KEYTRUDA® (pembrolizumab) In The Treatment Of Patients With Advanced (Unresectable Or Metastatic) Melanoma

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, UK (Tel: 0208 154 8000).

These slides are provided to UK healthcare professionals as a data resource for personal education.

To ensure compliance with all relevant codes and regulations, these slides are provided in PDF format and must not be amended.

Prescribing information can be found on slide 3, in the top right-hand corner of each slide, and at https://www.emcpi.com/pi/33162 (Great Britain) https://www.emcpi.com/pi/ni/378 (Northern Ireland). Always refer to the Summary of Product Characteristics and Risk Minimisation Materials before prescribing to help minimise the risks associated with the use of KEYTRUDA.

Images are illustrative of the range of patients diagnosed with melanoma.

Job number: GB-OOC-00756 Date of Preparation: April 2024

KEYTRUDA® (pembrolizumab)

KEYTRUDA Indications In Melanoma And Dosing[1]

GB PI | NI PI

Licensed melanoma indications:[1]

- **KEYTRUDA as monotherapy is indicated for the treatment of adults or adolescents aged 12 years and older with advanced (unresectable or metastatic) melanoma**
- **KEYTRUDA as monotherapy is indicated for the adjuvant treatment of adults and adolescents aged 12 years and older with Stage IIB, IIC or III melanoma and who have undergone complete resection**

Dosing information:[1]

- Patients with advanced melanoma should be treated with KEYTRUDA until disease progression or unacceptable toxicity
- For the adjuvant treatment of melanoma, KEYTRUDA should be administered until disease recurrence, unacceptable toxicity, or for a duration of up to 1 year
- The recommended dose of KEYTRUDA as monotherapy in adults is either 200 mg every 3 weeks or 400 mg every 6 weeks administered as an intravenous infusion over 30 minutes
- The recommended dose of KEYTRUDA as monotherapy in paediatric patients aged 12 years and older with melanoma is 2 mg/kg bodyweight (up to a maximum of 200 mg), every 3 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
- For any queries, please contact your local MSD contact at msdukoncology@msd.com

MSD does not recommend use of products outside their licensed indications, please refer to the Summary of Product Characteristics (and risk minimisation materials) available on the EMC website before prescribing.

KEYTRUDA® (pembrolizumab)

1. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

Prescribing Information

GB PI | NI PI

Prescribing information can be found at:

https://www.emcpi.com/pi/33162 (Great Britain)

https://www.emcpi.com/pi/ni/378 (Northern Ireland)

Pooled safety data of KEYTRUDA across all indications and AE management can be found in the Summary of Product Characteristics.

Please refer to the full KEYTRUDA Summary of Product Characteristics and Risk Minimisation Materials for Patients before prescribing KEYTRUDA.

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ (This link will direct you to a third-party website)* or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to MSD, UK (Tel: 0208 154 8000).

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KEYTRUDA® (pembrolizumab)

Learn How Patients May Benefit From KEYTRUDA Treatment

GB PI | NI PI

Pivotal KEYTRUDA trials in advanced melanoma

Phase Ib
Ipilimumab-naïve and ipilimumab-treated[1]

KEYTRUDA dose comparison
N=655

Phase II
Ipilimumab-treated[2]

KEYTRUDA vs chemotherapy
N=540

Phase III
Ipilimumab-naïve and ≤1 previous systemic therapy for advanced disease[3]

KEYTRUDA vs ipilimumab
N=834

KEYTRUDA® (pembrolizumab)

1. Ribas A, *et al. JAMA* 2016;315:1600–1609; **2.** Ribas A, *et al. Lancet Oncol* 2015;16:908–918; **3.** Robert C, *et al. N Engl J Med* 2015;372:2521–2532.

Dosing In Trials Differ From The Licensed Dose[1–6]

***These are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes. Data from KEYNOTE-001, 002 and 006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[1]**

Licensed dose[1]	KEYNOTE-001[2]	KEYNOTE-002[3]	KEYNOTE-006[4–6]
	Phase Ib trial *Primary endpoint: ORR* *Median follow-up: 21 months*	Phase II trial *Primary endpoints: PFS, OS* *Median follow-up: 10 months*	Phase III trial *Primary endpoints: PFS, OS* *Median follow-up: 22.9 months* *(post hoc analysis 57.7 months)*
200 mg Q3W or 400 mg Q6W	**2 mg/kg Q3W* or 10 mg/kg Q2W or Q3W***	**2 mg/kg Q3W* or 10 mg/kg Q3W***	**10 mg/kg Q2W* or 10 mg/kg Q3W***

ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024. **2.** Ribas A, *et al. JAMA* 2016;315:1600–1609; **3.** Ribas A, *et al. Lancet Oncol* 2015;16:908–918; **4.** Robert C, *et al. N Engl J Med* 2015;372:2521–2532; **5.** Schachter J, *et al. Lancet* 2017;390:1853–1862; **6.** Robert C, *et al. Lancet Oncol* 2019;20:1239–1251.

KEYTRUDA® (pembrolizumab)

KEYTRUDA Is An Immunotherapy Treatment That Could Support Eligible Stage IIB-IV Melanoma Patients[1]

Images are illustrative of the range of patients diagnosed with melanoma.

Licensed melanoma indications:[1]

- KEYTRUDA as monotherapy is indicated for the treatment of adults or adolescents aged 12 years and older with advanced (unresectable or metastatic) melanoma
- KEYTRUDA as monotherapy is indicated for the adjuvant treatment of adults and adolescents aged 12 years and older with Stage IIB, IIC or III melanoma and who have undergone complete resection

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1. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

Click On The Icons Below To Explore KEYTRUDA In Stage IV Melanoma

GB PI | NI PI

How is KEYTRUDA supporting patients with Stage IV melanoma?

- KEYNOTE-001
- KEYNOTE-002
- KEYNOTE-006

Using KEYTRUDA

GB PI | NI PI **Click on these icons to access KEYTRUDA prescribing information**

Click on this icon to return to this page

KEYTRUDA® (pembrolizumab)

Meet Farah, A Patient Who Has Stage IV Metastatic Melanoma*

GB PI | NI PI

Name: Farah
Age: 77
Medical history:

- Farah visited her GP in 2019 with concerns about a mole on her back and was referred to a dermatologist
- The mole was excised and histopathological review confirmed the diagnosis of Stage IIC melanoma
- Sentinel lymph node biopsy was conducted and no disease was detected
- Recently however, Farah discovered hardened lumps under her skin, has had shortness of breath along with chest pain
- A chest X-ray showed a suspicious right-sided nodule and a subsequent CT scan showed metastases to the lung and a soft-tissue nodule in the liver

Farah and other patients with unresectable advanced melanoma are at a high risk of mortality[1]

*Not a real patient.

1. Cancer Research UK. Available at: https://www.cancerresearchuk.org/about-cancer/melanoma/survival. Accessed April 2024.

KEYTRUDA® (pembrolizumab)

KEYNOTE-001:
Phase Ib Trial Of KEYTRUDA For The Treatment Of Patients With Unresectable Advanced Melanoma

Study design

Safety overview

Primary efficacy outcome results

KEYNOTE-001

Study Design[1]

GB PI | NI PI

- KEYNOTE-001 was a partially-randomised, independent, multicentre, international and open-label Phase Ib study designed to assess the efficacy and safety of several doses of KEYTRUDA
- KEYTRUDA was administered until disease progression or withdrawal was determined by an investigator for intolerable toxicity or protocol violation

Inclusion criteria:

- Advanced unresectable melanoma with measurable disease per investigator assessment
- Aged ≥18 years
- ECOG PS 0–1
- Adequate organ function

Exclusion criteria:

- Chemotherapy within 4 weeks of the first study dose
- Active infection
- Active autoimmune disease (or history thereof)
- Ongoing systemic corticosteroid therapy at treatment doses
- Previous treatment targeting the PD-1 pathway

Refer to the full protocol for the list of inclusion and exclusion criteria.

In KEYNOTE-001, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes. Data from KEYNOTE-001 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

ECOG PS, Eastern Cooperative Oncology Group performance status; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Ribas A, *et al. JAMA* 2016;315:1600–1609; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

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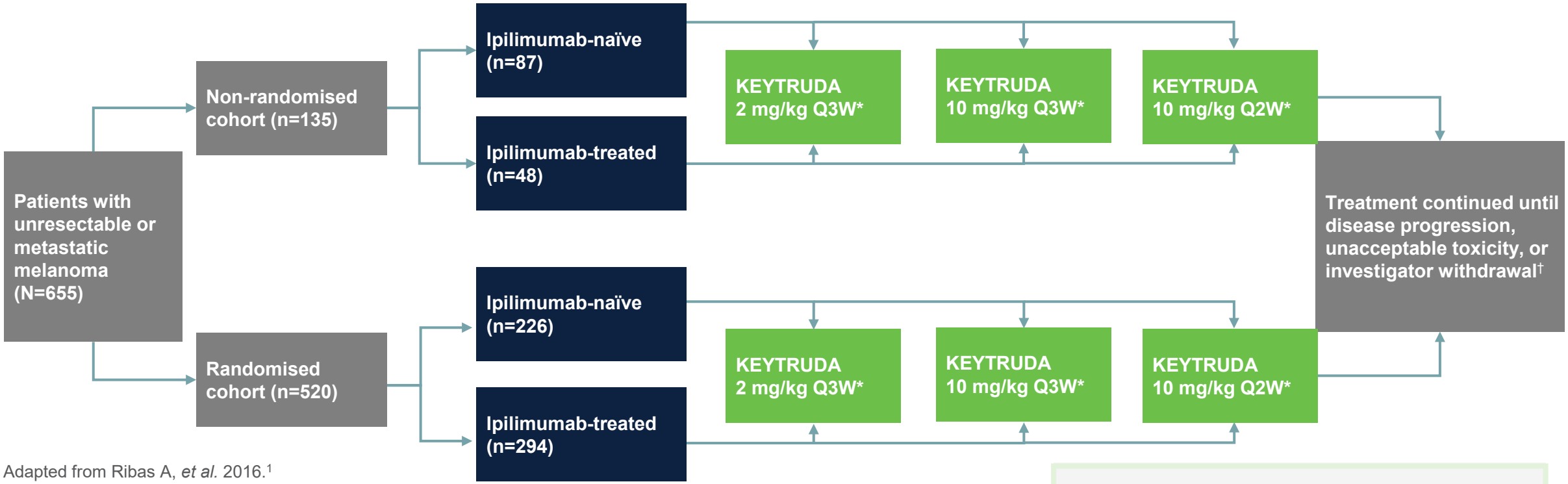
KEYNOTE-001

Study Design[1]



Adapted from Ribas A, *et al.* 2016.[1]

Baseline patient characteristics ›

***These are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes. Data from KEYNOTE-001, 002 and 006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]**

†Clinically stable patients with initial evidence of disease progression were permitted to remain on treatment until disease progression was confirmed.

Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Ribas A, *et al. JAMA* 2016;315:1600–1609; **2**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

KEYNOTE-001

Key Trial Endpoints[1]

GB PI | NI PI

Analysis of ORR was done in the full analysis set, defined as all patients with measurable disease per independent central review at baseline who received at least one dose of study treatment. All other analyses were performed in the all-patients-as-treated population (all patients who received at least one dose of study treatment).

1

Primary efficacy endpoint:

- Objective response rate (ORR): defined as the percentage of patients with a best overall response of complete or partial response*

2

Secondary endpoints:

- ORR as assessed by immune-mediated response criteria by investigators
- Duration of response (time from best overall response to first documentation of disease progression)
- Progression-free survival (PFS): time from start of treatment to documented disease progression or death due to any cause
- Overall survival (OS): time from start of treatment to death due to any cause

In KEYNOTE-001, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-001 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

*ORR was assessable only in patients with measurable disease at baseline and was assessed by independent central review using RECIST v1.1. For assessment of response rate, patients without post-baseline disease assessments were counted as non-responders. A pre-specified subgroup analysis of ORR was conducted.
ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Ribas A, *et al. JAMA* 2016;315:1600–1609; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Objective Response Rate Following Treatment With KEYTRUDA[1]

Median duration of follow-up was 21 months (range: 14–35 months)

	No. with objective response	Total no. of patients	Objective response rate, % (95% CI)*
Overall	**194**	**581**	**33.4 (29.6–37.4)**
Previous ipilimumab†			
Naïve	107	277	38.6 (32.9–44.6)
Treated	87	304	28.6 (23.6–34.1)
KEYTRUDA dose and schedule†			
2 mg/kg, Q3W	45	143	31.5 (24.0–39.8)
10 mg/kg, Q3W	86	272	31.6 (26.1–37.5)
10 mg/kg, Q2W	63	166	38.0 (30.5–45.8)

Adapted from Ribas A, *et al.* 2016.[1]

In KEYNOTE-001, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-001 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Data cut-off 18 October 2014. Full analysis set included 581 patients who had measurable disease assessed by central review at baseline (RECIST v1.1).
*Objective response rate was defined as the percentage of patients with a complete or partial response. †Original analysis additional subgroup data on objective response rate by sex, age, ECOG PS, LDH level, presence of brain metastases, BRAF status, M stage, number of previous therapies, type of previous therapies and baseline tumour size.
CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; LDH, lactate dehydrogenase; M, metastasis; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; RECIST, Response Evaluation Criteria in Solid Tumours.

