MSD Oncology

KEYNOTE-024: KEYTRUDA® (pembrolizumab) vs. chemotherapy for PD-L1 TPS ≥50% non-small cell lung cancer

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

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1. Garassino MC et al. J Clin Oncol 2023:41:1992–1998; 2. Novello S et al. J Clin Oncol 2023:41:1999–2006; 3. Reck M et al. J Clin Oncol 2021;39:2339–2349; 4. Jassem J, et al. J Thorac Oncol. 2021;16(11):1872-1882; 5. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available from: http://www.emcpi.com/pi/33162.

GB-PDO-03521 | Date of preparation: April 2025.

KEYTRUDA® (pembrolizumab)

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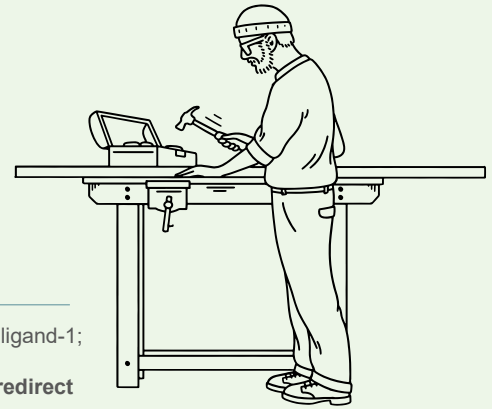
Abbreviations

Definitions of all abbreviations used in this deck can be found at the end of the presentation

KEYTRUDA® (pembrolizumab) advanced NSCLC indications[1]

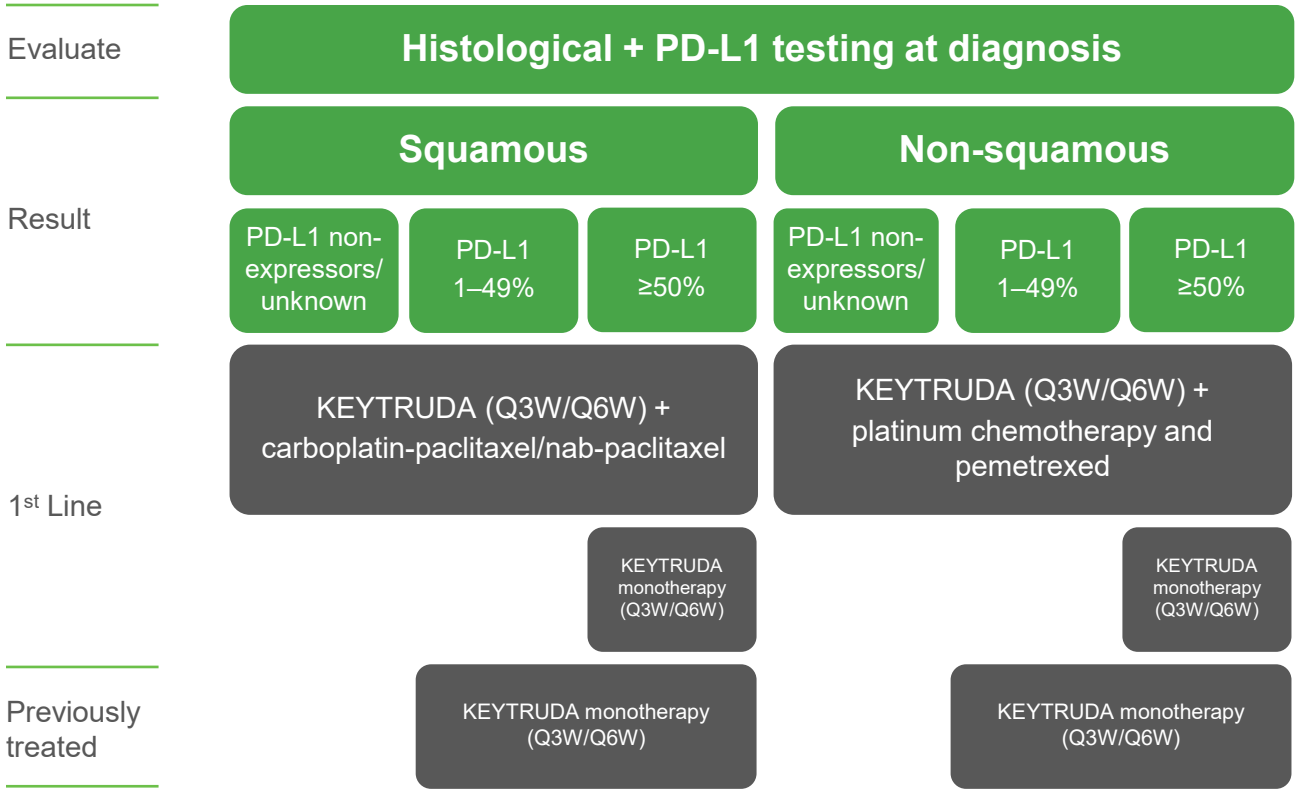
- KEYTRUDA as monotherapy is indicated for the first-line treatment of metastatic non-small cell lung carcinoma in adults whose tumours express PD-L1 with a ≥50% TPS with no *EGFR*- or *ALK*-positive tumour mutations
- KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of metastatic non-squamous non-small cell lung carcinoma 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 non-small cell lung carcinoma in adults
- KEYTRUDA as monotherapy is indicated for the treatment of locally advanced or metastatic non-small cell lung carcinoma 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 every 3 weeks or 400 mg every 6 weeks administered as an intravenous infusion over 30 minutes
- Refer to the Summary of Product Characteristics and Risk Minimisation materials available on the EMC website before prescribing in order to help reduce the risks associated with KEYTRUDA



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

1. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available from: https://www.medicines.org.uk/emc/product/2498/smpc. **Please note that clicking this link will redirect you to external websites, for which MSD does not review or control the content.**

KEYTRUDA licensed indications: Helping transform treatment expectations for patients with metastatic NSCLC[1]



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

NSCLC, non-small cell lung cancer; PD-L1, programmed death ligand-1; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available from: https://www.medicines.org.uk/emc/product/2498/smpc.

KEYNOTE-024: Definition of analyses

Analysis	Cut-off date	Slide symbol	Median follow up (range), months
Interim analysis 1 (1-year)	9 May 2016	1	11.2 (6.3–19.7)[1]
Interim analysis 2 (2-year)	10 July 2017	2	25.2 (20.4–33.7)[2]
Updated analysis (5-year)	1 June 2020	3	59.9 (55.1–68.4)[3]

1. Reck M *et al. N Engl J Med* 2016;375:1823–1833 (and supplementary appendix); 2. Reck M *et al. J Clin Oncol* 2019;37:537–546; 3. Reck M *et al. J Clin Oncol.* 2021;39(21):2339–2349.

KEYNOTE-024:

KEYTRUDA (pembrolizumab) vs. chemotherapy for PD-L1-positive non-small cell lung cancer[1,2]

1. Reck M *et al. N Engl J Med* 2016;375:1823–1833 (and supplementary appendix).
2. Reck M *et al. J Clin Oncol.* 2021;39(21):2339–2349.

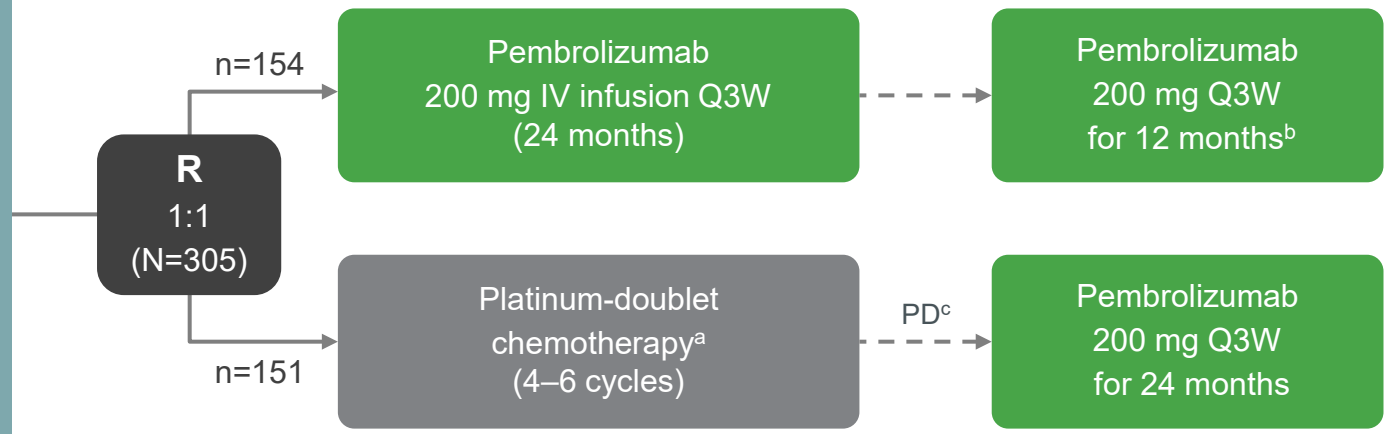
KEYNOTE-024: Study design[1,2]

Patients

- Untreated stage IV NSCLC
- PD-L1 TPS ≥50%
- ECOG PS 0–1
- No sensitising *EGFR* mutation or *ALK* translocation
- No untreated brain metastases
- No active autoimmune disease requiring systemic therapy
- No active immune ILD or pneumonitis requiring systemic therapy

Key endpoints:

- Primary: PFS (RECIST v1.1 per blinded, independent central review)
- Secondary: OS, ORR, safety
- Exploratory: DOR



Adapted from: Reck M et al. N Engl J Med 2016.

