defined as the percentage of patients who completed the PRO questionnaire among those who were expected to complete the instrument at each time point (e.g. those who had not discontinued study treatment).[1]

carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; PRO, patient-reported outcome; QLQ-C30, Quality of Life Questionnaire Core 30.

1. Mazieres J, *et al. J Clin Oncol* 2020;38:271–280.

KEYNOTE-407: Exploratory endpoint – QLQ-LC13 completion and compliance rates*†[1]

Median follow-up: 7.8 months. No statistical conclusions can be drawn from exploratory endpoints.

		KEYTRUDA + carb-pac/nabpac (n=275), n (%)	Placebo + carb-pac/nabpac (n=278), n (%)
Baseline		252 (91.6)	263 (94.6)
Week 3	Completion	227 (82.5)	237 (85.3)
	Compliance	227/265 (85.7)	237/266 (89.1)
Week 6	Completion	226 (82.2)	204 (73.4)
	Compliance	226/253 (89.3)	204/251 (81.3)
Week 9	Completion	187 (68.0)	197 (70.9)
	Compliance	187/233 (80.3)	197/225 (87.6)
Week 12	Completion	192 (69.8)	175 (62.9)
	Compliance	192/227 (84.6)	175/224 (78.1)
Week 15	Completion	191 (69.5)	164 (59.0)
	Compliance	191/224 (85.3)	164/201 (81.6)
Week 18	Completion	191 (69.5)	162 (58.3)
	Compliance	191/217 (88.0)	162/187 (86.6)

Adapted from Mazieres J, *et al.* 2020.[1]

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

*Completion rate was defined as the proportion of patients in the analysis population at each time point who completed ≥ one assessment.[1] †Compliance rate was defined as the percentage of patients who completed the PRO questionnaire among those who were expected to complete the instrument at each time point (e.g. those who had not discontinued study treatment).[1]

carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; PRO, patient-reported outcome; QLQ-LC13, Quality of Life Questionnaire Lung Cancer 13.

1. Mazieres J, *et al. J Clin Oncol* 2020;38:271–280.

KEYNOTE-407: Exploratory endpoint – change from baseline to Weeks 9 and 18 in EORTC QLQ-C30 GHS/QoL scores[1]

Median follow-up: 7.8 months. No statistical conclusions can be drawn from exploratory endpoints.

	KEYTRUDA + carb-pac/nabpac (n=276)	Placebo+ carb-pac/nabpac (n=278)
Baseline, mean (SD)	n=254 63.9 (20.4)	n=264 62.7 (21.3)
Week 9, mean (SD)	n=187 66.0 (18.5)	n=199 62.1 (19.6)
Change from baseline to Week 9,*† LS mean (95% CI)	n=276 1.8 (-0.9–4.4)	n=278 -1.8 (-4.4–0.7)
Difference in LS mean between treatment groups (95% CI)	3.6 (0.3–6.9) p=0.0337‡	
Week 18, mean (SD)	n=191 68.9 (19.3)	n=162 65.2 (17.1)
Change from baseline to Week 18,*† LS mean (95% CI)	n=276 4.3 (1.7–6.9)	n=278 -0.6 (-3.3–2.2)
Difference in LS mean between treatment groups (95% CI)	4.9 (1.4–8.3) p=0.0060‡	

Adapted from Mazieres J, *et al.* 2020.[1]