1. Ribas A, *et al. JAMA* 2016;315:1600–1609; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Treatment-Related Adverse Events With KEYTRUDA[1]

Median duration of follow-up was 55 months[1]

Treatment-related adverse events	KEYTRUDA, n (%)* N=655
Any grade	562 (86)
Grade 3–4†	114 (17)
Led to death	0
Led to discontinuation	51 (8)

Adapted from Hamid O, *et al.* 2019.[1]

In KEYNOTE-001, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[3] Data from KEYNOTE-001 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[3]

Data cut-off 1 September 2017.
*Grades are based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0.[2]
†Determined by the investigator to be related to treatment.[2]
Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.
1. Hamid O, *et al. Ann Oncol* 2019;30:582–588; **2.** Hamid O, *et al. Ann Oncol* 2019;30:582–588. Supplementary appendix; **3**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Click On The Arrows Below To View 55-month Follow-up Data For:[1]

- Overall survival
- Duration of response
- Progression-free survival
- Immune-mediated adverse events
- Objective response rates

In KEYNOTE-001, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-001 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Ribas A, *et al. JAMA* 2016;315:1600–1609; **2**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

KEYNOTE-002:
Phase II Trial Of KEYTRUDA For The Treatment Of Patients With Unresectable Advanced Melanoma

Study design

Safety overview

Primary efficacy outcome results

KEYNOTE-002

Study Design[1]

GB PI | NI PI

- KEYNOTE-002 was an international, randomised, controlled, Phase II study comparing KEYTRUDA with investigator-choice chemotherapy in patients previously treated with ipilimumab
- Randomisation was stratified by ECOG PS, LDH concentration (normal vs raised [≥110% ULN]) and BRAF status (wild-type vs V600 mutant-positive)

Inclusion criteria:

- Histologically or cytologically confirmed unresectable Stage III or Stage IV melanoma not amenable to local therapy
- Aged ≥18 years
- Confirmed disease progression within 24 weeks of the last ipilimumab dose
- Previous *BRAF* or *MEK* inhibitor therapy or both (if *BRAF V600* mutant-positive)
- ECOG PS 0–1
- Resolution or improvement of ipilimumab-related adverse events to Grade 0–1
- Measurable disease per RECIST v1.1

Exclusion criteria:

- Known active brain metastases or carcinomatous meningitis
- Active autoimmune disease
- Active infection requiring systemic therapy
- Known history of HIV infection
- Active hepatitis B or C virus infection
- History of Grade 4 ipilimumab-related adverse events or Grade 3 ipilimumab-related adverse events lasting longer than 12 weeks
- Previous treatment with any other anti-PD-1 or anti-PD-L1 therapy

Refer to the full protocol for the list of inclusion and exclusion criteria.

In KEYNOTE-002, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-002 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

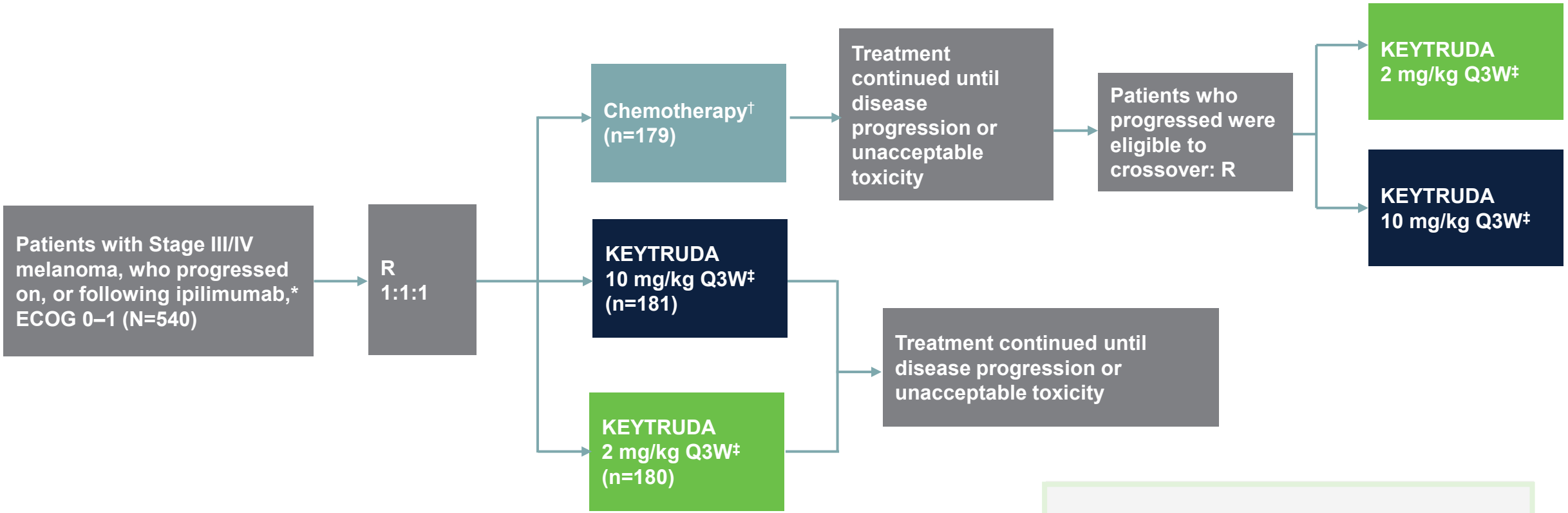
ECOG PS, Eastern Cooperative Oncology Group performance status; HIV, human immunodeficiency virus; LDH, lactate dehydrogenase; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; RECIST, Response Evaluation Criteria in Solid Tumours; ULN, upper limit of normal.

1. Ribas A, *et al. Lancet Oncol* 2015;16:908–918; **2**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

KEYNOTE-002

Study Design[1]



Adapted from Ribas A, *et al.* 2015.[1]

Baseline patient characteristics ›

*Patients with *BRAF V600* mutation were also previously treated with a *BRAF*- or *MEK*-inhibitor.
†The chemotherapy agent used for each patient in the chemotherapy arm was based on investigator choice, from five options (carboplatin alone, carboplatin + paclitaxel alone, dacarbazine, or temozolomide).
‡*These are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes. Data from KEYNOTE-001, 002 and 006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]
Data from KEYNOTE-002 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]
ECOG, Eastern Cooperative Oncology Group; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; R, randomisation.
1. Ribas A, *et al. Lancet Oncol* 2015;16:908–918; **2**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

KEYNOTE-002

Key Trial Endpoints[1]

GB PI | NI PI

The sample size of the study was determined based on the overall survival endpoint at the final analysis.

1

Primary efficacy endpoint:

- Progression-free survival: the time from randomisation to first documented disease progression as per RECIST v1.1 by independent central review or death from any cause, whichever occurred first
- Overall survival

2

Secondary endpoints:

- Proportion of patients who had an objective response
- Proportion of patients who had a complete or partial response (assessed per RECIST v1.1 by central review)
- Response duration
- Time from best overall response of complete or partial response until disease progression
- Safety

Assessment of tumour response was performed every 12 weeks by independent central review*

In KEYNOTE-002, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-002 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

*All scans were evaluated by independent central review. The independent radiologists were masked to treatment assignments, identifying patient characteristics and investigator-assessed findings.

Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; RECIST, Response Evaluation Criteria in Solid Tumours.

1. Ribas A, *et al. Lancet Oncol* 2015;16:908–918; **2**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

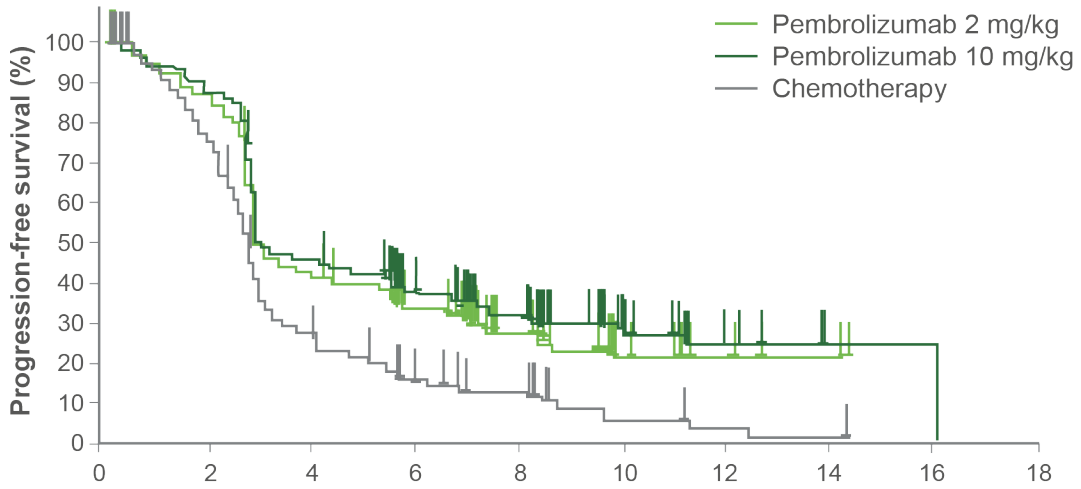
KEYTRUDA® (pembrolizumab)

PFS Following Treatment With KEYTRUDA vs Chemotherapy[1]

Median duration of follow-up was 10 months

PFS assessed by RECIST v1.1 by central review in the ITT population

Kaplan-Meier estimate of PFS in the ITT population



Number at risk

Pembrolizumab 2 mg/kg	180	153	74	53	26	9	4	2	0	0
Pembrolizumab 10 mg/kg	181	158	82	55	39	15	5	1	1	0
Chemotherapy	179	128	43	22	15	4	2	1	0	0

	KEYTRUDA 2 mg/kg (n=180)	KEYTRUDA 10 mg/kg (n=181)	Chemotherapy control (n=179)
Number of events,* n (%)	129 (72)	126 (70)	155 (87)
Median duration, months (range)	2.9 (2.8–3.8)	2.9 (2.8–4.7)	2.7 (2.5–2.8)
Proportion progression-free at 6 months, % (n)	34 (27–41)	38 (31–45)	16 (10–22)
Proportion progression-free at 9 months, % (n)	24 (17–31)	29 (23–37)	8 (4–14)
HR for death or disease progression* KEYTRUDA vs chemotherapy	0.57 (0.45–0.73); p<0.0001†	0.50 (0.39–0.64); p<0.0001†	

Adapted from Ribas A, *et al.* 2015.[1]

In KEYNOTE-002, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-002 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Cut-off 12 May 2014. *HRs and associated 95% CIs were based on Cox regression models with treatment as a covariate stratified by ECOG performance status (0 vs 1), lactate dehydrogenase concentration (normal vs raised), and *BRAFV600* status (mutant vs wild-type). †One-sided p-value on the log-rank test.
CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; ITT, intention-to-treat; PFS, progression-free survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks. RECIST, Response Evaluation Criteria in Solid Tumours.

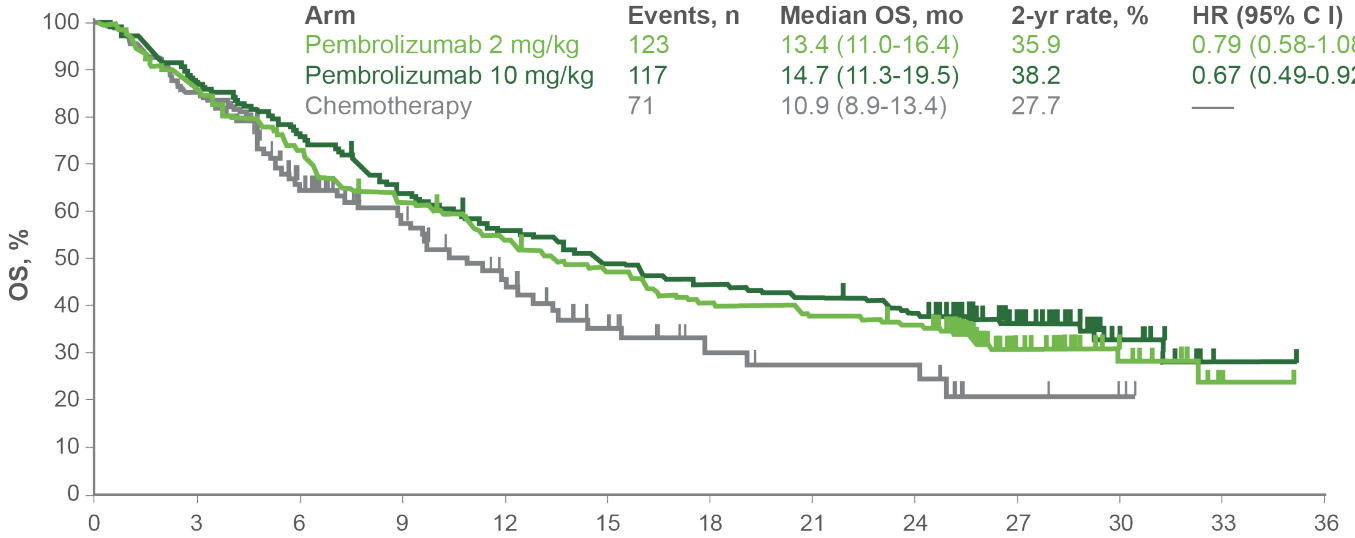
1. Ribas A, *et al. Lancet Oncol* 2015;16:908–918; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

OS Following Treatment With KEYTRUDA vs Chemotherapy[1]

Median duration of follow-up was 28 months[1]

Kaplan-Meier estimate of overall survival adjusted for crossover in KEYNOTE-002[1]



Adapted from Hamid O, *et al.* 2017.[1]

In KEYNOTE-002, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-002 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Cut-off 16 November 2015.

CI, confidence interval; HR, hazard ratio; OS, overall survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; yr, year.

1. Hamid O, *et al. Eur J Cancer* 2017;86:37–45; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Treatment-Related Adverse Events With KEYTRUDA[1]

Median time on treatment was 112.5 days (range: 1.0–988.0) and 145.0 days (range: 1.0–967.0) for patients receiving KEYTRUDA 2 mg/kg and 10 mg/kg, respectively

Treatment-related adverse events with KEYTRUDA*[1]

Treatment-related adverse events, n (%)	KEYTRUDA 2 mg/kg (n=178)			KEYTRUDA 10 mg/kg (n=179)			Chemotherapy (n=171)		
	Grade 1–2	Grade 3–4	Grade 5	Grade 1–2	Grade 3–4	Grade 5	Grade 1–2	Grade 3–4	Grade 5
Any	101 (56.7)	24 (13.5)	0	106 (59.2)	29 (16.2)	1 (<1)	93 (54.3)	45 (26.3)	0
Led to discontinuation	2 (1.1)	6 (3.3)	0	4 (2.2)	11 (6.1)	0	5 (2.9)	4 (2.3)	0

Adapted from Hamid O, *et al.* 2017.[1]

Detailed treatment-related adverse events ›

Immune-mediated adverse events ›

In KEYNOTE-002, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-002 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Cut-off 16 November 2015.
*Safety was assessed in all patients who received ≥1 dose of study treatment.

Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Hamid O, *et al. Eur J Cancer* 2017;86:37–45; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

KEYNOTE-006:
Phase III Trial Of KEYTRUDA For The Treatment Of Patients With Unresectable Advanced Melanoma

Study design

Safety overview

Primary efficacy outcome results

KEYNOTE-006

Study Design[1]

GB PI | NI PI

- KEYNOTE-006 was an international, randomised, open-label, controlled Phase III trial in patients with unresectable Stage III or IV melanoma of KEYTRUDA vs ipilimumab
- Randomisation was stratified according to ECOG PS (0 vs 1), line of therapy (first vs second) and PD-L1 expression (positive vs negative)
- Treatment continued until disease progression, onset of unacceptable side effects, investigator decision to discontinue treatment, withdrawal of patient consent or 24 months of therapy

Inclusion criteria:

- Histologically confirmed, unresectable Stage III or IV melanoma
- ≤1 previous systemic therapy for advanced disease
- ECOG PS 0–1
- Tumour sample adequate for assessing PD-L1 expression

Additional eligibility criteria:

- Aged ≥18 years
- Known *BRAF V600* mutational status
- Previous BRAF inhibitor therapy not required for patients with normal LDH levels and no clinically significant tumour-related symptoms or evidence of rapidly progressive disease

Exclusion criteria:

- Prior therapy with CTLA-4, PD-1 or PD-L1 inhibitors
- Ocular melanoma
- Active brain metastases
- History of serious autoimmune disease

Refer to the full protocol for the list of inclusion and exclusion criteria.

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

CTLA-4, cytotoxic T-lymphocyte-associated protein 4; ECOG PS, Eastern Cooperative Oncology Group performance status; LDH, lactate dehydrogenase; PD1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

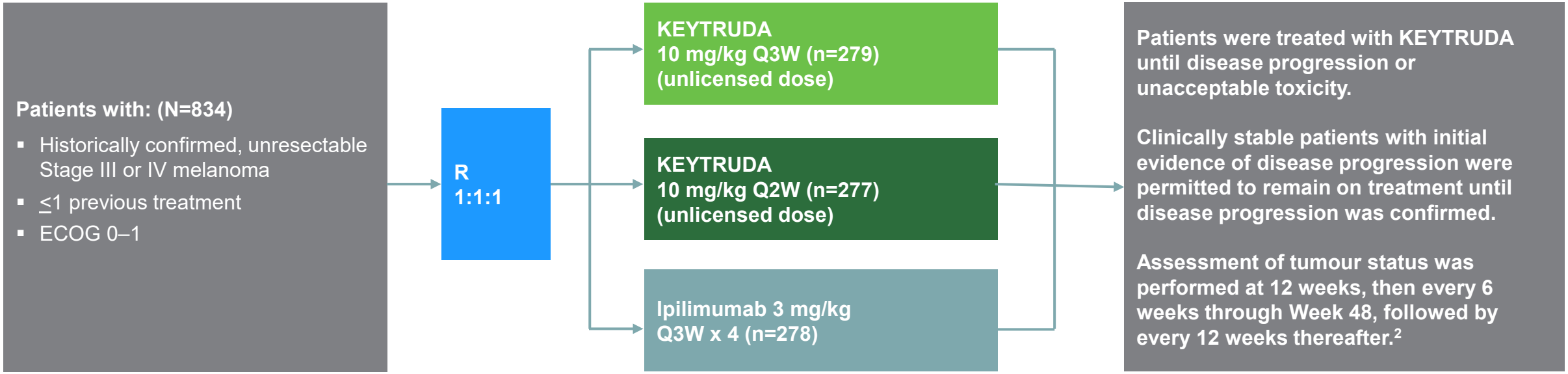
1. Robert C, *et al. N Engl J Med* 2015;372:2521–2532; **2**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Study Design[1,2]

Study design from the original trial

Minimum duration of follow-up of key efficacy measures was 21 months[1]



Adapted from Robert C, *et al.* 2015.[1]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[3] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[3]

Baseline patient characteristics ›

ECOG, Eastern Cooperative Oncology Group; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; R, randomisation.

1. Robert C, *et al. N Engl J Med* 2015;372:2521–2532; **2.** Robert C, *et al. Lancet Oncol* 2019;20:1239–1251; 3. **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

KEYNOTE-006

Key Trial Endpoints[1]

GB PI | NI PI

- Efficacy was assessed in the intention-to-treat population, with all patients included in the treatment group to which they were randomly assigned
- No formal statistical power calculations were done for the 5-year follow-up post hoc exploratory analyses of this trial[2]

1

Primary efficacy endpoint:

- Progression-free survival (PFS): time from randomisation to documented disease progression according to RECIST v1.1 or death from any cause
- Overall survival: time from randomisation to death from any cause

2

Secondary endpoints:

- Objective response rate: percentage of patients with complete or partial response according to RECIST
- Duration of response: time from first documented response to radiologic progression according to RECIST
- Safety

Assessment of tumour status was performed at 12 weeks, then every 6 weeks through Week 48, followed by every 12 weeks thereafter[1,2]

One-sided alpha of 0.002 was given to the primary objective of KEYTRUDA vs ipilimumab for PFS for the initial analysis

Safety was assessed in the as-treated population, which was defined as all patients who underwent randomisation and who received at least one dose of a study drug.

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[3] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[3]

Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; RECIST, Response Evaluation Criteria in Solid tumours.

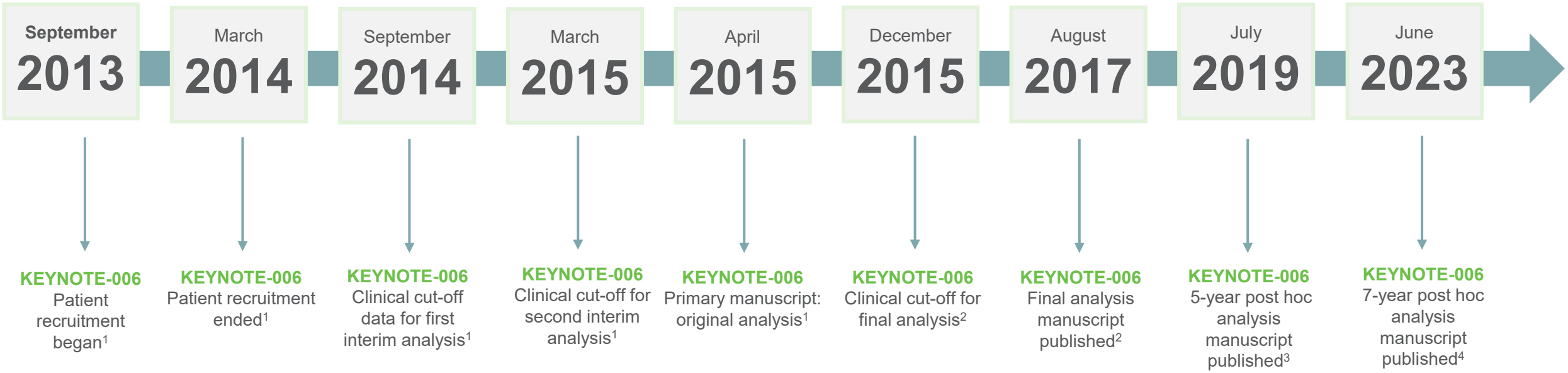
1. Robert C, *et al. N Engl J Med* 2015;372:2521–2532; **2.** Robert C, *et al. Lancet Oncol* 2019;20:1239–1251; **3**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

KEYNOTE-006

KEYNOTE-006 Trial Timeline

GB PI | NI PI



In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[5] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[5]

Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Robert C, *et al. N Engl J Med* 2015;372:2521–2532; **2.** Schachter J, *et al. Lancet* 2017;390:1853–1862; **3.** Robert C, *et al. Lancet Oncol* 2019;20:1239–1251; **4**. Robert C, *et al. J Clin Oncol* 2023;41:3998-4003; **5.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

KEYNOTE-006

Trial Analyses[1]

GB PI | NI PI

1

Initial analysis (IA1)[1,2]

- Cut-off date: 3 September 2014
- 502 PFS events and 202 deaths across all treatment groups
- PFS for KEYTRUDA reached p<0.001 for both groups vs ipilimumab
- Did not reach one-sided p-value for OS

2

Interim analysis (IA2)[1,2]

- Cut-off date: 3 March 2015
- 289 deaths
- OS for KEYTRUDA reached p-values of 0.00052 for Q2W and 0.00358 for Q3W vs ipilimumab
- Reached criteria for stopping (one-sided p-value for OS <0.005 for both arms)

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[3] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[3]

OS, overall survival; PFS, progression-free survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Robert C, *et al. N Engl J Med* 2015;372:2521–2532; **2.** Robert C, *et al. N Engl J Med* 2015;372:2521–2532. Supplementary appendix; **3**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

KEYNOTE-006

Trial Analyses[1]

GB PI | NI PI

3

Final analysis[1]

- Cut-off date: 3 December 2015
- Median follow-up: 22.9 months
- 435 deaths (88% of the target number of events at final analysis)
- Powered by a one-sided alpha of 0.02 as the superiority threshold for overall survival
- 566 PFS events reported; 65% of these occurred in the pooled KEYTRUDA group

4

5-year post hoc analysis[2]

- Post hoc exploratory analyses of the efficacy and safety of KEYTRUDA or ipilimumab in patients with 5 years of follow-up, efficacy of KEYTRUDA in patients who received 2 years of treatment and efficacy and safety of second-course KEYTRUDA
- Cut-off date: 3 December 2018
- Median follow-up: 57.7 months
- No formal statistical power calculations were done for analyses

5

7-year post hoc analysis[3]

- Post hoc analysis of the efficacy of KEYTRUDA or ipilimumab in patients with 7 years of follow-up
- Cut-off date: 19 April 2021
- Median follow-up: 85.3 months
- No formal statistical power calculations were done for analyses

Click here to view the final analysis data ›

Click here to view the 5-year post hoc analysis data ›

Click here to view the 7-year post hoc analysis data ›

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[4] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[4]

PFS, progression-free survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Schachter J, *et al. Lancet* 2017;390:1853–1862; **2.** Robert C, *et al. Lancet Oncol* 2019;20:1239–1251; **3**. Robert C, *et al. J Clin Oncol* 2023; 4. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

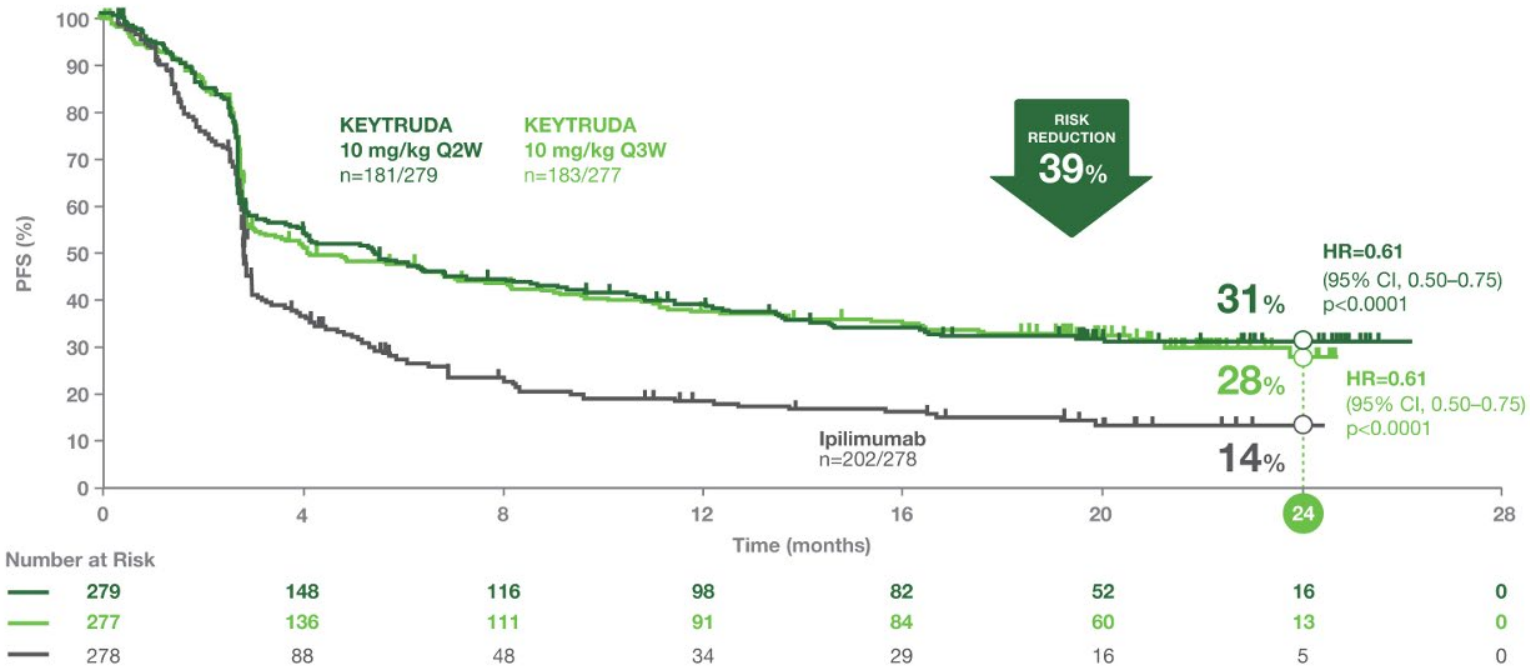
KEYNOTE-006 Final Analysis

Efficacy Data At Minimum Follow-up Of 21 Months

Patients Treated With KEYTRUDA Had Significantly Improved PFS vs Ipilimumab[1]