[a]Investigator's choice of chemotherapy, [b]Patients randomised to pembrolizumab who completed 2 years of therapy or who stopped pembrolizumab after achieving CR and then had PD were eligible for a second course of pembrolizumab monotherapy. [c]To be eligible for crossover, PD had to be confirmed by blinded, independent central radiology review and all safety criteria had to be met.
ALK, anaplastic lymphoma kinase; CR, complete response; DOR, duration of response; ECOG PS, Eastern Co-operative Oncology Group Performance Status; *EGFR*, epidermal growth factor receptor; ILD, interstitial lung disease; IV, intravenous; 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; R, randomised; RECIST v1.1, Response Evaluation Criteria In Solid Tumors Version 1.1; Q3W, every 3 weeks; TPS, tumour proportion score.
1. Reck M *et al. N Engl J Med* 2016;375:1823–1833 (and supplementary appendix); 2. Reck M *et al. J Clin Oncol.* 2021;39(21):2339–2349.

KEYNOTE-024: Investigator's choice of platinum-doublet chemotherapy[a,1]

For first-line therapy, non-squamous NSCLC only

- **Pemetrexed** 500 mg/m^2 on Day 1 of 21-day cycles + **Carboplatin** AUC 5 or 6 on Day 1 of 21-day cycles — n=67
- **Pemetrexed** 500 mg/m^2 on Day 1 of 21-day cycles + **Cisplatin** 75 mg/m^2 on Day 1 of 21-day cycles — n=36
- **Paclitaxel** 200 mg/m^2 on Day 1 of 21-day cycles + **Carboplatin** AUC 5 or 6 on Day 1 of 21-day cycles — n=17
- **Gemcitabine** 1,250 mg/m^2 on Days 1 and 8 of 21-day cycles + **Carboplatin** AUC 5 or 6 on Day 1 of 21-day cycles — n=20
- **Gemcitabine** 1,250 mg/m^2 on Days 1 and 8 of 21-day cycles + **Cisplatin** 75 mg/m^2 on Day 1 of 21-day cycles — n=11

Optional pemetrexed maintenance therapy 500 mg/m^2 Q3W permitted for non-squamous NSCLC

Adapted from: Reck M et al. N Engl J Med 2016 (and supplementary appendix).

[a]All chemotherapy regimens were given for up to 4–6 cycles.
AUC, area under the curve; NSCLC, non-small cell lung cancer; Q3W, every 3 weeks.
1. Reck M *et al. N Engl J Med* 2016;375:1823–1833 (and supplementary appendix).

KEYNOTE-024: Assessments and treatments[1]

Assessments:[a]

- PD-L1 expression was assessed centrally in core needle or excisional biopsies, or in resected tissue, using the Dako 22C3 platform
- Tumour imaging: scheduled every 9 weeks
- Response: RECIST v1.1 by blinded, independent, central radiologic review

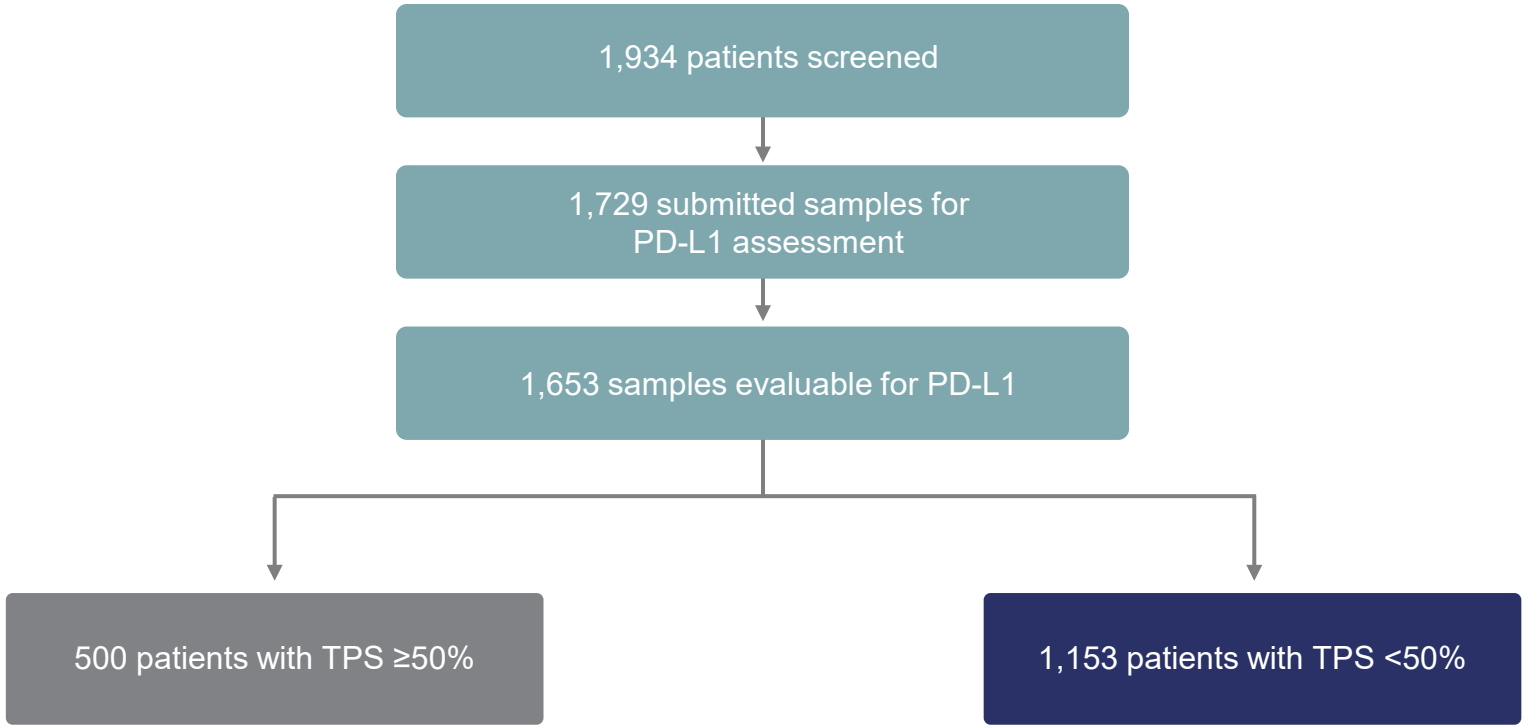
Treatment: patients with radiological PD could continue treatment if clinically stable

[a]Other assessments included: adverse events review, physical examination, vital signs, a complete blood count with a differential count, and a comprehensive blood panel were assessed every 3 weeks during treatment and at the time of treatment discontinuation; T3, free T4, and thyrotropin were assessed every 6 weeks. During the survival follow-up phase, patients were contacted every 2 months for an assessment of survival.

IHC, immunohistochemistry; PD, progressive disease; PD-L1, programmed death ligand-1; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1.

1. Reck M *et al. N Engl J Med* 2016;375:1823–1833 (and supplementary appendix).

KEYNOTE-024: PD-L1 screening[1]



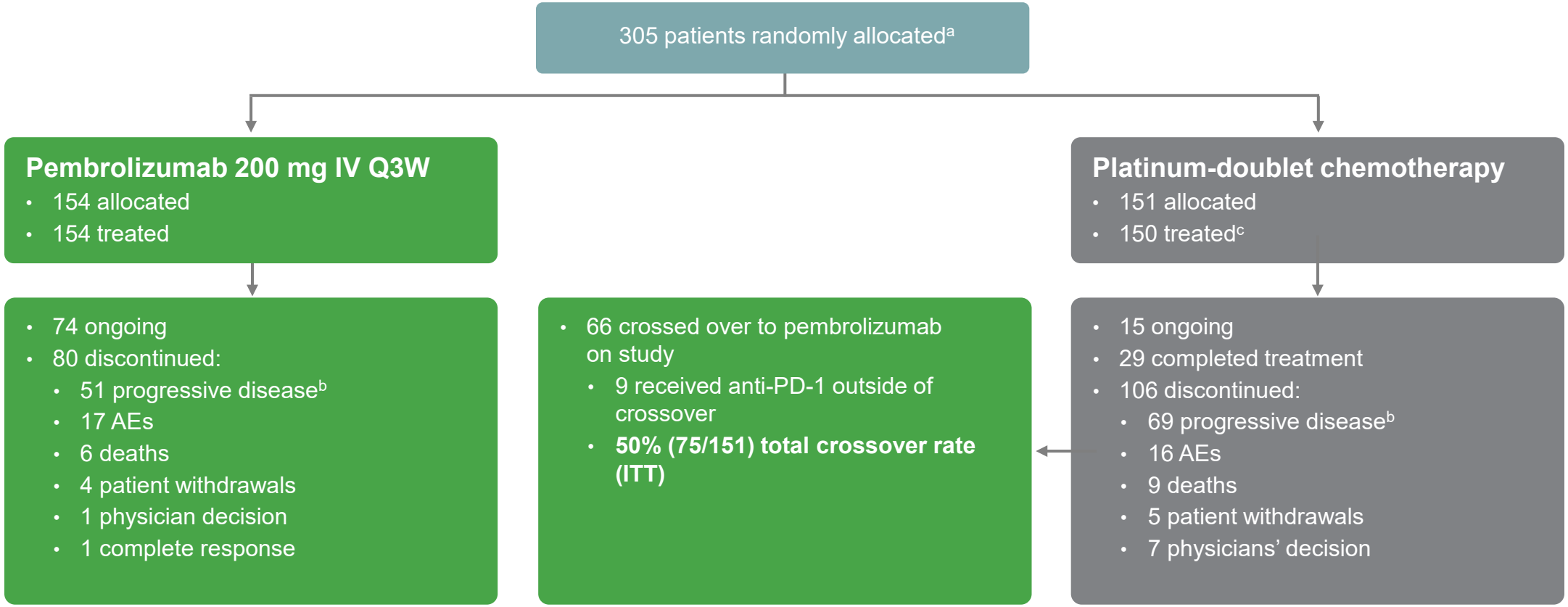
Adapted from: Reck M et al. N Engl J Med 2016.