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

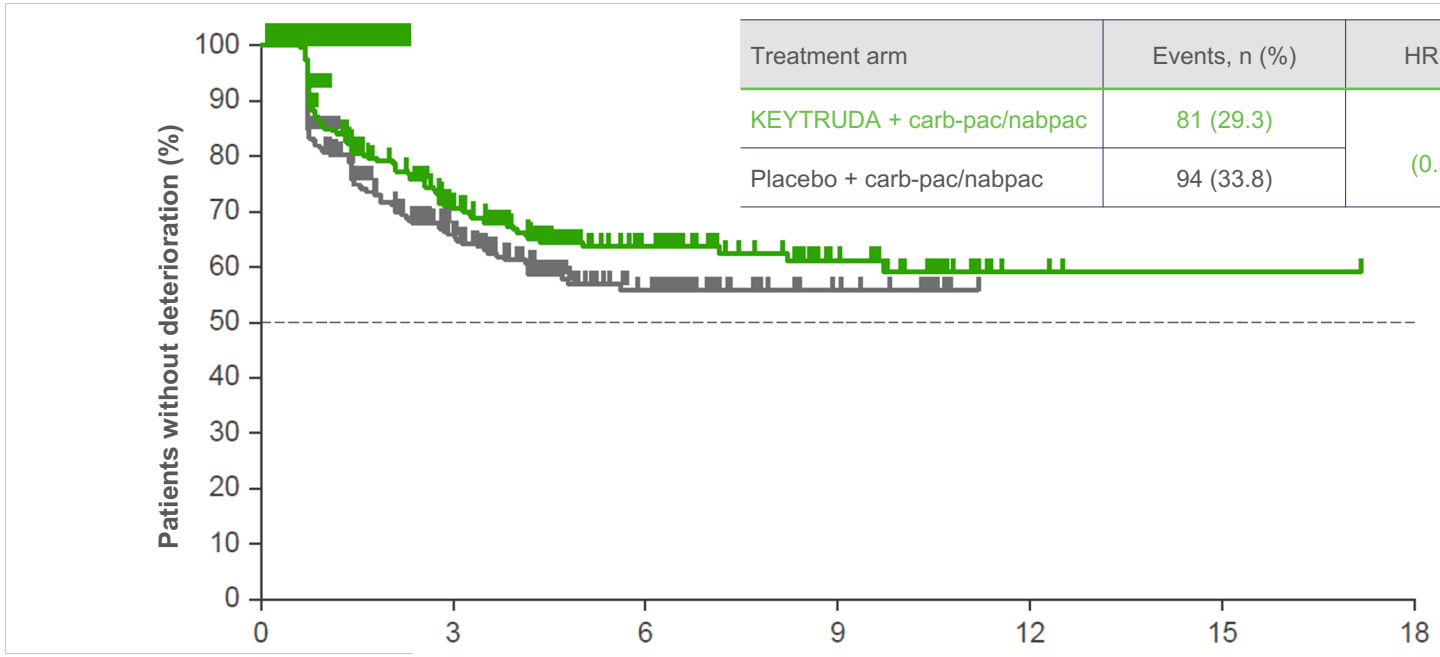
*Key PRO endpoint.[1] †Based on cLDA model with EORTC QLQ-C30 GHS/QoL scores as the response variable and treatment-by-study-visit interaction, and randomisation stratification factors as covariates.[1] ‡P values are 2-sided and nominal.[1]

carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; CI, confidence interval; cLDA, Constrained longitudinal data analysis; EORTC, European Organisation for Research and Treatment of Cancer; GHS, global health status; LS, least squares; PRO, patient-reported outcome; QLQ-C30, Quality of Life Questionnaire Core 30; SD, standard deviation.

1. Mazieres J, *et al. J Clin Oncol* 2020;38:271–280.

KEYNOTE-407: Exploratory endpoint – time to deterioration in composite endpoint of cough, chest pain or dyspnoea*[1]

Median follow-up: 7.8 months. No statistical conclusions can be drawn from exploratory endpoints.



Treatment arm	Events, n (%)	HR (95% CI)	P value
KEYTRUDA + carb-pac/nabpac	81 (29.3)	0.79 (0.58–1.06)	0.125†
Placebo + carb-pac/nabpac	94 (33.8)		

Number at risk

KEYTRUDA + carb-pac/nabpac	276	139	78	32	3	1	0
Placebo + carb-pac/nabpac	278	121	49	16	0	0	0

Adapted from Mazieres J, *et al.* 2020.[1]

Data cut-off date: 3 April 2018.[1]
*Key PRO endpoint.[1] †P values are 2-sided and nominal, based on the stratified log-rank test.[1]
carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; CI, confidence interval; HR, hazard ratio; PRO, patient-reported outcome.
1. Mazieres J, *et al. J Clin Oncol* 2020;38:271–280.

KEYNOTE-407: Exploratory endpoint – EORTC QLQ-C30 GHS/QoL[1]

Median follow-up: 7.8 months. No statistical conclusions can be drawn from exploratory endpoints.