Median follow-up: 22.9 months

Kaplan-Meier estimate of progression-free survival in KEYNOTE-006[1]



Adapted from Schachter J, *et al.* 2017.[1]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

CI, confidence interval; HR, hazard ratio; PFS, progression-free survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

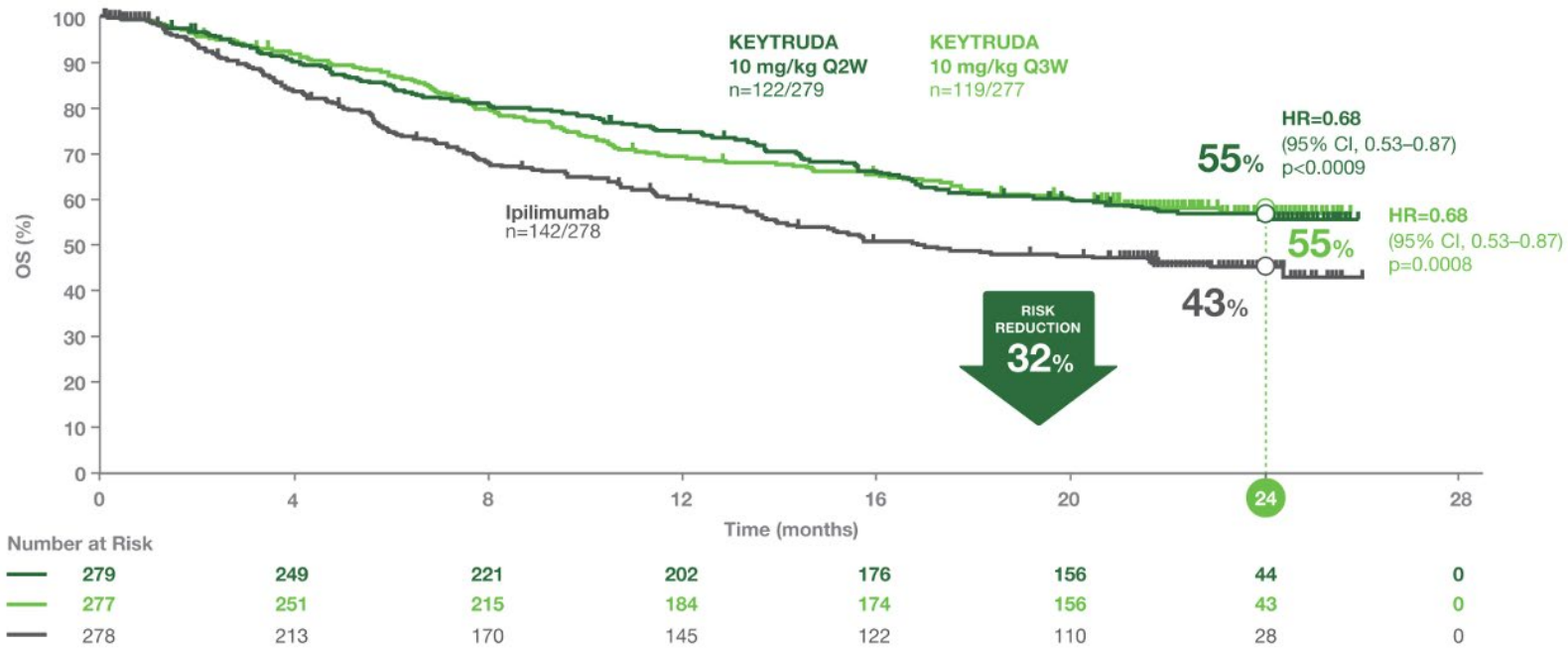
1. Schachter J, *et al. Lancet* 2017;390:1853–1862; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

OS Rates For Patients With Advanced Melanoma Receiving KEYTRUDA Or Ipilimumab[1]

Median follow-up: 22.9 months

Kaplan-Meier estimate of overall survival in KEYNOTE-006[1]



Adapted from Schachter J, *et al.* 2017.[1]

ORR data

Subgroup analysis by *BRAF* status

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

CI, confidence interval; HR, hazard ratio; ORR, overall response rate; OS, overall survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Schachter J, *et al. Lancet* 2017;390:1853–1862; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

KEYNOTE-006 5-year Post Hoc Analysis

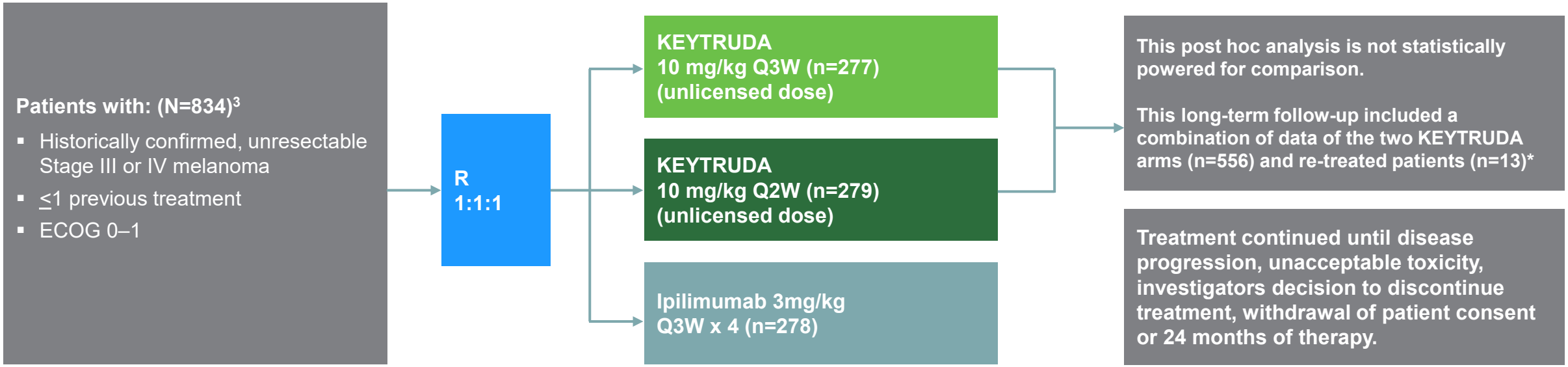
Post Hoc Analysis At 5-year Follow-Up

Study Design[1]

- This is a post hoc analysis and no statistical conclusions can be drawn from these results

Study design from the 5-year post hoc follow-up (not specified)[1]

Medium duration of follow-up for efficacy endpoints of surviving was 57.7 months[1]



Adapted from Robert C, *et al.* 2019.[1]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

All protocol-prespecified response assessments were done according to RECIST V1.1 by blinded independent central review; subsequent analyses reported here were per immune-mediated response criteria by investigator review. Adverse events were collected throughout the study and until 30 days (90 days for serious adverse events) after the last dose of study drug or before initiation of a new anti-cancer treatment, whichever occurred first, and were graded per NCI-CTCAE V4.0.

*Retreatment of patients: a second course (≤1 year) of KEYTRUDA was available for patients who achieved stable disease or better with the first course of KEYTRUDA and had documented disease progression after cessation of therapy. Completion of second-course treatment was defined as receipt of 17 cycles of KEYTRUDA. Second-course participants were treated with a fixed dose of 200 mg Q3W following amendment of the original protocol.

ECOG, Eastern Cooperative Oncology Group; NCI-CTCAE, National Cancer Institute-Common Terminology Criteria for Adverse Events; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; R, Randomisation. RECIST, Response Evaluation Criteria in Solid Tumours.

1. Robert C, *et al. Lancet Oncol* 2019;20:1239–1251; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

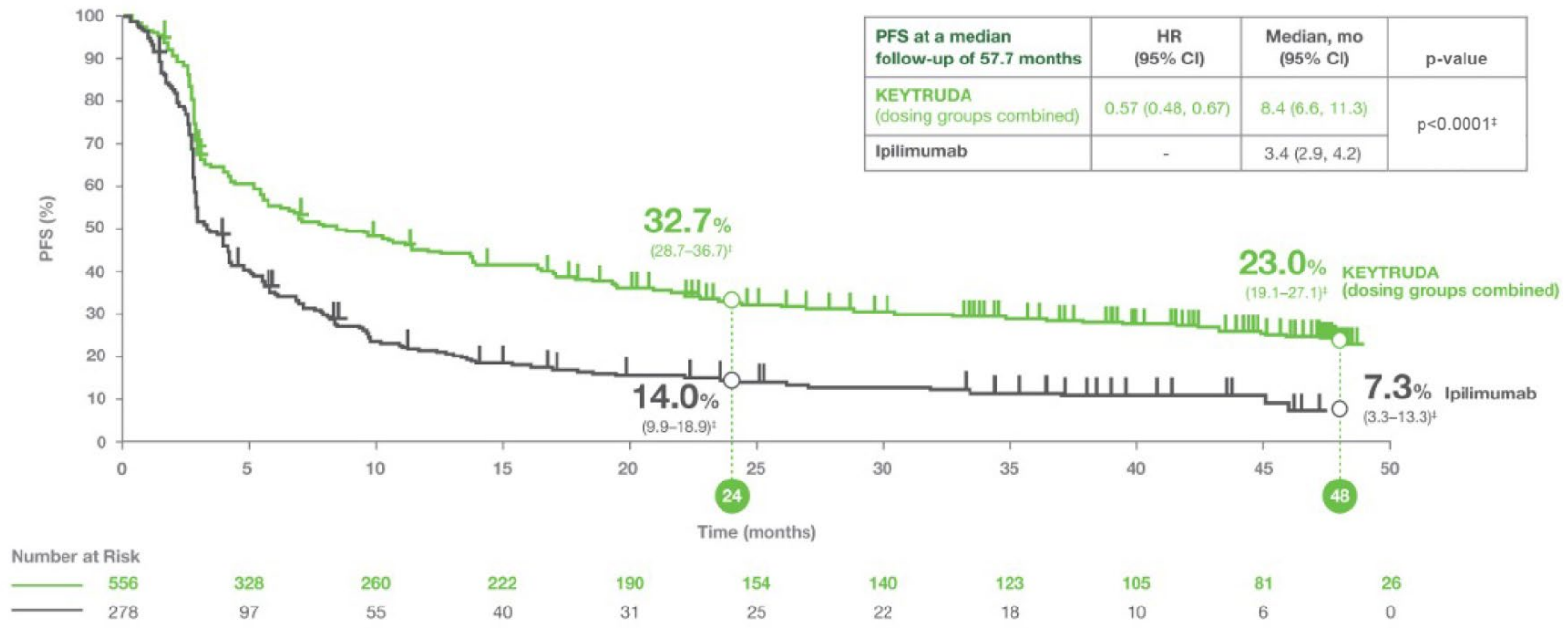
KEYTRUDA® (pembrolizumab)

KEYTRUDA vs Ipilimumab PFS At 5 Years In The Total Study Population Per irRC By Investigator Review[1,2]

- This is a 5-year follow-up post hoc analysis and no statistical conclusions can be drawn from these results

Mean duration of follow-up of surviving patients was 57.7 months (IQR: 56.7–59.2)

Post hoc analysis: Kaplan-Meier of PFS† in all patients per irRC by investigator in KEYNOTE-006[1]



PFS at a median follow-up of 57.7 months	HR (95% CI)	Median, mo (95% CI)	p-value
KEYTRUDA (dosing groups combined)	0.57 (0.48, 0.67)	8.4 (6.6, 11.3)	p<0.0001‡
Ipilimumab	-	3.4 (2.9, 4.2)	

Data pooled from 10 mg/kg Q2W + 10 mg/kg Q3W dosing groups; included 13 patients who received a second course of KEYTRUDA; (n=556).

Adapted from Robert C, *et al.* 2019.[1]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[3] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[3]

Cut-off 3 December 2018. *Based on Cox regression model with treatment as a covariate stratified by line of therapy (first vs second), PD-L1 status (positive vs negative), and ECOG PS (0 vs 1). If no patients are in one of the treatment groups involved in a comparison for a particular stratum, that stratum is excluded for the treatment comparison. †From product-limit (Kaplan-Meier) method for censored data. ‡One-sided p-value based on log-rank test.