PD-L1, programmed death ligand-1; TPS, tumour proportion score.

1. Reck M *et al. N Engl J Med* 2016;375:1823–1833 (and supplementary appendix).

KEYNOTE-024: Interim analysis 1 – Patient disposition[1,2]

Median follow up: 11.2 months



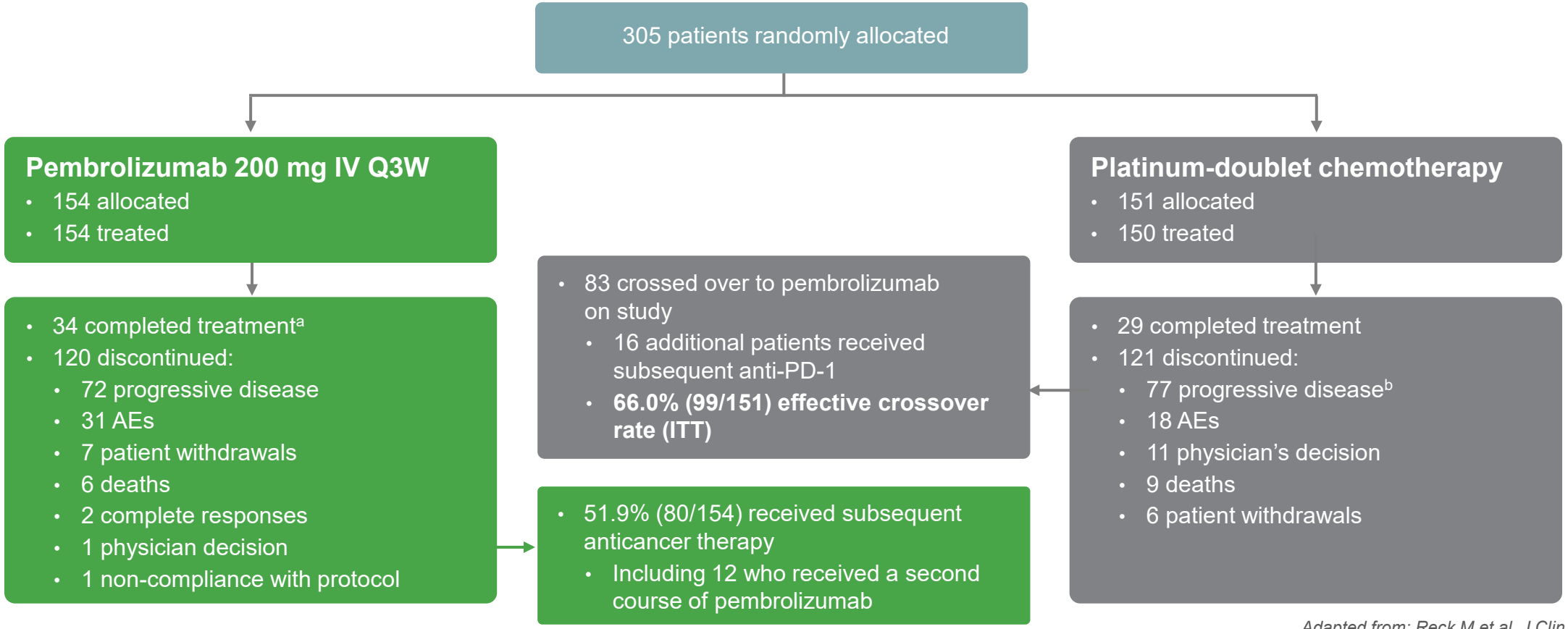
Adapted from: Reck M et al. N Engl J Med, 2016 (and supplementary appendix) and Reck M et al. ESMO 2016.

[a]Reasons for screen failure were untreated brain metastases (n=59), *EGFR* or *ALK* aberration (n=30), ECOG PS 2 or 3 (n=27), inadequate organ function (n=19), prohibited intercurrent condition (n=16), NSCLC not confirmed (n=13), and other (n=33). [b]Includes patients with clinical progression or progressive disease. [c]46 patients received pemetrexed maintenance therapy. AE, adverse event; d, days; ECOG PS, Eastern Co-operative Oncology Group Performance Status; ITT, intention to treat; IV, intravenous; PD-1, programmed death protein 1; NSCLC, non-small cell lung cancer; Q3W, every 3 weeks.

1. Reck *M et al*. Presented at the European Society for Medical Oncology (ESMO) 2016 Congress, 7–11 October, 2016, Copenhagen, Denmark; 2. Reck M *et al. N Engl J Med* 2016;375:1823–1833 (and supplementary appendix).

KEYNOTE-024: Updated analysis – Patient disposition[1]

Median follow up: 59.9 months



Adapted from: Reck M et al. J Clin Oncol. 2021.

[a]Number of patients who completed treatment, as reported by investigator.
AE, adverse event; d, days; ITT, intention-to-treat; IV, intravenous; PD-1, programmed death 1; Q3W, every 3 weeks.
1. Reck M *et al. J Clin Oncol.* 2021;39(21):2339–2349.

KEYNOTE-024: Updated analysis – Selected baseline characteristics[1]

Median follow up: 59.9 months

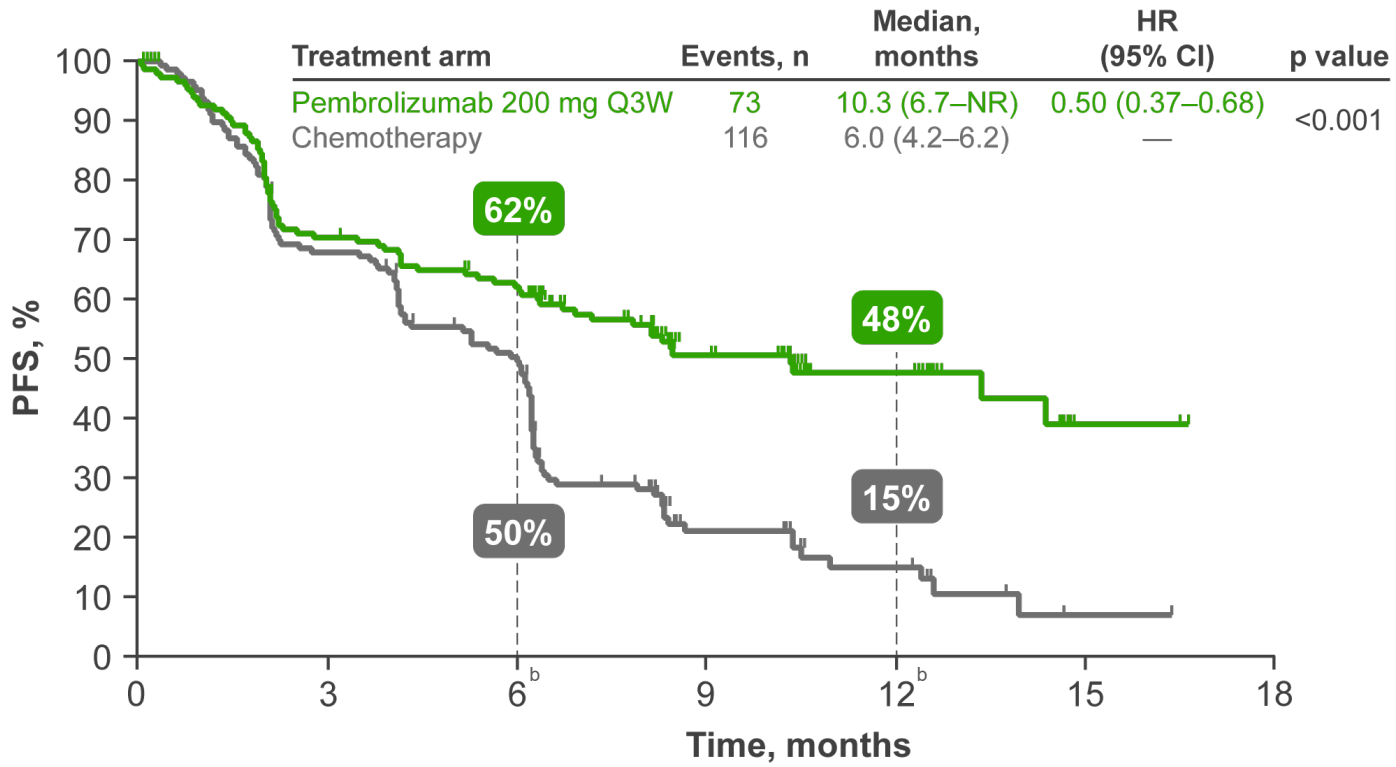
Characteristic, n (%)[a]	Pembrolizumab 200 mg Q3W (n=154)	Chemotherapy (n=151)	35 cycles (2 years) of pembrolizumab (n=39)[c]	Second course of pembrolizumab (n=12)[d]
Age, median (range), years	64.5 (33–90)	66.0 (38–85)	61.0 (43–80)	60.0 (43–77)
Male	92 (59.7)	95 (62.9)	25 (64.1)	8 (66.7)
ECOG PS 1	99 (64.3)	98 (64.9)	23 (59.0)	9 (75.0)
Enrolled in East Asia	21 (13.6)	19 (12.6)	8 (20.5)	3 (25.0)
Squamous histology	29 (18.8)	27 (17.9)[b]	2 (5.1)	1 (8.3)
Current/former smoker	149 (96.8)	132 (87.4)	37 (94.9)	12 (100.0)
Treated brain metastases	18 (11.7)	10 (6.6)	9 (23.1)	1 (8.3)
Prior neoadjuvant therapy	3 (1.9)	1 (0.7)	0	0
Prior adjuvant therapy	6 (3.9)	3 (2.0)	0	0

Adapted from: Reck M et al. J Clin Oncol. 2021.