Mean QLQ-C30 GHS/QoL scores:*

- Were above baseline at all time points for the KEYTRUDA + carb-pac/nabpac group (Weeks 3–36)
  - The largest improvements were observed from Weeks 18–36
- Below baseline at all time points for the placebo + carb-pac/nabpac group (Weeks 3–36)

Changes in QLQ-C30 GHS/QoL status:

- In comparison to placebo + carb-pac/nabpac group:
  - Fewer patients reported a deterioration in GHS/QoL status (Week 9: 26.1% vs 29.5%; Week 18: 22.8% vs 31.3%) in the KEYTRUDA + carb-pac/nabpac group
  - More patients reported an improvement in GHS/QoL status (Week 9: 30.4% vs 24.5%; Week 18: 36.2% vs 27.7%) in the KEYTRUDA + carb-pac/nabpac group

Data cut-off date: 3 April 2018.[1]
*Key PRO endpoint.[1]
carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; EORTC, European Organisation for. Research and Treatment of Cancer; GHS, global health status; PRO, patient-reported outcome; QLQ-C30, Quality of Life Questionnaire Core 30; QoL, quality of life.

1. Mazieres J, *et al. J Clin Oncol* 2020;38:271–280.

KEYNOTE-407: Exploratory endpoint – EORTC QLQ-C30 functional and symptom subscale scores[1]

Median follow-up: 7.8 months. No statistical conclusions can be drawn from exploratory endpoints.

QLQ-C30 functional scales:

- Change from baseline scores were numerically superior for the KEYTRUDA + carb-pac/nabpac group vs. the placebo + carb-pac/nabpac group for all functional scales at Week 9 and Week 18
  - In the KEYTRUDA + carb-pac/nabpac group, there were minimal changes from baseline in physical, cognitive, role and social function scales at Weeks 9 and 18. Improvements in emotional functioning scores occurred at both time points in this group
  - Scores declined from baseline for physical and role functioning in the placebo + carb-pac/nabpac group at Week 9 and Week 18. Minimal changes were also reported for cognitive and social functioning, but improvements in emotional functioning occurred at both time points

QLQ-C30 symptom scales:

- Change from baseline scores improved in most scales at Week 9, with further improvements at Week 18 in both treatment groups
- At Week 9 and 18, the KEYTRUDA + carb-pac/nabpac group was numerically superior with regard to fatigue, pain, dyspnoea and insomnia, whereas the placebo + carb-pac/nabpac group was numerically superior in the nausea/vomiting, appetite loss, constipation and diarrhoea scales
- Financial difficulties were worse in KEYTRUDA + carb-pac/nabpac group at Week 9 compared to the placebo + carb-pac/nabpac; however, at Week 18 these were worse in the placebo + carb-pac/nabpac vs the KEYTRUDA + carb-pac/nabpac group

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

carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; EORTC, European Organisation for Research and Treatment of Cancer; QLQ-C30, Quality of Life Questionnaire Core 30.

1. Mazieres J, *et al. J Clin Oncol* 2020;38:271–280.

KEYNOTE-407: Efficacy and safety summary

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

Efficacy of KEYTRUDA in KEYNOTE-407[1,2]

- **At IA2,** KEYTRUDA + carb-pac/nabpac demonstrated a superior OS and PFS benefit vs placebo + carb-pac/nabpac (median follow-up: 7.8 months):[1]

  36% reduced risk of death, HR; 0.64; 95% CI: 0.49–0.85) p<0.001 (dual primary endpoint, statistically significant)

  44% reduced risk of progression, HR; 0.56; 95% CI: 0.45–0.70) p<0.001 (dual primary endpoint, statistically significant)

  - Treatment effect on OS was consistent across all PD-L1 subgroups, including the <1% and 1–49% subgroups*[1]
  - Improved ORR (57.9% vs 38.4%) and median DOR (7.7 vs 4.8 months) was observed†‡[1]

Safety profile of KEYTRUDA in KEYNOTE-407[1,2]

- KEYTRUDA + carb-pac/nabpac displayed a generally manageable tolerability profile[1]
- The frequency of AEs for the combination was observed to be higher than that for each agent alone, reflecting the contributions of each agent[1]
- Rates of discontinuation due to AEs were shown to be higher with KEYTRUDA + carb-pac/nabpac[1]
- In the 5-year follow-up, toxicity was manageable, which was consistent with previous reports[2]