CI, confidence interval; HR, hazard ratio; irRC, immune-related response criteria; IQR, interquartile range; OS, overall survival; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Robert C, *et al. Lancet Oncol* 2019;20:1239–1251; **2.** Robert C, *et al. Lancet Oncol* 2019;20:1239–51. Supplementary appendix; **2**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

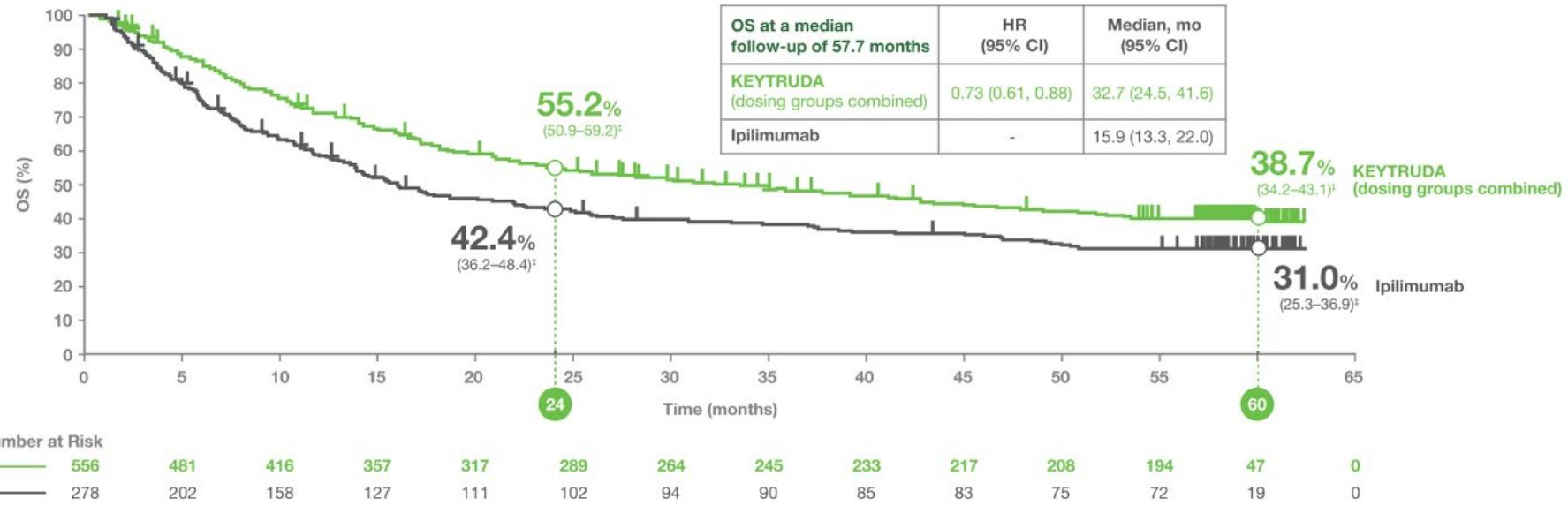
KEYTRUDA® (pembrolizumab)

KEYTRUDA vs Ipilimumab OS At 5 Years In The Total Study Population[1,2]

- This is a 5-year follow-up post hoc analysis and no statistical conclusions can be drawn from these results

Mean duration of follow-up of surviving patients was 57.7 months (IQR: 56.7–59.2)

Post hoc analysis: Kaplan-Meier estimate of OS† in all patients in KEYNOTE-006 (dosing groups combined)[1,2]



Data pooled from 10 mg/kg Q2W + 10 mg/kg Q3W dosing groups; included 13 patients who received a second course of KEYTRUDA; (n=556).

Adapted from Robert C, *et al.* 2019.[1]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[3] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[3]

Cut-off 3 December 2018. *Based on Cox regression model with treatment as a covariate stratified by line of therapy (first vs second), PD-L1 status (positive vs negative), and ECOG PS (0 vs 1). If no patients are in one of the treatment groups involved in a comparison for a particular stratum, that stratum is excluded for the treatment comparison. †From product-limit (Kaplan-Meier) method for censored data. ‡One-sided p-value based on log-rank test.

CI, confidence interval; HR, hazard ratio; IQR, interquartile range; OS, overall survival; PD-L1, programmed cell death ligand 1; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

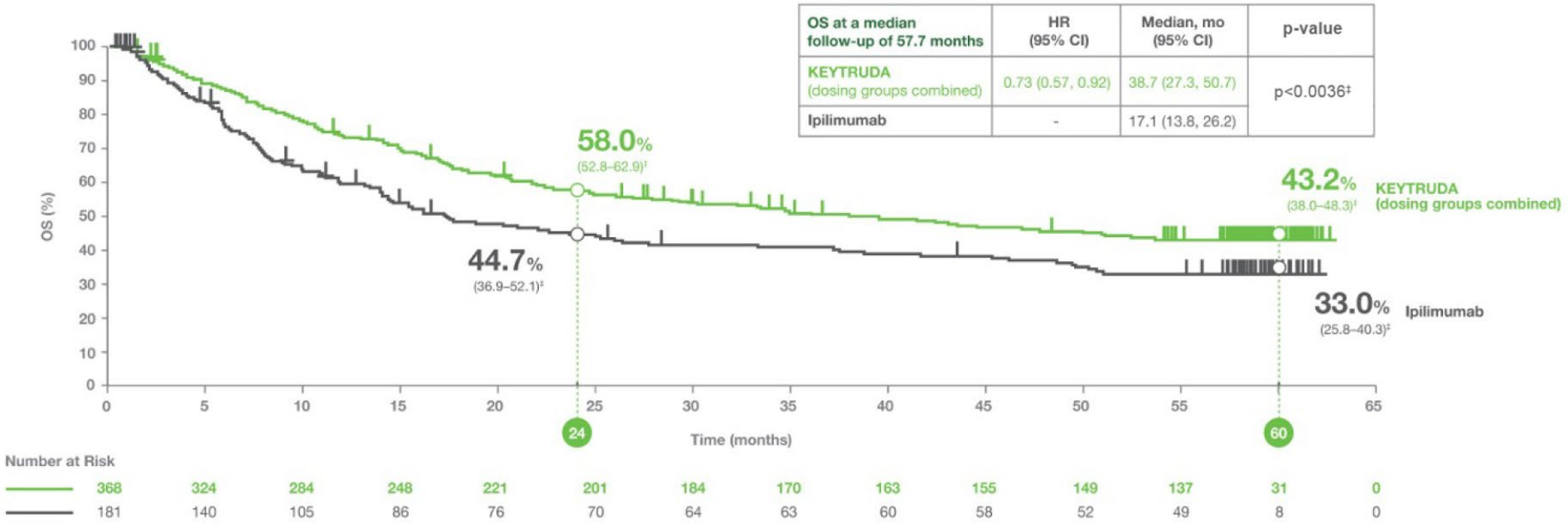
1. Robert C, *et al. Lancet Oncol* 2019;20:1239–51; **2.** Robert C, *et al. Lancet Oncol* 2019;20:1239–51. Supplementary appendix; **3**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

OS At 5 Years In Patients Receiving KEYTRUDA vs Ipilimumab As First-line Therapy[1,2]

Median duration of follow-up of surviving patients was 57.7 months (IQR: 56.7–59.2)

Post hoc analysis: Kaplan-Meier estimate of OS† in all patients receiving first-line KEYTRUDA or ipilimumab for advanced disease[1,2]



Data pooled from 10 mg/kg Q2W + 10 mg/kg Q3W dosing groups; included 13 patients who received a second course of KEYTRUDA; (n=556).

Adapted from Robert C, *et al.* 2019.[1]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[3] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[3]

Cut-off 3 December 2018. *Based on Cox regression model with treatment as a covariate stratified by line of therapy (first vs second), PD-L1 status (positive vs negative), and ECOG PS (0 vs 1). If no patients are in one of the treatment groups involved in a comparison for a particular stratum, that stratum is excluded for the treatment comparison. †From product-limit (Kaplan-Meier) method for censored data. ‡One-sided p-value based on log-rank test.
CI, confidence interval; HR, hazard ratio; IQR, interquartile range; OS, overall survival; PD-L1, programmed cell death ligand 1; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Robert C, *et al. Lancet Oncol* 2019;20:1239–1251; **2.** Robert C, *et al. Lancet Oncol* 2019;20:1239–51. Supplementary appendix; **3**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Objective Response Rates In Patients From Combined KEYTRUDA Groups vs Ipilimumab At 5-years Of Follow-Up[1]

- This is a 5-year follow-up post hoc analysis and no statistical conclusions can be drawn from these results

Data cut-off 3 December 2018

	KEYTRUDA (pooled, n=556)	Ipilimumab (n=278)
Objective response rate (95% CI)	42% (38.1–46.5)	17% (12.4–21.4)
Complete response	14%	3%
Partial response	28%	13%

Objective response rate was a secondary endpoint and not powered for statistical comparison

Data pooled from 10 mg/kg Q2W + 10 mg/kg Q3W dosing groups; included 13 patients who received a second course of KEYTRUDA; n=556).

Note that retreatment with KEYTRUDA is not licensed.

Adapted from Robert C, *et al.* 2019.[1]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

CI, confidence interval; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Robert C, *et al. Lancet Oncol* 2019;20:1239–1251; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

KEYNOTE-006
Safety Data

Treatment-Related Adverse Events Were Observed With KEYTRUDA And Ipilimumab*[1]

Cut-off 3 September 2014

	KEYTRUDA Q2W (n=278)		KEYTRUDA Q3W (n=277)		Ipilimumab (n=256)	
Related to treatment, n (%)	**Any grade**	**Grade 3–5**	**Any grade**	**Grade 3–5**	**Any grade**	**Grade 3–5**
Any	221 (79.5)	37 (13.3)	202 (72.9)	29 (10.1)	187 (73.0)	51 (19.9)
Occurring in ≥10% in any study group						
Fatigue	58 (20.9)	0	53 (19.1)	1 (0.4)	39 (15.2)	3 (1.2)
Diarrhoea	47 (16.9)	7 (2.5)	40 (14.4)	3 (1.1)	58 (22.7)	8 (3.1)
Rash	41 (14.7)	0	37 (13.4)	0	37 (14.5)	2 (0.8)
Pruritus	40 (14.4)	0	39 (14.1)	0	65 (25.4)	1 (0.4)
Asthenia	32 (11.5)	1 (0.4)	31 (11.2)	0	16 (6.3)	2 (0.8)
Nausea	28 (10.1)	0	31 (11.2)	1 (0.4)	22 (8.6)	1 (0.4)
Arthralgia	26 (9.4)	0	32 (11.6)	1 (0.4)	13 (5.1)	2 (0.8)
Vitiligo	25 (9.0)	0	31 (11.2)	0	4 (1.6)	0

Adapted from Robert C, *et al.* 2019.[1]

Please refer to the pooled safety data for KEYTRUDA in the SmPC for a full list of adverse events across multiple studies.[2]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

*The relationship between an adverse event and a study drug was attributed by the investigator. Safety was assessed in the as-treated population, which was defined as all patients who underwent randomisation and who received at least one dose of a study drug.
Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; SmPC, Summary of Product Characteristics.

1. Robert C, *et al. N Engl J Med* 2015;372:2521–2532; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Adverse Events Of Special Interest In The As-Treated Population[1]

Cut-off 3 September 2014

	KEYTRUDA Q2W (n=278)		KEYTRUDA Q3W (n=277)		Ipilimumab (n=256)	
AEOSI,* n (%)	**Any grade**	**Grade 3–5**	**Any grade**	**Grade 3–5**	**Any grade**	**Grade 3–5**
Hypothyroidism	28 (10.1)	1 (0.4)	24 (8.7)	0	5 (2.0)	0
Hyperthyroidism	18 (6.5)	0	9 (3.2)	0	6 (2.3)	1 (0.4)
Colitis	5 (1.8)	4 (1.4)	10 (3.6)	7 (2.5)	21 (8.2)	18 (7.0)
Hepatitis	3 (1.1)	3 (1.1)	5 (1.8)	5 (1.8)	3 (1.2)	1 (0.4)
Hypophysitis	1 (0.4)	1 (0.4)	2 (0.7)	1 (0.4)	6 (2.3)	4 (1.6)
Pneumonitis	1 (0.4)	0	5 (1.8)	1 (0.4)	1 (0.4)	1 (0.4)
Type 1 diabetes mellitus	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.4)	0	0
Uveitis	1 (0.4)	0	3 (1.1)	0	0	0
Myositis	0	0	2 (0.7)	0	1 (0.4)	0
Nephritis	0	0	1 (0.4)	0	1 (0.4)	1 (0.4)

Adapted from Robert C, *et al.* 2019.[1]

Please refer to the pooled safety data for KEYTRUDA in the SmPC for a full list of adverse events across multiple studies.[2]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Safety was assessed in the as-treated population, which was defined as all patients who underwent randomisation and who received at least one dose of a study drug.
*The listed adverse events of special interest include related terms and are provided regardless of attribution to a study drug.
AEOSI, adverse events of special interest; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; SmPC, Summary of Product Characteristics.
1. Robert C, *et al. N Engl J Med* 2015;372:2521–2532; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Treatment-Related Adverse Events Were Observed With KEYTRUDA And Ipilimumab[1*]

Cut-off 3 December 2018

	KEYTRUDA (pooled 10 mg/kg Q2W + 10 mg/kg Q3W dosing groups; n=555)		Ipilimumab group (n=256)	
Related to treatment, n (%)	**Grade 1-2**	**Grade 3–5**	**Grade 1-2**	**Grade 3–5**
Any	436 (79)	103 (19)	183 (71)	54 (21)
Diarrhoea	92 (17)	10 (2)	55 (21)	7 (3)
Nausea	73 (13)	1 (<1)	23 (9)	1 (<1)
Asthenia	68 (12)	2 (<1)	14 (5)	2 (<1)
Fatigue	141 (25)	4 (<1)	40 (16)	3 (1)
Arthralgia	70 (13)	3 (<1)	12 (5)	1 (<1)
Pruritus	111 (20)	1 (<1)	65 (25)	2 (<1)
Rash	92 (17)	0	38 (15)	2 (<1)
Vitiligo	71 (13)	0	4 (2)	0

Adapted from Robert C, *et al.* 2019.[1]

Please refer to the pooled safety data for KEYTRUDA in the SmPC for a full list of adverse events across multiple studies.[2]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

*Safety was assessed in the as-treated population, which was defined as all patients who underwent randomisation and who received at least one dose of a study drug.
Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; SmPC, Summary of Product Characteristics.

1. Robert C, *et al. Lancet Oncol* 2019;20:1239–1251; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Immune-Mediated Adverse Events In The As-treated Population[1]

Cut-off 3 December 2018

	KEYTRUDA (pooled 10 mg/kg Q2W + 10 mg/kg Q3W dosing groups; n=555)	Ipilimumab group (n=256)
Immune-mediated AEs summary, n (%)		
Any grade	148 (27)	48 (19)
Grade 3–4	53 (10)	31 (12)
Led to death	0 (0)	0 (0)
Led to discontinuation	30 (5)	14 (6)
Immune-mediated AEs occurring in >2% of patients, n (%)		
Hypothyroidism	60 (11)	5 (2)
Hyperthyroidism	29 (5)	6 (2)
Colitis	18 (3)	19 (7)
Skin disorders	14 (3)	5 (2)
Pneumonitis	13 (2)	1 (<1)

One case of death occurred in the KEYTRUDA 10 mg/kg Q2W arm that was considered by the investigator to be drug-related (sepsis).[2]

Adapted from Robert C, *et al.* 2019.[1]

Please refer to the pooled safety data for KEYTRUDA in the SmPC for a full list of adverse events across multiple studies.[3]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[3] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[3]

*Not adjusted for exposure. Immune-mediated AEs are based on a list of terms specified by the sponsor and were considered regardless of attribution by the investigator.
Safety was assessed in the as-treated population, which was defined as all patients who underwent randomisation and who received at least one dose of a study drug.
AE, adverse event; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; SmPC, Summary of Product Characteristics.