[a]Unless otherwise stated. [b]Includes patients with squamous cell carcinoma and poorly differentiated squamous cell carcinoma. [c]Only includes patients who were initially allocated to pembrolizumab who received 35 cycles of pembrolizumab according to actual exposure assessment. [d]Only includes patients initially allocated to pembrolizumab who received a second course of pembrolizumab therapy according to actual exposure assessment.
ECOG PS, Eastern Cooperative Oncology Group Performance Status; Q3W, every 3 weeks.
1. Reck M *et al. J Clin Oncol.* 2021;39(21):2339–2349.

KEYNOTE-024: Interim analysis 1 – 1-year landmark PFS[a,1,2]

Median follow up: 11.2 months



No. at risk							
Pembrolizumab 200 mg Q3W	154	104	89	44	22	3	1
Chemotherapy	151	99	70	18	9	1	0

KEYTRUDA monotherapy demonstrated a **superior PFS benefit** vs. platinum-based chemotherapy with a 50% reduced risk of progression or death (HR 0.50, P<0.001)[1,2]

Adapted from: Reck M et al. ESMO 2016 and Reck M et al. N Engl J Med, 2016.

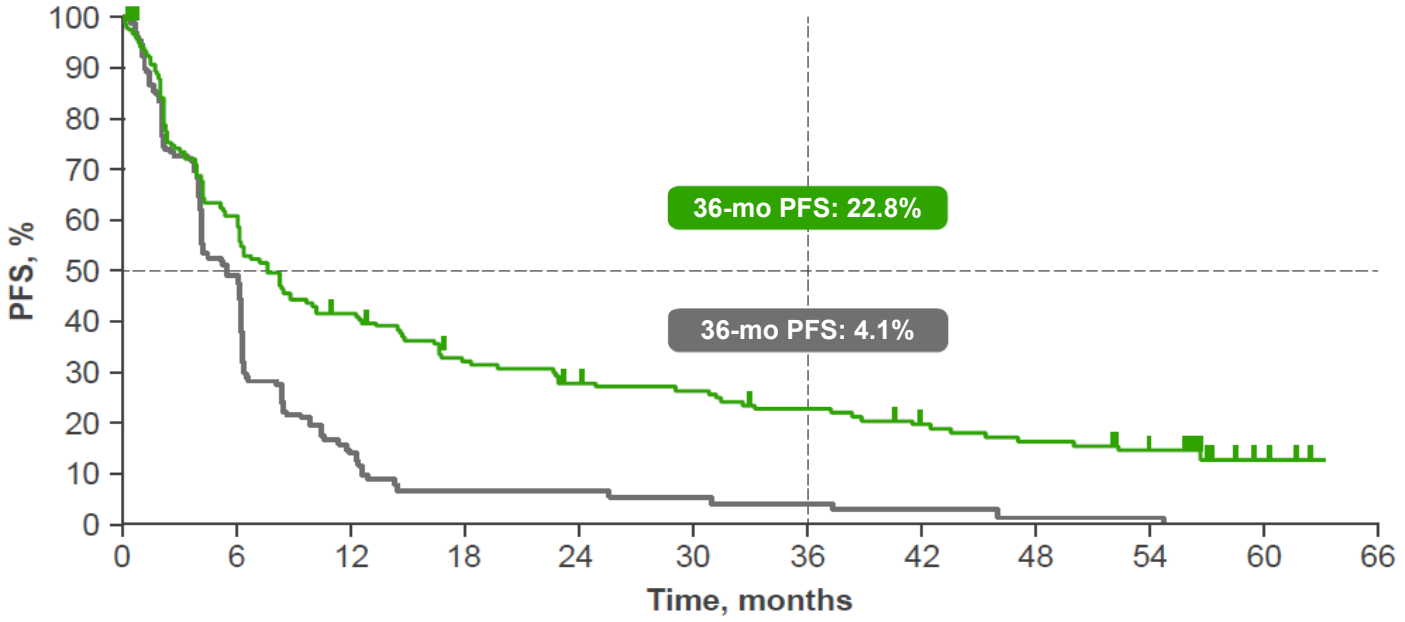
[a]Assessed per RECIST v1.1 by blinded, independent central review. [b]The estimated percentage of patients who were alive and had no disease progression at 6 or 12 months.
CI, confidence interval; HR, hazard ratio; NR, not reached; PFS, progression-free survival; Q3W, every 3 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1.

1. Reck *M et al*. Presented at the European Society for Medical Oncology (ESMO) 2016 Congress, 7–11 October, 2016, Copenhagen, Denmark; 2. Reck M *et al. N Engl J Med* 2016;375:1823–1833 (and supplementary appendix).

KEYNOTE-024: Updated analysis – 5-year median PFS[a,b,1]

Median follow up: 59.9 months

Treatment arm	Events, n (%)	Median (95% CI), months	HR (95% CI)
Pembrolizumab 200 mg Q3W	126 (81.8)	7.7 (6.1–10.2)	0.50 (0.39–0.65)
Chemotherapy	141 (93.4)	5.5 (4.2–6.2)	



No. at risk

Pembrolizumab 200 mg Q3W	154	92	62	46	38	36	30	24	20	15	3	0
Chemotherapy	151	73	20	6	5	4	3	2	1	1	0	0

No statistical conclusions can be drawn from exploratory analyses

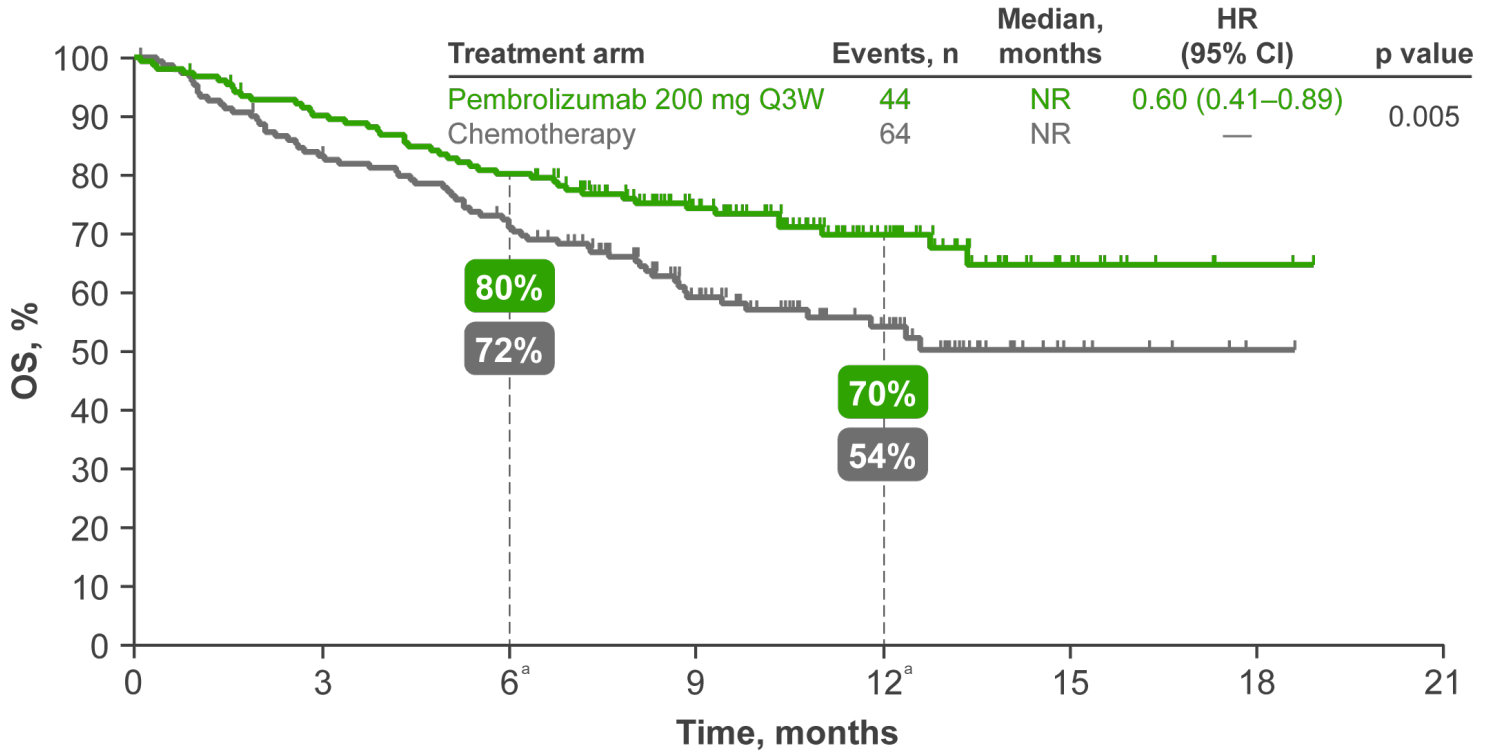
Statistical significance was met for primary and secondary endpoints in interim analysis 1 (2016)

Adapted from: Reck M et al. J Clin Oncol. 2021.

[a]Assessed per RECIST v1.1 by blinded, independent central review.
CI, confidence interval; HR, hazard ratio; mo, month; PFS, progression-free survival; Q3W, every 3 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1.
1. Reck M *et al. J Clin Oncol.* 2021;39(21):2339–2349.