In the 5-year follow-up, treatment with KEYTRUDA + carb-pac/nabpac continued to demonstrate an OS and PFS benefit vs placebo + carb-pac/nabpac (median follow-up: 56.9 months; p not tested)[2]

- Benefits were observed despite an effective crossover rate of 50.9%[2]
- OS and PFS benefits were seen irrespective of baseline PD-L1 expression[2]
- Patients who received 35 cycles of KEYTRUDA had durable responses and experienced long-term OS[2]

*PD-L1 subgroup analyses were exploratory endpoints – no statistical conclusions can be drawn.[1] †Not tested for significance – no statistical conclusions can be drawn.[1] ‡At the first interim analysis (Data cut-off date: 27 October 2017), the response rate was formally tested and shown to be significantly higher in the KEYTRUDA + carb-pac/nabpac group of 101 patients (58.4% [95% CI: 48.2–68.1%]) than in the placebo + carb-pac/nabpac group of 103 patients (35.0% [95% CI: 25.8–45.0%]), p<0.001.[1]

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

1. Paz-Ares L, *et al. N Engl J Med* 2018;379:2040–2051 (and supplementary appendix). **2.** Novello S, *et al. J Clin Oncol* 2023;41:1999–2006.

KEYNOTE-407: HRQoL summary

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

HRQoL of KEYTRUDA in KEYNOTE-407:[1]

- KEYTRUDA + carb-pac/nabpac maintained or improved QoL compared with baseline and improved QoL compared with placebo + carb-pac/nabpac[1]
- At Weeks 9 and 18, patients who received KEYTRUDA + carb-pac/nabpac had improved GHS/QoL scores compared with baseline and those who received placebo + carb-pac/nabpac[1]
- KEYTRUDA + carb-pac/nabpac showed a numerical improvement in time to deterioration in cough, chest pain or dyspnoea compared with the control group (HR: 0.79; 95% CI: 0.58–1.06; p=0.125); the median time to deterioration in this endpoint was not reached in either group[1]
- In KEYNOTE-407, the HRQoL findings, along with the improved efficacy seen in the KEYTRUDA + carb-pac/nabpac, support its use as first-line therapy for patients with metastatic squamous NSCLC[1]

carb-pac/nabpac, carboplatin and either paclitaxel or nab-paclitaxel; CI, confidence interval; GHS, global health status; HR, hazard ratio; HRQoL, health-related quality of life; NSCLC, non-small cell lung cancer; QoL, quality of life.

1. Mazieres J, *et al. J Clin Oncol* 2020;38:271–280.

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.

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.

Appendices

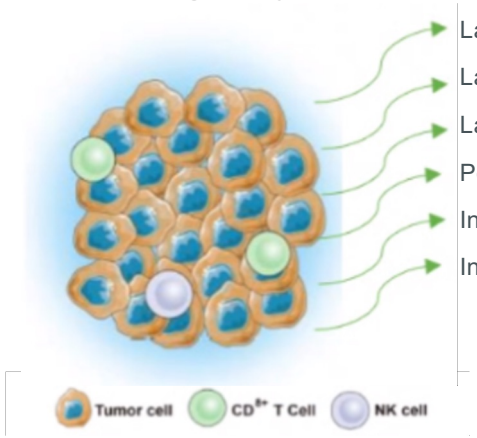
Immune checkpoint inhibitors, in combination with chemotherapy, can help improve outcomes, harnessing the patient's immune system against cancer[1]

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]

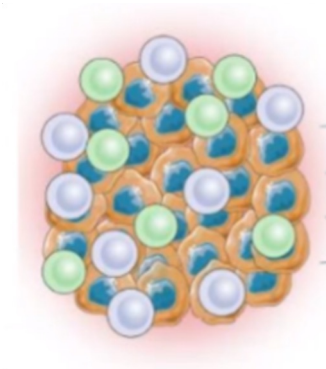
Chemotherapy, through its induction of immunogenic cell death (ICD), can turn a cold tumour into a hot tumour:
Converting a cold tumour microenvironment into a hot tumour can enable increased expression of PD-L1 and sensitise the tumour to PD-1 blockade[3,4]

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

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

AE, adverse event; DOR, duration of response; HRQoL, health-related quality of life; ITT, intent-to-treat; 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.