1. Robert C, *et al. Lancet Oncol* 2019;20:1239–1251. Supplementary appendix; **2.** Robert C, *et al. Lancet Oncol* 2019;20:1239–1251; **3.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

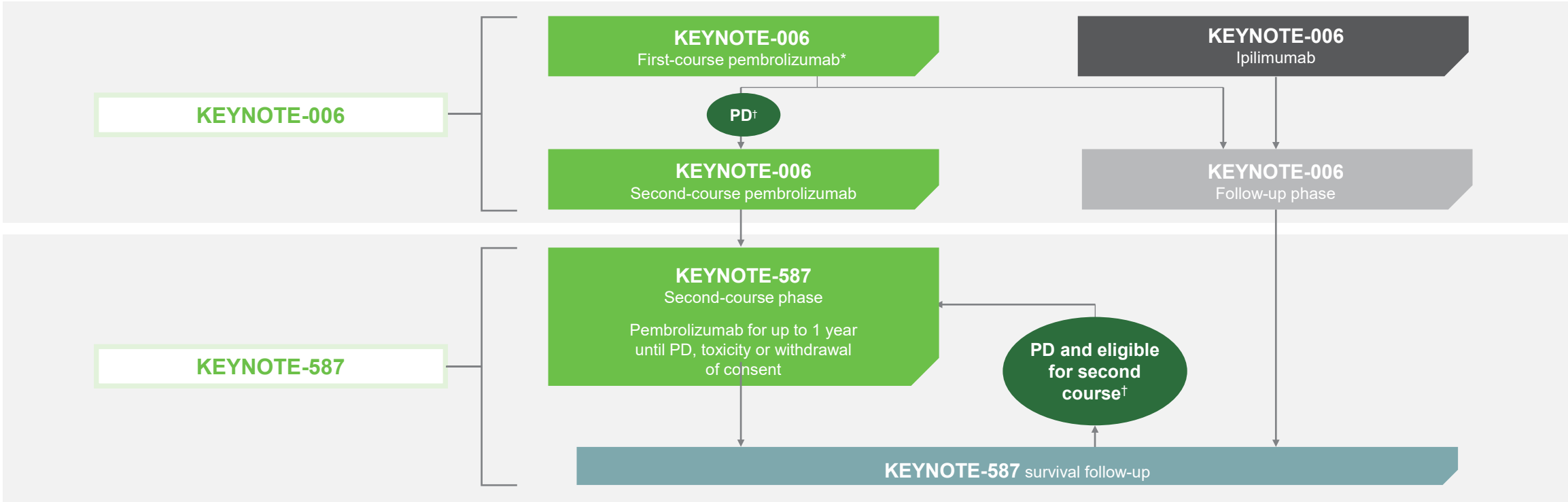
KEYNOTE-006 7-year Post Hoc Analysis (KEYNOTE-587)

Post Hoc Analysis At 7-year Follow-Up

Study Design[1]

Patient flow from KEYNOTE-006 to KEYNOTE-587 (extension study)[1]

Median duration of follow-up was 85.3 months[1]



Adapted from Robert C, *et al.* 2023.[1]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

*All patients from KEYNOTE-006 who enrolled in KEYNOTE-587 had completed the first course of pembrolizumab.
†Patients with SD or better on first-course pembrolizumab who had subsequent PD were eligible for a second course of pembrolizumab in KEYNOTE-006 or KEYNOTE-587. Patients in the survival follow-up phase were contacted over 12 weeks to assess for survival status and start of a new anti-cancer therapy until death, withdrawal or the end of the trial.
SD, stable disease; PD, progressive disease; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.
1. Robert C, *et al. J Clin Oncol* 2023;41:3998-4003; **2**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Patient Pathway From KEYNOTE-006 To KEYNOTE-587

Characteristic	Pembrolizumab no. (%)	Ipilimumab no. (%)
Randomly assigned to treatment in KEYNOTE-006	556 (100)	278 (100)
Died during KEYNOTE-006	328 (59.0)	173 (62.2)
Eligible to enrol in KEYNOTE-587	228 (41.0)	105 (37.8)
Alive, but did not enrol in KEYNOTE-587*	70 (30.7)	53 (50.5)
Enrolled in KEYNOTE-587	158 (69.3)	52 (49.5)

Adapted from Robert C, *et al.* 2023.[1]

For PFS and OS analysis, patients in KEYNOTE-006 who did not enrol in KEYNOTE-587 were censored at the date last known alive.

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

*70 patients in the pembrolizumab arm and 53 patients in the ipilimumab arm were alive after KEYNOTE-006 but did not enrol in KEYNOTE-587.
OS, overall survival; PFS, progression-free survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.
1. Robert C, *et al. J Clin Oncol* 2023; 41:3998-4003; **2**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Key Trial Endpoints[1]

1

Primary efficacy endpoint:

- Overall survival: time from randomisation to death from any cause

2

Secondary endpoints:

- Duration of response per evaluation criteria used in the parent study
- Progression-free survival
- Duration of complete response per evaluation criteria used in the parent study
- Safety

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Robert C, *et al. J Clin Oncol* 2023;41:3998-4003; **2**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

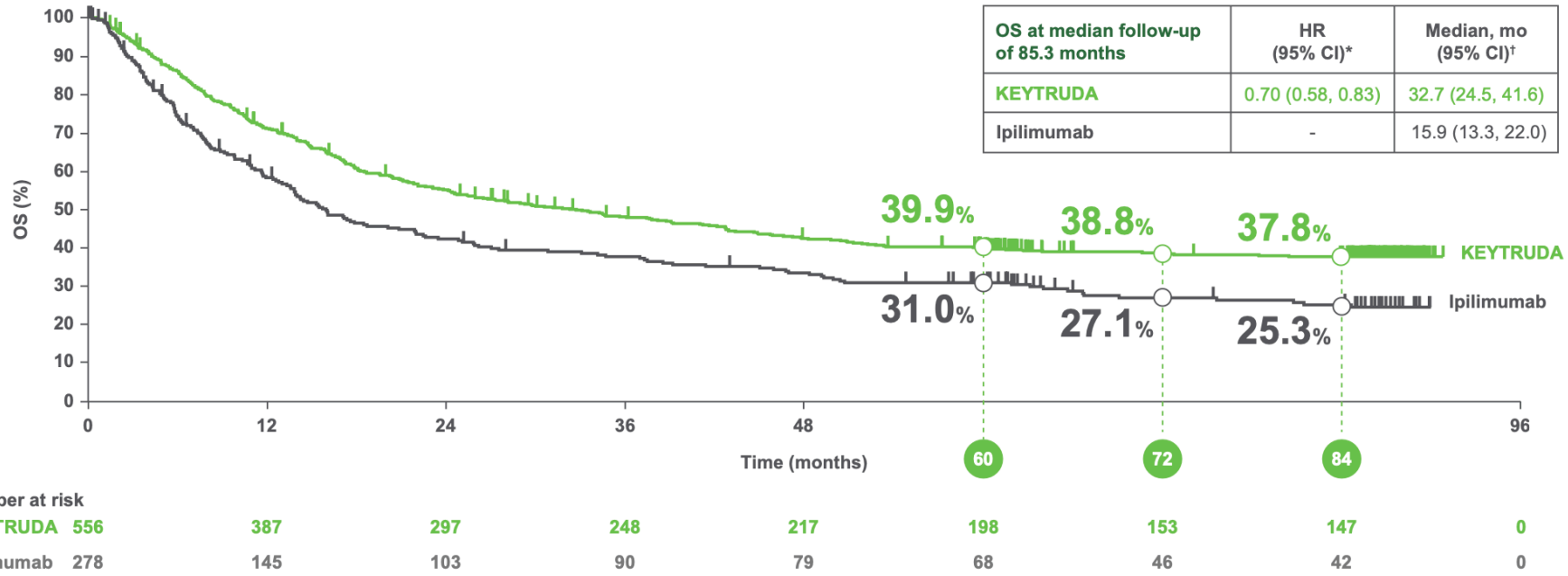
KEYTRUDA® (pembrolizumab)

OS At 7 Years In The Overall KEYNOTE-006 Population[1]

- This is a 7-year follow-up post hoc analysis and no statistical conclusions can be drawn from these results

Median duration of follow-up of surviving patients was 85.3 months

Post hoc analysis: Kaplan-Meier estimate of OS in all patients in KEYNOTE-006[1]



OS at median follow-up of 85.3 months	HR (95% CI)*	Median, mo (95% CI)†
KEYTRUDA	0.70 (0.58, 0.83)	32.7 (24.5, 41.6)
Ipilimumab	-	15.9 (13.3, 22.0)

Number at risk									
KEYTRUDA	556	387	297	248	217	198	153	147	0
Ipilimumab	278	145	103	90	79	68	46	42	0

- **Patients in KEYNOTE-006 who did not enrol in KEYNOTE-587 were censored at the date last known alive.**
- **For OS, patients who had survival follow-up after the data cut-off date were censored at the time of data cut-off**

Adapted from Robert C, *et al.* 2023.[1]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Cut-off 19 April 2021. *From product-limit (Kaplan-Meier) method for censored data. †On the basis of Cox regression model with the Efron method of tie handling with treatment as a covariate.
CI, confidence interval; HR, hazard ratio; OS, overall survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Robert C, *et al. J Clin Oncol* 2023; 41:3998-4003; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

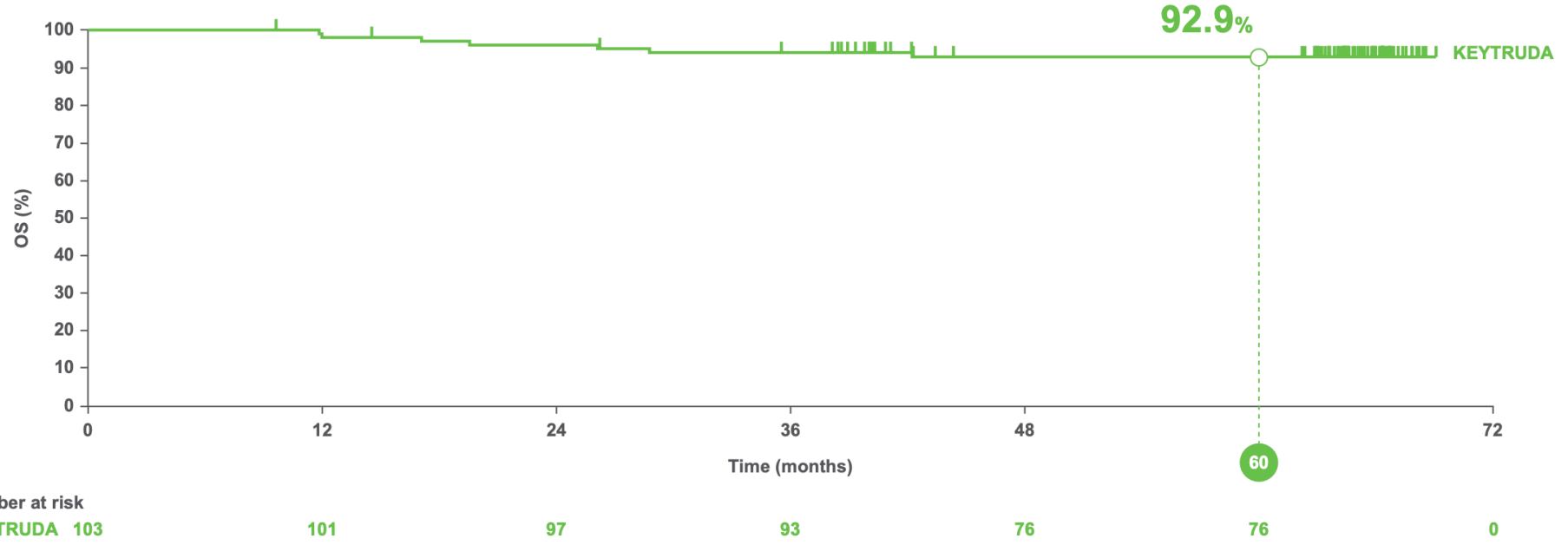
KEYTRUDA® (pembrolizumab)

OS From Week 94[1]

- This is a 7-year follow-up post hoc analysis and no statistical conclusions can be drawn from these results

Median duration of follow-up of surviving patients was 85.3 months

Post hoc analysis: Kaplan-Meier of OS in patients who completed ≥ 94 weeks of treatment with pembrolizumab in KEYNOTE-006 and had SD or better



- **Patients in KEYNOTE-006 who did not enrol in KEYNOTE-587 were censored at the date last known alive.**
- **For OS, patients who had survival follow-up after the data cut-off date were censored at the time of data cut-off**

Adapted from Robert C, *et al.* 2023.[1]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Cut-off 19 April 2021.

CI, confidence interval; HR, hazard ratio; OS, overall survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; SD, stable disease.