KEYNOTE-024: Interim analysis 1 – 1-year landmark OS[1,2]

Median follow up: 11.2 months



No. at risk								
Pembrolizumab 200 mg Q3W	154	136	121	82	39	11	2	0
Chemotherapy	151	123	106	64	34	7	1	0

KEYTRUDA monotherapy demonstrated a **superior OS benefit** vs. platinum-based chemotherapy with a 40% reduced risk of death (HR 0.60, P=0.005)[2]

DSMC recommended stopping the trial because of superior efficacy observed with pembrolizumab vs. chemotherapy[1]

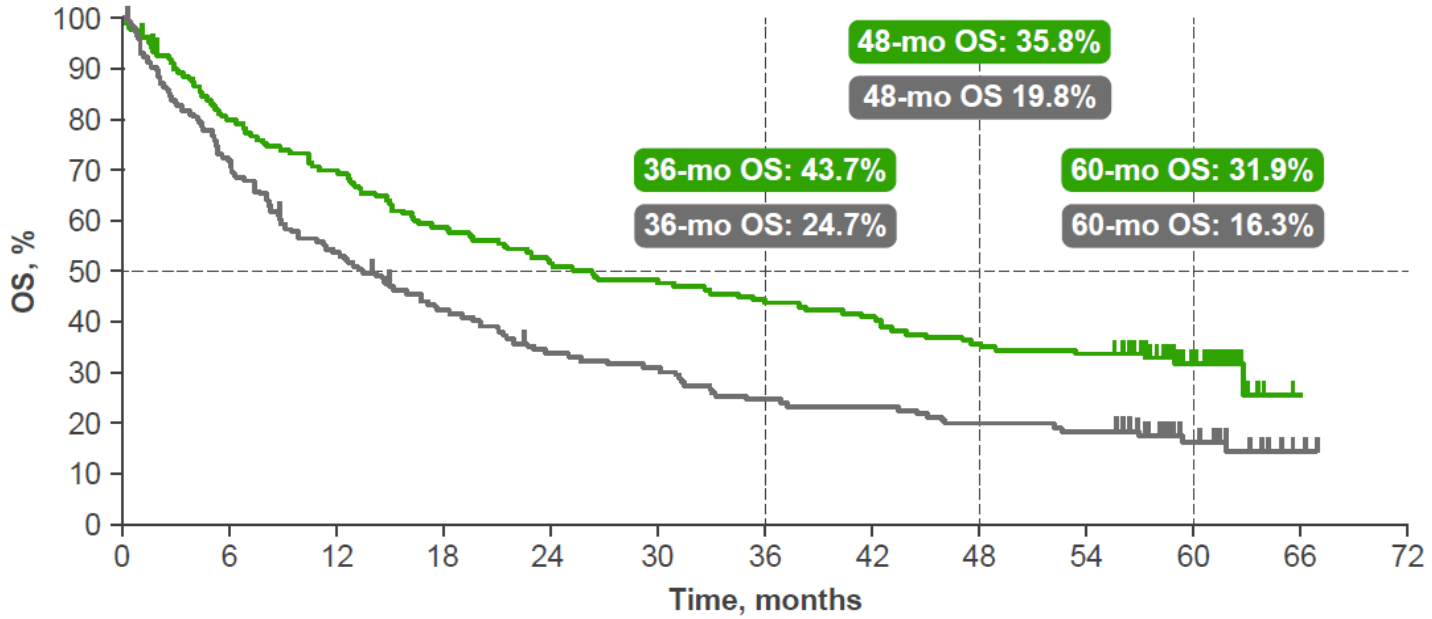
Adapted from: Reck M et al. ESMO 2016 and Reck M et al. N Engl J Med 2016.

[a]The estimated percentage of patients who were alive at 6 or 12 months.
CI, confidence interval; DSMC, Data Safety Monitoring Committee; HR, hazard ratio; NR, not reached; OS, overall survival; Q3W, every 3 weeks.
1. Reck M *et al.* Presented at the European Society for Medical Oncology (ESMO) 2016 Congress, 7–11 October, 2016, Copenhagen, Denmark; 2. Reck M *et al. N Engl J Med* 2016;375:1823–1833 (and supplementary appendix).

KEYNOTE-024: Updated analysis – 5-year median OS[a,1]

Median follow up: 59.9 months

Treatment arm	Events, n (%)	Median (95% CI), months	HR (95% CI)
Pembrolizumab 200 mg Q3W	103 (66.9)	26.3 (18.3–40.4)	0.62 (0.48–0.81)
Chemotherapy[b]	123 (81.5)	13.4 (9.4–18.3)	



No. at risk

Pembrolizumab 200 mg Q3W	154	121	106	89	78	73	66	62	54	51	20	0	0
Chemotherapy	151	168	80	61	48	44	35	33	28	26	13	3	0

No statistical conclusions can be drawn from exploratory analyses

Statistical significance was met for primary and secondary endpoints in interim analysis 1 (2016)

5-year OS rate numerically doubled with KEYTRUDA: 31.9% vs. 16.3% with chemotherapy (with a 66% effective crossover rate)

Median OS was numerically more than 1 year longer in the KEYTRUDA group (26.3 months, 95% CI: 18.3 to 40.4) than in the chemotherapy group (13.4 months, 95% CI: 9.4 to 18.3) HR, 0.62; 95% CI, 0.48 to 0.81

Adapted from: Reck M et al. J Clin Oncol. 2021.

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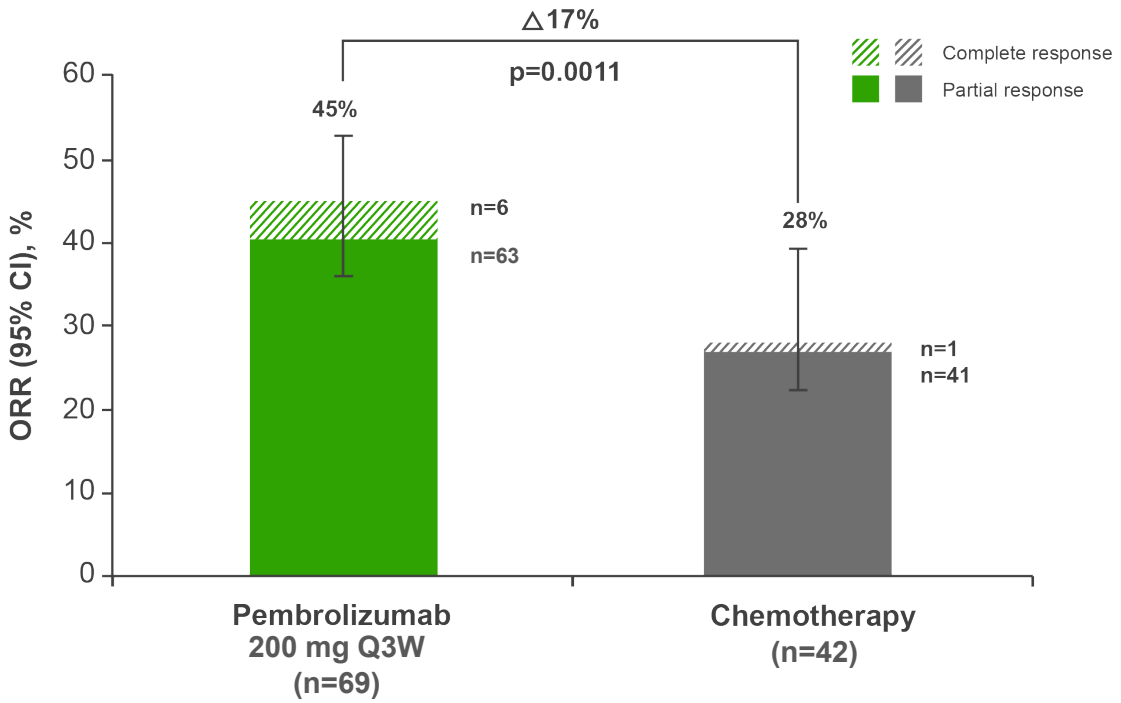
[a]Effective crossover rate from chemotherapy to anti-PD-L1 therapy: 66.0% (99 patients in total crossed over to anti-PD-1 or PD-L1 therapy: 83 patients crossed over to pembrolizumab during the study and 16 additional patients received anti-PD-1 or PD-L1 therapy outside of the crossover).
CI, confidence interval; HR, hazard ratio; mo, month; OS, overall survival; PD-1, programmed deatlh-1; PD-L1, programmed death ligand-1; Q3W, every 3 weeks.
1. Reck M *et al. J Clin Oncol.* 2021;39(21):2339–2349.

KEYNOTE-024: Interim analysis 1 – Summary of responses[a,1,2]

Median follow up: 11.2 months



	Pembrolizumab 200 mg Q3W responders (n=69)	Chemotherapy responders (n=42)
TTR, median (range), months	2.2 (1.4–8.2)	2.2 (1.8–12.2)
DOR,[b] median (range), months	NR (1.9+–14.5+)	6.3 (2.1+–12.6+)

Adapted from: Reck M et al. ESMO 2016 and Reck M et al. N Engl J Med 2016.

[a]Assessed per RECIST v1.1 by blinded, independent central review. [b]+ denotes a response that was ongoing at the data cut-off.
CI, confidence interval; CR, complete response; DOR, duration of response; NR, not reached; ORR, objective response rate; PR, partial response; Q3W, every 3 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1; TTR, time to response.

1. Reck M *et al*. Presented at the European Society for Medical Oncology (ESMO) 2016 Congress, 7–11 October, 2016, Copenhagen, Denmark; 2. Reck M *et al. N Engl J Med* 2016;375:1823–1833 (and supplementary appendix).