1. Robert C, *et al. J Clin Oncol* 2023; 41:3998-4003; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

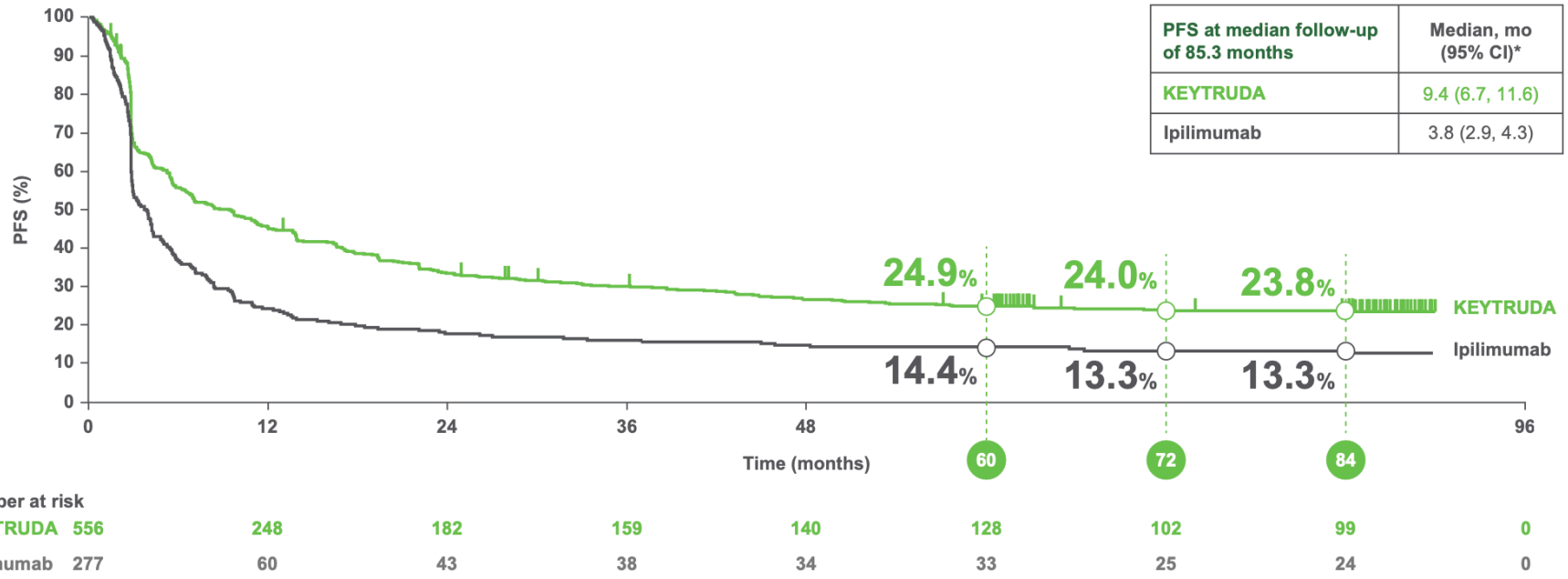
KEYTRUDA® (pembrolizumab)

PFS At 7 Years In The Total KEYNOTE-006 Population Per imRC By Investigator Review[1]

- This is a 7-year follow-up post hoc analysis and no statistical conclusions can be drawn from these results

Median duration of follow-up of surviving patients was 85.3 months

Post hoc analysis: Kaplan-Meier of PFS in all patients per imRC by investigator in KEYNOTE-006[1]



PFS at median follow-up of 85.3 months	Median, mo (95% CI)*
KEYTRUDA	9.4 (6.7, 11.6)
Ipilimumab	3.8 (2.9, 4.3)

- **Patients in KEYNOTE-006 who did not enrol in KEYNOTE-587 were censored at the date last known alive.**
- **For PFS, patients without progressive disease were censored at the date last known alive**

Adapted from Robert C, *et al.* 2023.[1]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Cut-off 19 April 2021. *From product-limit (Kaplan-Meier) method for censored data.
CI, confidence interval; HR, hazard ratio; imRC, immune-mediated response criteria; PFS, progression-free survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.
1. Robert C, *et al. J Clin Oncol* 2023; 41:3998-4003; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

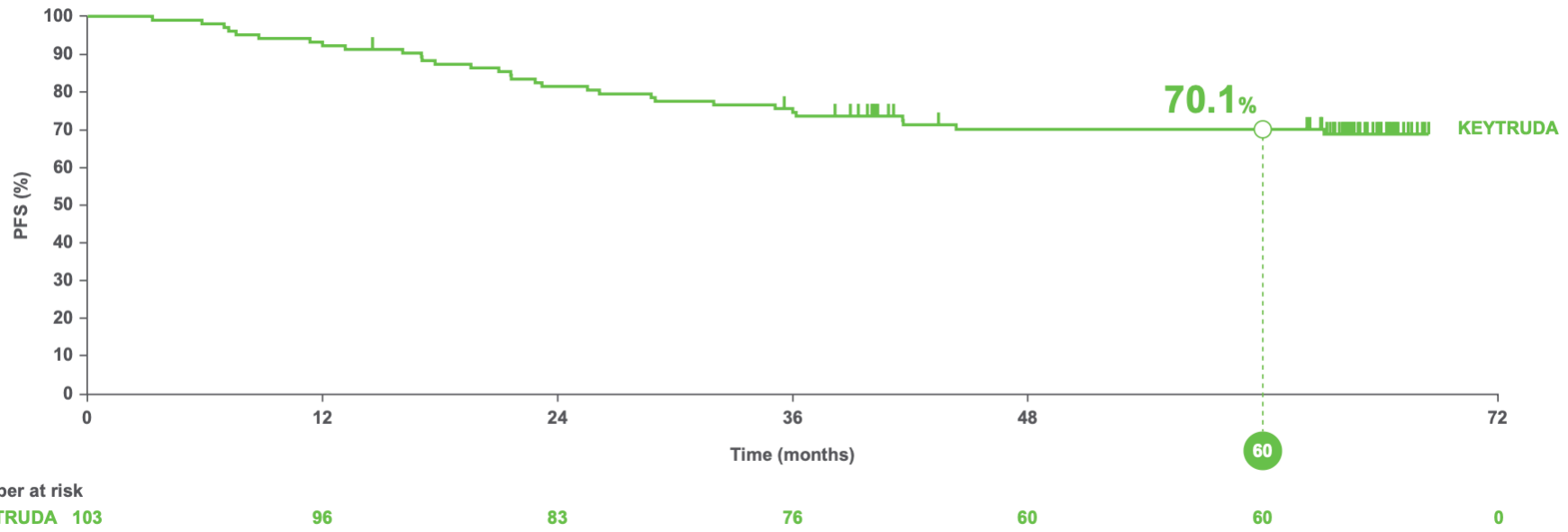
KEYTRUDA® (pembrolizumab)

PFS Per imRC By Investigator Review From Week 94[1]

- This is a 7-year follow-up post hoc analysis and no statistical conclusions can be drawn from these results

Median duration of follow-up of surviving patients was 85.3 months

Post hoc analysis: Kaplan-Meier of PFS in patients who completed ≥94 weeks of treatment with pembrolizumab in KEYNOTE-006 and had SD or better per imRC by investigator in KEYNOTE-006[1]



- **Patients in KEYNOTE-006 who did not enrol in KEYNOTE-587 were censored at the date last known alive.**
- **For PFS, patients without progressive disease were censored at the date last known alive**

Adapted from Robert C, *et al.* 2023.[1]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Cut-off 19 April 2021.
CI, confidence interval; HR, hazard ratio; imRC, immune-mediated response criteria; PFS, progression-free survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; SD, stable disease.

1. Robert C, *et al. J Clin Oncol* 2023; 41:3998-4003; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

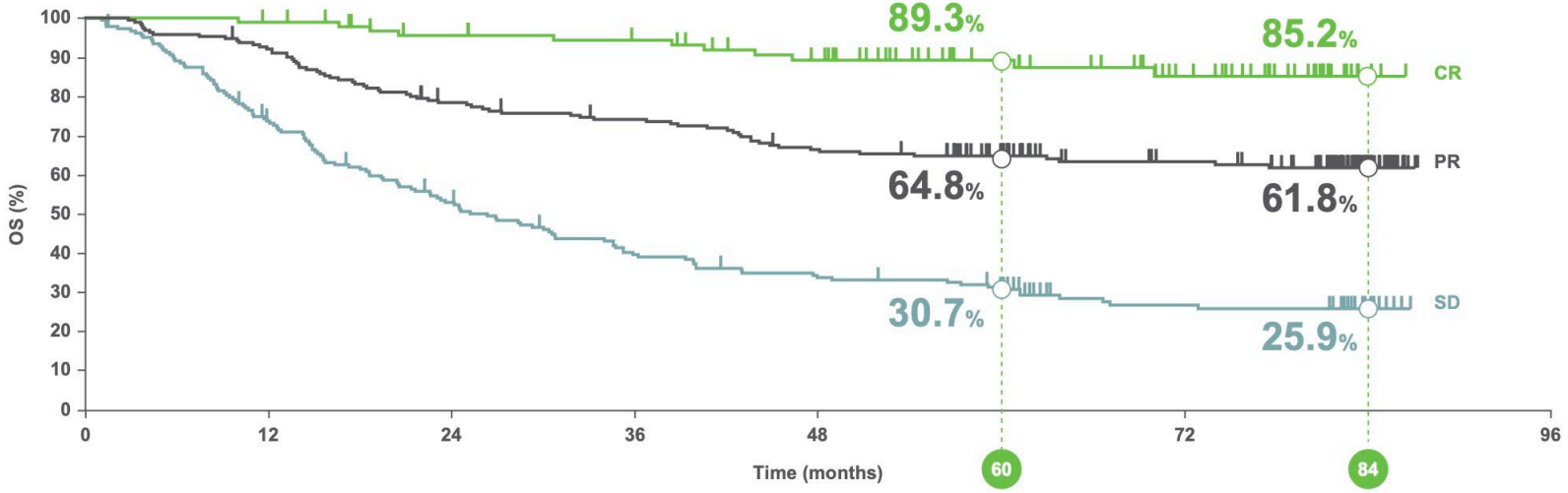
KEYTRUDA® (pembrolizumab)

OS By Best Overall Response In Patients Treated With Pembrolizumab In KEYNOTE-006[1]

- This is a 7-year follow-up post hoc analysis and no statistical conclusions can be drawn from these results

Median duration of follow-up of surviving patients was 85.3 months

Post hoc analysis: Kaplan-Meier estimate of OS by best overall response in patients treated with pembrolizumab in KEYNOTE-006[1]



Adapted from Robert C, *et al.* 2023.[1]

- **Patients in KEYNOTE-006 who did not enrol in KEYNOTE-587 were censored at the date last known alive.**
- **For OS, patients who had survival follow-up after the data cut-off date were censored at the time of data cut-off**

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Cut-off 19 April 2021.
CI, confidence interval; CR, complete response; HR, hazard ratio; OS, overall survival; PR, partial response; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; SD, stable disease.
1. Robert C, *et al. J Clin Oncol* 2023; 41:3998-4003; **2**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

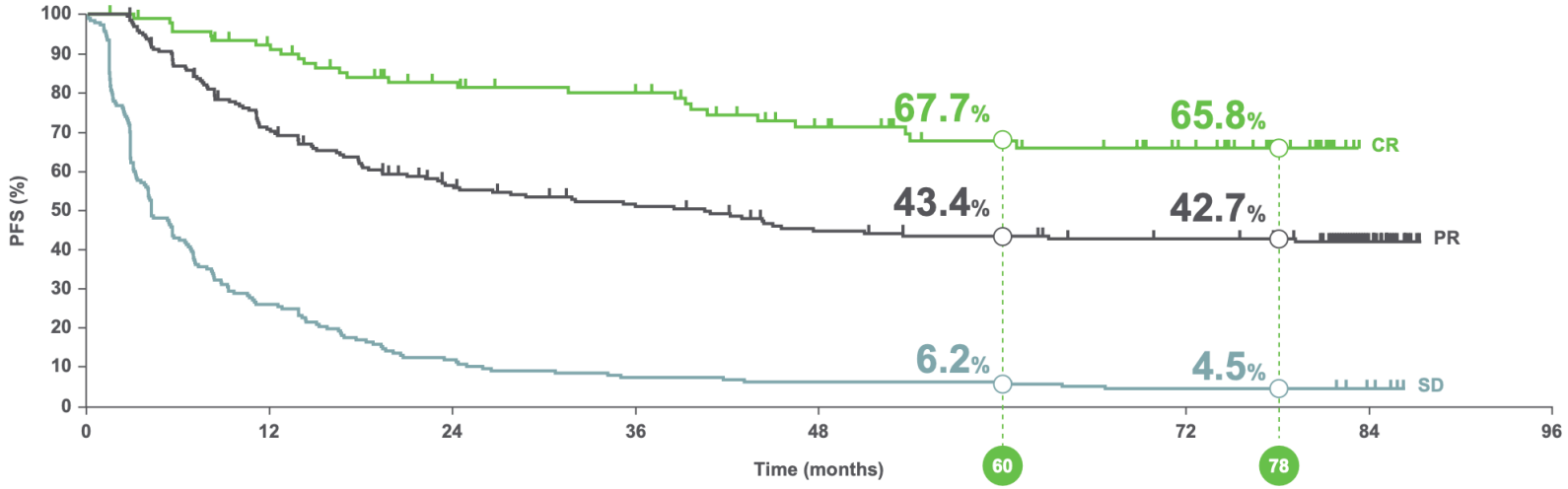
KEYTRUDA® (pembrolizumab)

PFS By Best Overall Response In Patients Treated With Pembrolizumab In KEYNOTE-006[1]

- This is a 7-year follow-up post hoc analysis and no statistical conclusions can be drawn from these results

Median duration of follow-up of surviving patients was 85.3 months

Post hoc analysis: Kaplan-Meier estimate of PFS by best overall response in patients treated with pembrolizumab in KEYNOTE-006[1]



Number at risk									
CR	93	78	64	58	45	37	28	0	0
PR	191	130	97	84	70	66	61	26	0
SD	184	46	21	13	11	11	8	4	0

Adapted from Robert C, *et al.* 2023.[1]

- **Patients in KEYNOTE-006 who did not enrol in KEYNOTE-587 were censored at the date last known alive.**
- **For PFS, patients without progressive disease were censored at the date last known alive**

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Cut-off 19 April 2021.
CR, complete response; PFS, progression-free survival; PR, partial response; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; SD, stable disease.