KEYNOTE-024: Updated analysis – Summary of responses[a,1]

Median follow up: 59.9 months

No statistical conclusions can be drawn from exploratory analyses

Statistical significance was met for primary and secondary endpoints in interim analysis 1 (2016)

	Pembrolizumab 200 mg Q3W (n=154)	Chemotherapy (n=151)
OR, n (%)	71 (46.1)	47 (31.1)
Best OR, n (%)		
CR	7 (4.5)	0
PR	64 (41.6)	47 (31.1)
SD	37 (24.0)	60 (39.7)
PD	35 (22.7)	25 (16.6)
NE	0	1 (0.7)
NA	11 (7.1)	18 (11.9)
Median time to response, mo (range)	2.1 (1.4–14.6)	2.1 (1.1–12.2)
DOR, median, mo (range)	29.1 (2.2–60.8+)[b]	6.3 (3.1–52.4)

Adapted from: Reck M et al. J Clin Oncol. 2021.

[a]Assessed by RECIST v1.1 by investigator review. [b]"+" indicates response duration is censored.
CI, confidence interval; CR, complete response; DOR, duration of response; mo, month; NA; no assessment; NE, not evaluable; OR, objective response; PD, progressive disease; PR, partial response; Q3W, every 3 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1; SD, stable disease.

1. Reck M *et al. J Clin Oncol.* 2021;39(21):2339–2349.

KEYNOTE-024: Updated analysis – Best OR after second course of pembrolizumab[1]

Median follow up: 59.9 months

No statistical conclusions can be drawn from exploratory analyses

	Pembrolizumab 200 mg Q3W (n=12)
Alive at data cut-off, n (%)	8 (66.7)
OR during second course, n (%)	4 (33.3)
Best OR, n (%)	
CR	0
PR	4 (33.3)
SD	6 (50.0)
PD	1 (8.3)
Not evaluable	1 (8.3)

At data cut-off, **5/12 patients (41.7%)** were alive without PD per investigator assessment

3 patients (25.0%) did not receive subsequent therapy

CR, complete response; NE, not evaluable, OR, objective response; PD, progressive disease; PR, partial response, SD, stable disease.

1. Reck M *et al. J Clin Oncol.* 2021;39(21):2339–2349.

KEYNOTE-024: Updated analysis – Best OR after 35 cycles (2-years) of pembrolizumab[1]

Median follow up: 59.9 months

No statistical conclusions can be drawn from exploratory analyses

	Pembrolizumab 200 mg Q3W (n=39)
3-year OS rate from completion of pembrolizumab, %	81.4
OR, n (%)	32 (82.1)
Best OR, n (%)	
CR	4 (10.3)
PR	28 (71.8)
SD	6 (15.4)
PD	1 (2.6)

At data cut-off, **18/39 patients (46.2%)** were alive without PD or subsequent therapy for NSCLC per investigator assessment

1 patient developed a secondary malignancy and was treated accordingly

CR, complete response; NSCLC, non-small cell lung cancer; PD, progressive disease; PR, partial response; OR, objective response; OS, overall survival; Q3W, every 3 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1; SD, stable disease.

1. Reck M *et al. J Clin Oncol.* 2021;39(21):2339–2349.

KEYNOTE-024: Interim analysis 2 – AE summary[a,1,2]

Median follow up: 25.2 months

No statistical conclusions can be drawn from exploratory analyses

	Pembrolizumab 200 mg Q3W (n=154)	Chemotherapy (n=150)
Median (range) duration of initially assigned treatment	7.9 (0.03–28.8)	3.5 (0.03–30.5)
Treatment-related AEs, n (%)	118 (76.6)	135 (90.0)
Grade 3–5	48 (31.2)	80 (53.3)
Serious	35 (22.7)	31 (20.7)
Led to discontinuation	21 (13.6)	16 (10.7)
Led to death	2 (1.3)	3 (2.0)
Immune-mediated AEs,[b] n (%)	52 (33.8)	8 (5.3)
Grade 3–5	21 (13.6)	1 (0.7)
Led to death	1 (0.6)	0

Adapted from: Brahmer JR et al. IASLC 2017 and Reck M et al. J Clin Oncol 2019.

KEYTRUDA monotherapy had fewer grade 3–5 treatment-related AEs, but a higher frequency of grade 3–5 immune-mediated AEs and infusion reactions, vs. chemotherapy[2]

[a]During treatment with the initially assigned therapy. [b]Irrespective of attribution to treatment by the investigator.
AE, adverse event; Q3W, every 3 weeks.

1. Brahmer JR *et al.* Presented at the International Association for the Study of Lung Cancer (IASLC) 18th World Conference on Lung Cancer, 15–18 October, 2017, Yokohama, Japan; 2. Reck M *et al. J Clin Oncol* 2019;37:537–546.

KEYNOTE-024: Updated analysis – AE summary[a,1]

Median follow up: 59.9 months

No statistical conclusions can be drawn from exploratory analyses

	Pembrolizumab 200 mg Q3W (n=154)[a]	Chemotherapy (n=150)[a]	35 cycles (2 years) of pembrolizumab 200 mg Q3W (n=39)[a]
Treatment-related AEs, n (%)	118 (76.6)	135 (90.0)	34 (87.2)
Grade 3–5[b]	48 (31.2)	80 (53.3)	6 (15.4)
Serious	35 (22.7)	31 (20.7)	4 (10.3)
Led to discontinuation	21 (13.6)	16 (10.7)	0
Led to death	2 (1.3)	3 (2.0)	0
Immune-mediated AEs[c], n (%)	53 (34.4)	8 (5.3)	12 (30.8)
Grade 3–5	21 (13.6)	1 (0.7)	3 (7.7)
Led to death	1 (0.6)	0	0

Exposure-adjusted AE rates in the ITT population decreased over time in both treatment groups

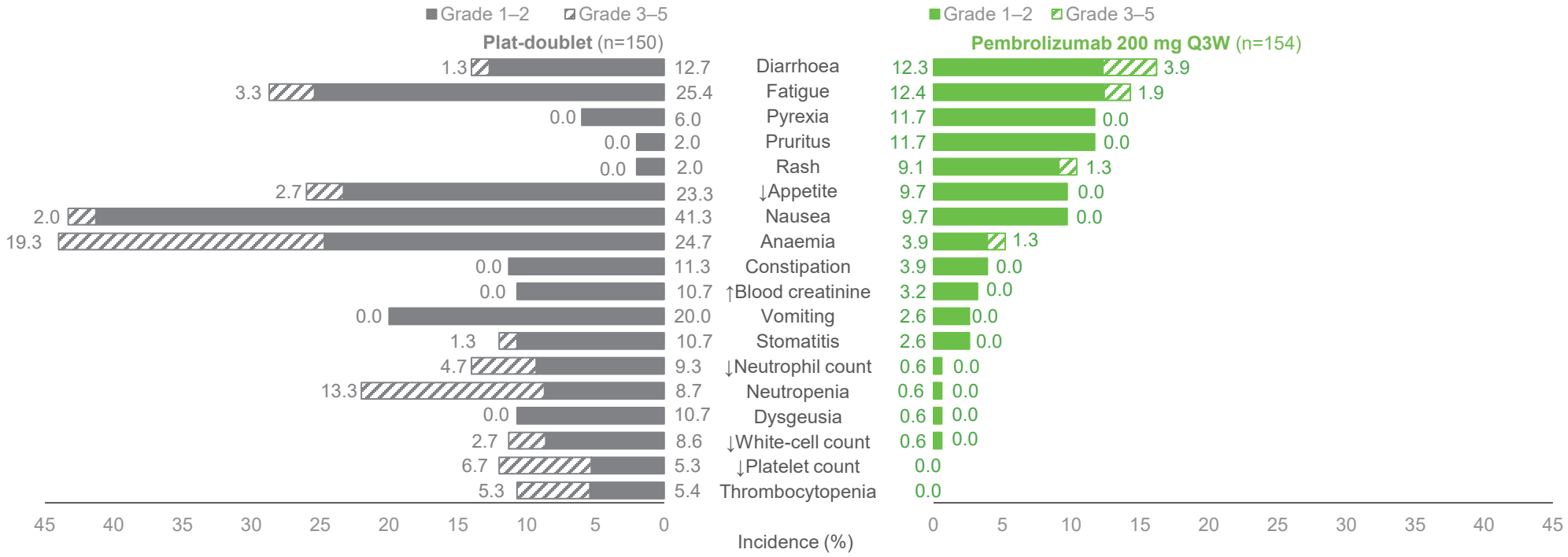
Adapted from: Reck M et al. J Clin Oncol. 2021.

[a]During treatment with the initially assigned therapy. [b]7 additional patients in the pembrolizumab arm and no additional patients in the chemotherapy arm had treatment-related grade 3–5 AEs since the initial publication of KEYNOTE-024 (Reck M, *et al*. *N Engl J Med*. 2016;375:1823–1833). There was no change since the updated analysis at 25.2 months median follow-up.
[c]Irrespective of attribution to treatment by the investigator.
AE, adverse event; ITT, intention-to-treat; Q3W, every 3 weeks.
1. Reck M *et al. J Clin Oncol*. 2021;39(21):2339–2349.

KEYNOTE-024: Interim analysis 2 – TRAEs occurring in ≥10 patients in either treatment arm[a,1,2]

Median follow up: 25.2 months

No statistical conclusions can be drawn from exploratory analyses



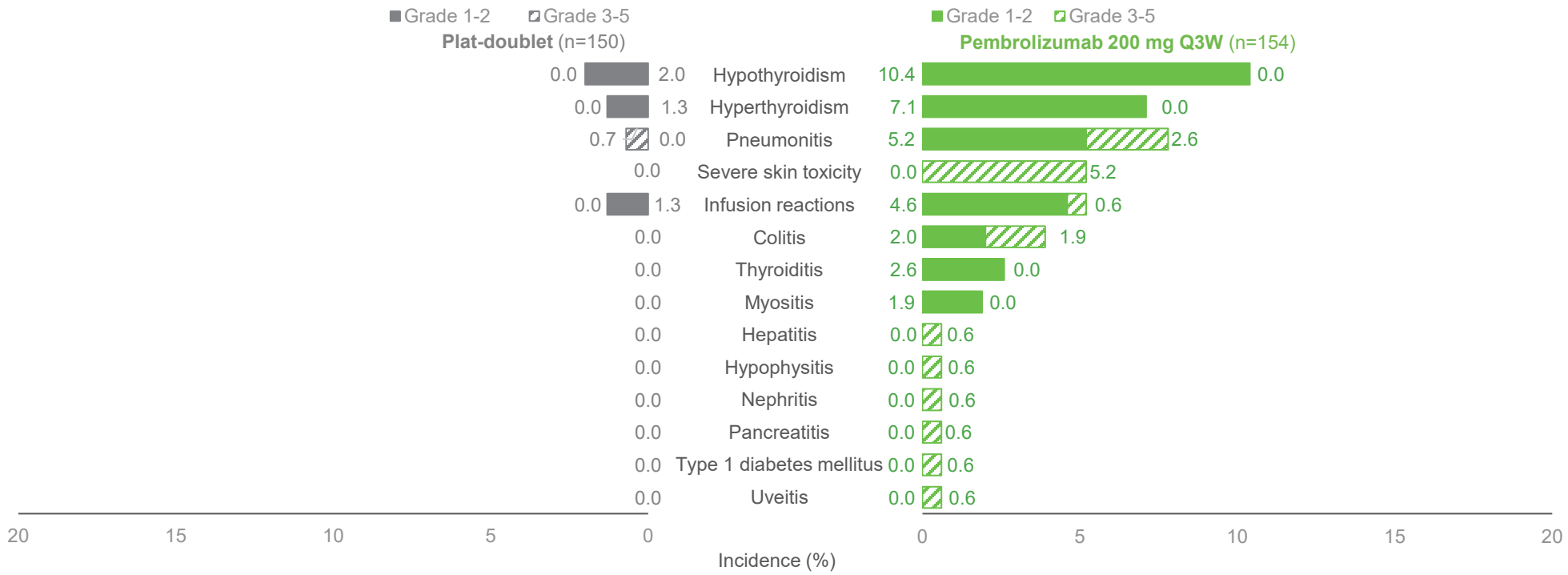
Adapted from: Brahmer JR et al. IASLC 2017 and Reck M et al. J Clin Oncol 2019.

[a]During treatment with the initially assigned therapy. [b]Two Grade 5 treatment-related AEs occurred in the pembrolizumab arm (pneumonitis and sudden death) and three in the chemotherapy arm (death, pulmonary sepsis and pulmonary alveolar haemorrhage).
TRAE, treatment-related adverse event.
1. Brahmer JR *et al*. Presented at the International Association for the Study of Lung Cancer (IASLC) 18th World Conference on Lung Cancer, 15–18 October, 2017, Yokohama, Japan; 2. Reck M *et al. J Clin Oncol* 2019;37:537–546.

KEYNOTE-024: Interim analysis 2 – Immune-mediated AEs[a,1,2]

Median follow up: 25.2 months

No statistical conclusions can be drawn from exploratory endpoints



Adapted from: Brahmer JR et al. IASLC 2017; Reck M et al. J Clin Oncol 2019.

[a]Irrespective of attribution to treatment by the investigator and occurring during treatment with the initially assigned therapy. [b]One Grade 5 event occurred in the pembrolizumab arm (pneumonitis).
AE, adverse event.
1. Brahmer JR *et al.* Presented at the International Association for the Study of Lung Cancer (IASLC) 18th World Conference on Lung Cancer, 15–18 October, 2017, Yokohama, Japan; 2. Reck M *et al. J Clin Oncol* 2019;37:537–546.

KEYNOTE-024: HRQoL[1]
EORTC QLQ-C30 GHS

No statistical conclusions can be drawn from exploratory endpoints

	Pembrolizumab 200 mg Q3W (n=151)	Chemotherapy (n=148)
Mean score at baseline (SDev) n	62.2 (22.3) 145	59.9 (22.3) 137
Mean score at Week 15 (SDev) n	71.0 (21.2) 109	63.7 (20.6) 92
LS mean change from baseline (95% CI) n[a]	6.9 (3.3–10.6) 150	−0.9 (−4.8–3.0) 147
Difference in LS mean (95% CI) p value	7.8 (2.8–12.8) p=0.0020	

Adapted from: Brahmer JR et al. Lancet Oncol 2017.

HRQoL was an exploratory endpoint.

[a]Based on a cLDA model. For baseline and Week 15, n is the number of patients in each treatment group with non-missing assessments at the specific time point; for change from baseline, n is the number of patients in the analysis population in each treatment group.

CI, confidence interval; cLDA, constrained longitudinal data analysis; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 items; GHS, global health status; HRQoL, health-related quality of life; LS, least squares; n, number of patients; Q3W, every 3 weeks; SDev, standard deviation.

1. Brahmer JR *et al. Lancet Oncol* 2017;18:1600–1609.

KEYNOTE-024: HRQoL[1]
EORTC QLQ-C30 and QLQ-LC13

No statistical conclusions can be drawn from exploratory endpoints

- The mean change from baseline in EORTC QLQ-C30 GHS/QoL scores improved more over 33 weeks in patients who received pembrolizumab compared with those who received chemotherapy
- In most EORTC QLQ-C30 functioning and symptom domains, changes from baseline to Week 15 were better for patients who received pembrolizumab compared with those who received chemotherapy
- Overall, changes from baseline to Week 15 in EORTC QLQ-LC13 symptom domains were also better for the pembrolizumab group than the chemotherapy group
  - Neuropathy, alopecia and chest pain were nominally significantly different between groups[a]

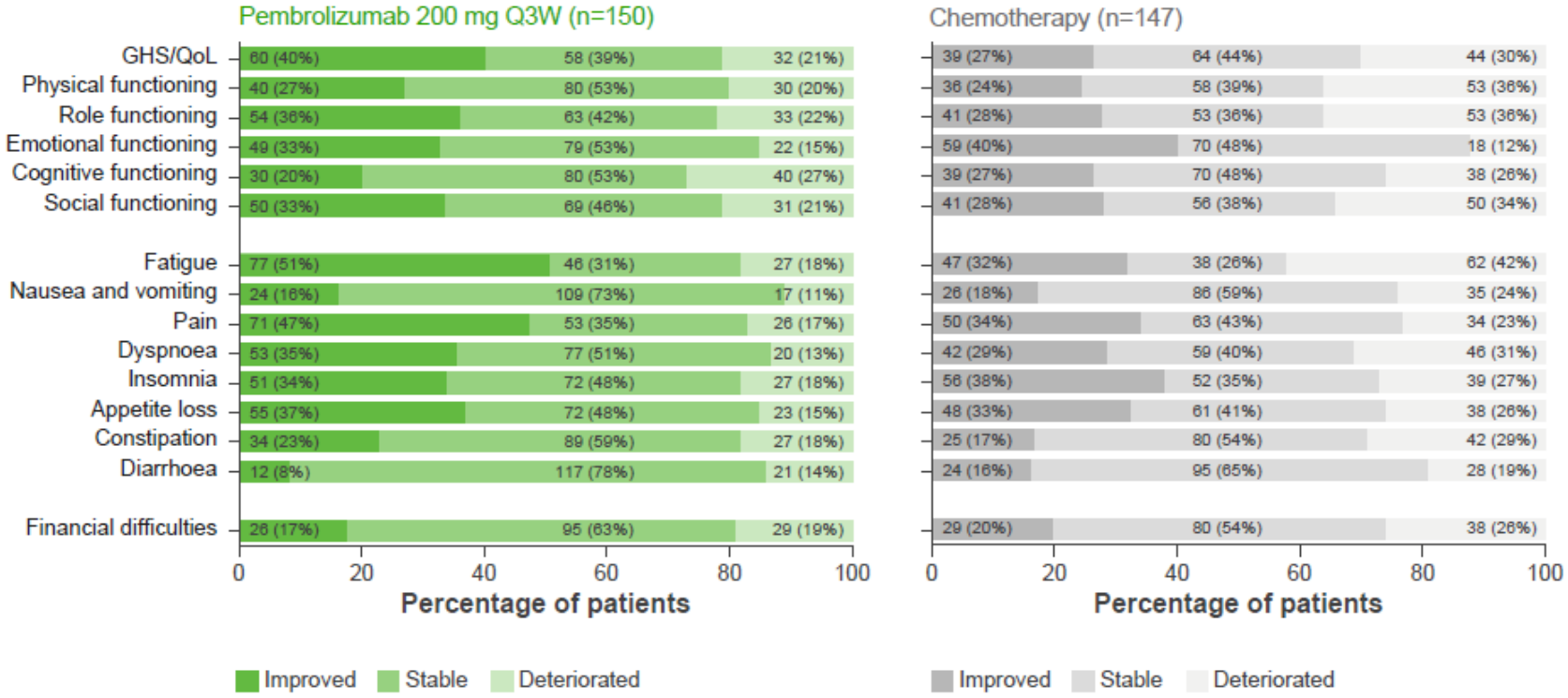
[a]Described by no overlaps within the 95% CI interval between the pembrolizumab and chemotherapy groups.
EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 items; HRQoL, health-related quality of life; GHS, global health status; QoL, quality of life; QLQ-LC13, Quality of Life Questionnaire Lung Cancer 13 items.

1. Brahmer JR *et al. Lancet Oncol* 2017;18:1600–1609.

KEYNOTE-024: HRQoL[1]

Proportion of patients with improved, stable and deteriorated QLQ-C30 scores at 15 weeks

No statistical conclusions can be drawn from exploratory endpoints



Adapted from: Brahmer JR et al. Lancet Oncol. 2017.

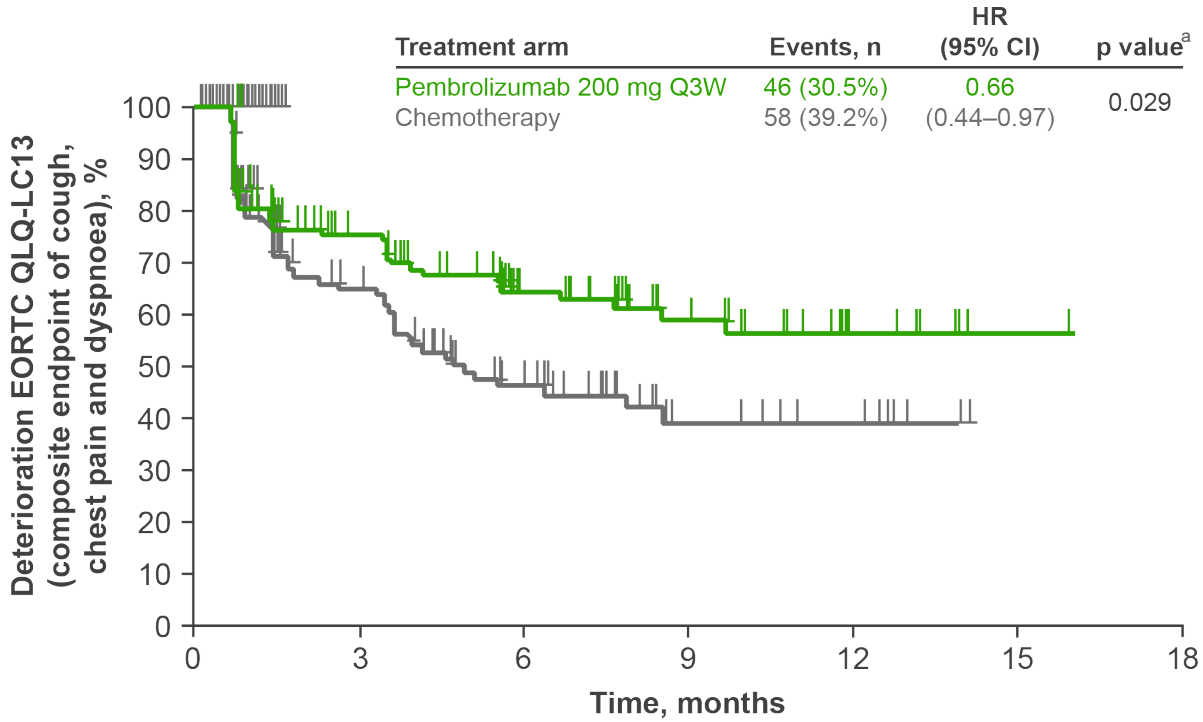
GHS, global health status; HRQoL, health-related quality of life; QoL; quality of life; QLQ-C30, Quality of Life Questionnaire Core 30 items.

1. Brahmer JR *et al. Lancet Oncol* 2017;18:1600–1609.

KEYNOTE-024: Time to deterioration analysis[1]

Composite endpoint of cough, chest pain and dyspnoea

No statistical conclusions can be drawn from exploratory endpoints



Time to deterioration was longer with pembrolizumab than with chemotherapy (median not reached [95% CI: 8.5–NR] vs 5.0 months [95% CI: 3.6–NR])

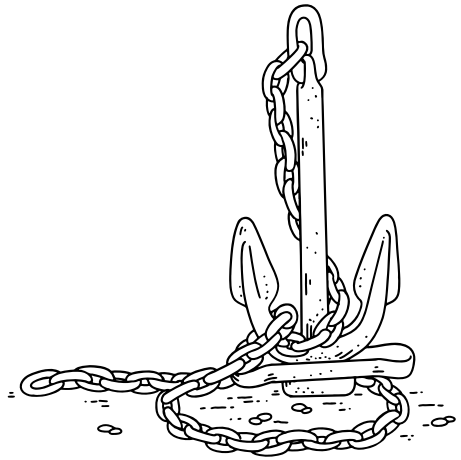
Adapted from: Brahmer JR et al. Lancet Oncol 2017.

[a]Two-sided nominal p value.
CI, confidence interval; EORTC QLQ-LC13, The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Lung Cancer 13 Module; HR, hazard ratio; NR, not reached; Q3W, every 3 weeks.

1. Brahmer JR *et al. Lancet Oncol* 2017;18:1600–1609.

KEYNOTE-024: Summary

- Pembrolizumab demonstrated a superior PFS and OS benefit vs. platinum-based chemotherapy as first-line therapy for metastatic NSCLC with PD-L1 TPS ≥50% (original analysis)[1]
- With 5 years of follow up, pembrolizumab continues to show meaningful improvements in OS and durable responses vs. chemotherapy[2]
  - The 5-year OS rate was approximately doubled in the pembrolizumab arm vs the chemotherapy arm (31.9% vs. 16.3%), with a median DOR of 29.1 months (despite the 66% effective crossover rate)[2]
- Patients who completed 35 cycles (2 years) of pembrolizumab experienced long-term OS[2]
- Pembrolizumab continues to demonstrate a generally manageable tolerability profile[2,3]
  - No new safety signals were identified with long-term treatment with pembrolizumab[2]
- Pembrolizumab improves or maintains HRQoL compared with that for chemotherapy[4]
- These data support:
  - Pembrolizumab monotherapy as a standard of care for first-line treatment in advanced NSCLC with PD-L1 TPS ≥50%, including both squamous and non-squamous tumours



DOR, duration of response; HRQoL, health-related quality of life; NSCLC, non-small cell lung cancer; OS, overall survival; PD-L1, programmed death ligand 1; PFS: progression-free survival; TPS, tumour proportion score.

1. Reck M *et al. N Engl J Med* 2016;375:1823–1833; 2. Reck M *et al. J Clin Oncol.* 2021;39(21):2339–2349; 3. Reck M *et al. J Clin Oncol* 2019;37:537–546; 4. Brahmer JR *et al. Lancet Oncol* 2017;18:1600–1609.

Abbreviations

Abbreviation	Definition
AE	Adverse event
ALK	Anaplastic lymphoma kinase
AUC	Area under the curve
CI	Confidence interval
cLDA	Constrained longitudinal data analysis
CR	Complete response
d	Day
DSMC	Data Safety Monitoring Committee
DOR	Duration of response
ECOG	Eastern Cooperative Oncology Group
EGFR	Epidermal growth factor receptor
EMC	Electronic Medicines Compendium
EORTC	European Organisation for Research and Treatment of Cancer
GHS	Global health status
HR	Hazard ratio
HRQoL	Health-related quality of life
IHC	Immunohistochemistry
ILD	Interstitial lung disease
ITT	Intention-to-treat

Abbreviation	Definition
IV	Intravenous
LS	Least squares
mg	Milligram(s)
mo	Month
MHRA	Medicines and Healthcare Products Regulatory Agency
n	Number of patients
NA	No assessment
NE	Not evaluable
NR	Not reached
NSCLC	Non-small cell lung cancer
OR	Objective response
ORR	Objective response rate
OS	Overall survival
PD	Progressive disease
PD-1	Programmed death-1
PD-L1	Programmed death ligand-1
PFS	Progression-free survival
Pembro–plat–pem	Pembrolizumab + platinum + pemetrexed
Placebo–plat–pem	Placebo + platinum + pemetrexed

Abbreviations

Abbreviation	Definition
PR	Partial response
PS	Performance status
Q3W	Every 3 weeks
Q6W	Every 6 weeks
QLQ-C30	Quality of Life Questionnaire Core 30
QLQ-LC3	Quality of Life Questionnaire Lung Cancer 13
QoL	Quality of life
RECIST v1.1	Response Evaluation Criteria in Solid Tumors version 1.1
SD	Stable disease
SDev	Standard deviation
TPS	Tumour proportion score
TRAE	Treatment-related adverse event

Data dive[1]

PFS	OS	Responses	Safety	HRQoL
Interim analysis 1 (1-year)	Interim analysis 1 (1-year)	Interim analysis 1 – Summary (1-year)	Interim analysis 2 – AEs (2-year)	EORTC QLQ-C30 GHS
Updated analysis (5-year)	Updated analysis (5-year)	Updated analysis – Summary (5-year)	Updated analysis – AEs (5-year)	EORTC QLQ-C30 and QLQ-LC13
		Updated analysis – Best OR after 2nd course of pembrolizumab	Interim analysis 2 – TRAEs (2-year)	Breakdown of QLQ-C30 scores
		Updated analysis – Best OR after 35 cycles of pembrolizumab	Interim analysis 2 – Immune-mediated AEs (2-year)	Time to deterioration analysis

AE, adverse event; EORTC, European Organisation for Research and Treatment of Cancer; HRQoL, health-related quality of life; OS, overall survival; OR, objective response; PFS, progression-free survival; QLQ-C30,Quality of Life Questionnaire Core 30; QLQ-LC13,Quality of Life Questionnaire Lung Cancer 13; TRAE, treatment-related adverse event.

1. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available from: https://www.medicines.org.uk/emc/product/2498/smpc.

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 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 dosing for monotherapy and combination therapy.

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

1. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available from: https://www.medicines.org.uk/emc/product/2498/smpc.