1. Robert C, *et al. J Clin Oncol* 2023; 41:3998-4003; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

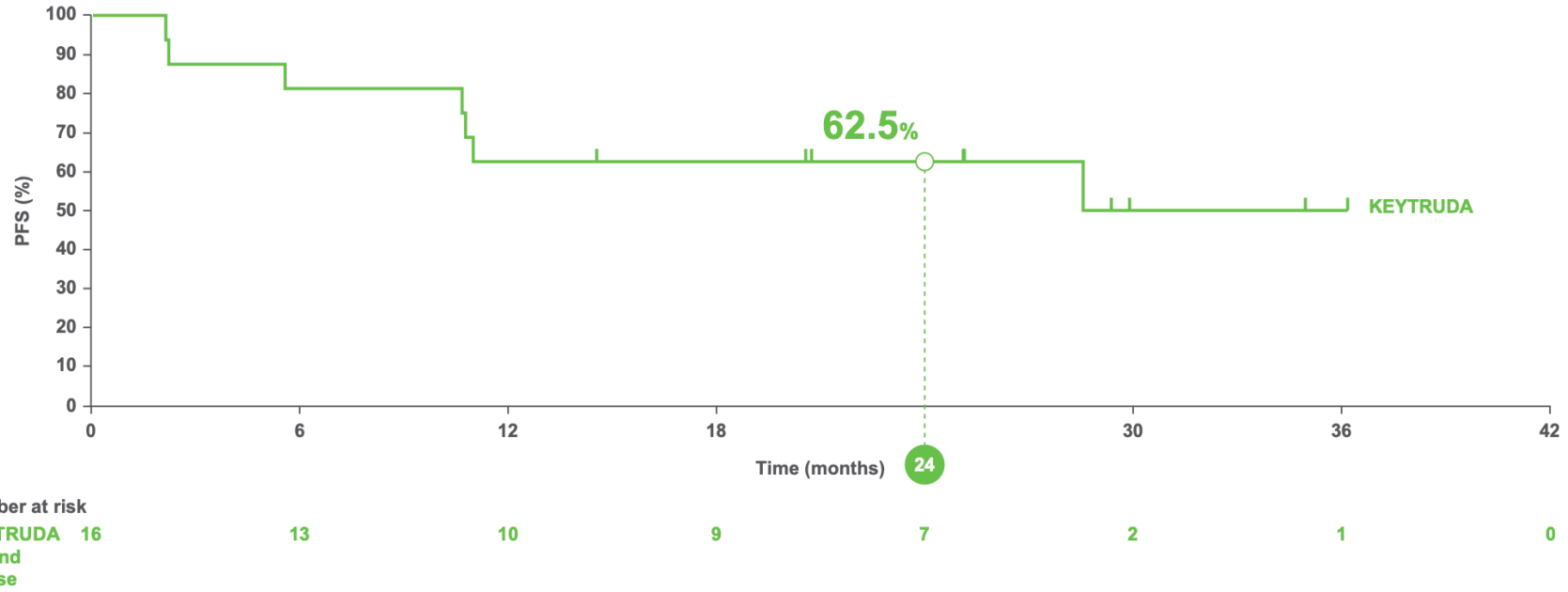
KEYTRUDA® (pembrolizumab)

PFS By Investigator Review Per RECIST V1.1 In Patients Receiving Second-Course Pembrolizumab In KEYNOTE-006 Or KEYNOTE-587[1]

- This is a 7-year follow-up post hoc analysis and no statistical conclusions can be drawn from these results

Median duration of follow-up of surviving patients was 85.3 months

Post hoc analysis: Kaplan-Meier estimate of PFS from start of second-course pembrolizumab by investigator review per RECIST v1.1 in patients receiving second-course pembrolizumab in KEYNOTE-006 or KEYNOTE-587[1]



- **Patients in KEYNOTE-006 who did not enrol in KEYNOTE-587 were censored at the date last known alive.**
- **For PFS, patients without progressive disease were censored at the date last known alive**

Adapted from Robert C, *et al.* 2023.[1]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Cut-off 19 April 2021.

PFS, progression-free survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; RECIST, Response Evaluation Criteria in Solid Tumours.

1. Robert C, *et al. J Clin Oncol* 2023; 41:3998-4003; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Patients Such As Farah* Could Benefit From KEYTRUDA Treatment Similar To Patients In KEYNOTE-006

See Farah's profile here

GB PI | NI PI

- Patients with advanced stage melanoma achieved:

Significant improvements in OS and PFS with KEYTRUDA vs ipilimumab at minimum follow-up of 21 months[1,2]

Durable improvement in OS and PFS rates with KEYTRUDA vs ipilimumab at a median follow-up of 5 years[2]

KEYTRUDA provides long-term survival benefit at a median follow-up of 7 years[3]

- KEYTRUDA demonstrated **a generally manageable safety profile** in advanced melanoma patients, consistent with previous studies of KEYTRUDA in melanoma[2]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[4] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[4]

*Not a real patient.
OS, overall survival; PFS, progression-free survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.
1. Schachter J, *et al. Lancet* 2017;390:1853–1862; **2.** Robert C, *et al. Lancet Oncol* 2019;20:1239–51; **3.** Robert C, *et al. J Clin Oncol* 2023; 41:3998-4003; **4**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

KEYTRUDA Offers Flexibility Of Dosing[1]

Administered as an IV infusion[1]

Over 30 minutes[1]

Adult patients

200 mg every **3** weeks

OR

400 mg every **6** weeks

Paediatric patients*

2 mg/kg bw every **3** weeks, up to a maximum of 200 mg

The 200 mg once every 3 weeks regimen has been assessed in Phase II and Phase III 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 once every 6 weeks dosing for monotherapy and combination therapy.[1]

The recommended dose of KEYTRUDA as monotherapy in paediatric patients aged 12 years and older with melanoma is 2 mg/kg body weight (up to a maximum of 200 mg), every 3 weeks administered as an intravenous infusion over 30 minutes.[1]

What does the flexibility of dosing mean for you and your patients?

Please refer to the KEYTRUDA Summary of Product Characteristics and patient Risk Minimisation Materials before prescribing KEYTRUDA.

*Paediatric patients must be 12 years or older.
bw, bodyweight; IV, intravenous.

1. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Find Out More About KEYTRUDA In Melanoma

GB PI | NI PI

Click here or scan the QR code to sign up for MSD emails and be the first to hear updates about KEYTRUDA in melanoma.

This link will take you to an MSD website within which you can give your consent to receive marketing or promotional emails from MSD about our products, services and events.

KEYTRUDA® (pembrolizumab)

Appendices

KEYNOTE-001 Appendix

KEYNOTE-002 Appendix

KEYNOTE-006 Appendix

Patient Baseline Characteristics (1/3)[1]

Return to study design

GB PI | NI PI

	Total (N=655)	Ipilimumab-treated (n=342)	Ipilimumab-naïve (n=313)	Treatment-naïve (n=152)*
Age, median (range), years	61 (18–94)	61 (18–88)	61 (23–94)	63 (26–90)
Male, %	62	63	61	68
Race, n (%)				
White	636 (97)	334 (98)	302 (96)	144 (95)
Asian	10 (2)	3 (1)	7 (2)	4 (3)
Black or African American	5 (1)	3 (1)	2 (1)	2 (1)
Other	4 (1)	2 (1)	2 (1)	2 (1)
ECOG PS, n (%)				
0	444 (68)	215 (63)	229 (73)	113 (74)
1	210 (32)	126 (37)	84 (27)	39 (26)
Unknown	1 (0.2)	1 (0.3)	0	0
BRAF-mutation status, n (%)				
Mutant	155 (24)	64 (19)	91 (29)	25 (16)
Wild-type	494 (75)	277 (81)	217 (69)	125 (82)
Unknown	6 (1)	1 (0.3)	5 (2)	2 (1)

Adapted from Ribas A, *et al.* 2016.[1]

In KEYNOTE-001, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-001 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Due to rounding, some sections may not add up to 100%. *Indicates patients without any prior systemic treatment for advanced melanoma.
ECOG PS, Eastern Cooperative Oncology Group Performance status; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Ribas A, *et al. JAMA* 2016;315:1600–1609; **2**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Patient Baseline Characteristics (2/3)[1]

Return to study design

GB PI | NI PI

	Total (N=655)	Ipilimumab-treated (n=342)	Ipilimumab-naïve (n=313)	Treatment-naïve (n=152)*
Brain metastasis, n (%)				
Yes	54 (8)	37 (11)	17 (5)	7 (5)
No	600 (9.2)	305 (89)	295 (94)	145 (95)
Unknown	1 (0.2)	0	1 (0.3)	0
LDH, n (%)				
Normal (≤100% ULN)	393 (60)	199 (58)	194 (62)	95 (63)
Elevated (>100% ULN)	250 (38)	139 (41)	111 (35)	50 (33)
Unknown	12 (2)	4 (1)	8 (3)	7 (5)
Baseline tumour size, median (range), mm	102 (10–895)	120 (10–895)	90 (11–752)	87 (11–752)
M category, n (%)				
M0	8 (1)	2 (1)	6 (2)	3 (2)
M1a	50 (8)	30 (9)	20 (6)	12 (8)
M1b	89 (14)	38 (11)	51 (16)	28 (18)
M1b	508 (78)	272 (80)	236 (75)	109 (72)

Adapted from Ribas A, *et al.* 2016.[1]

In KEYNOTE-001, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-001 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Due to rounding, some sections may not add up to 100%. *Indicates patients without any prior systemic treatment for advanced melanoma.
LDH, lactate dehydrogenase; M, metastasis; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; ULN, upper limit of normal.
1. Ribas A, *et al. JAMA* 2016;315:1600–1609; **2**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Patient Baseline Characteristics (3/3)[1]

Return to study design

GB PI | NI PI

	Total (N=655)	Ipilimumab-treated (n=342)	Ipilimumab-naïve (n=313)	Treatment-naïve (n=152)*
Previous systemic therapies, n (%)				
0	161 (25)	0	161 (51)	152 (100)
1	206 (31)	103 (30)	103 (33)	0
2	174 (27)	128 (37)	46 (15)	0
≥3	114 (17)	111 (32)	3 (1)	0
Previous treatments, n (%)†				
Ipilimumab	342 (52)	342 (100)	0	0
Chemotherapy	215 (33)	155 (45)	60 (19)	0
BRAF or *MEK* inhibitor	110 (17)	63 (18)	47 (15)	0
Other immunotherapy‡	173 (26)	105 (31)	68 (22)	0
Other therapy	94 (14)	66 (19)	28 (9)	0

Adapted from Ribas A, *et al.* 2016.[1]

In KEYNOTE-001, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-001 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Due to rounding, some sections may not add up to 100%. *Indicates patients without any prior systemic treatment for advanced melanoma.
†Excludes neoadjuvant therapies. Patients may have received more than one type of previous therapy. ‡Excludes ipilimumab.
Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Ribas A, *et al. JAMA* 2016;315:1600–1609; **2**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

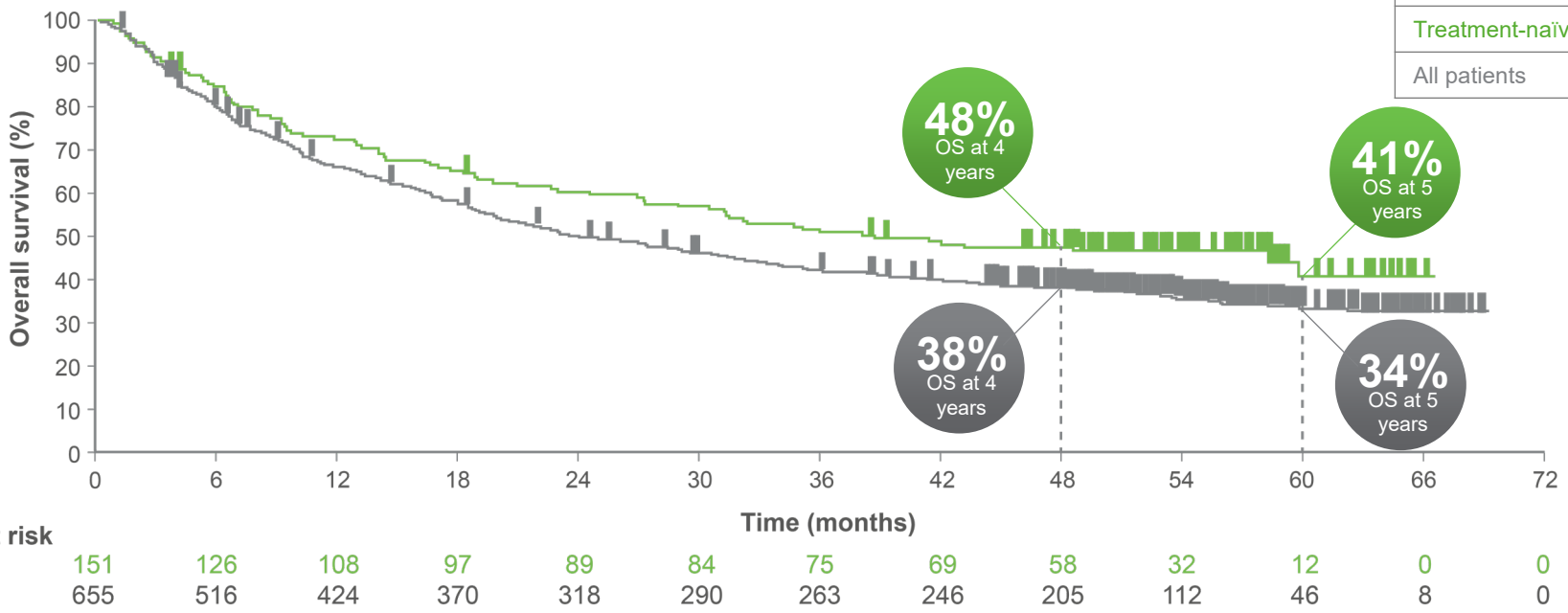
Return to data selection | Progression free survival | GB PI | NI PI

OS After 5 Years In All Patients And In Treatment-Naïve Patients With KEYTRUDA[1]

Median duration of follow-up was 55 months[1]

Kaplan-Meier estimate of OS in KEYNOTE-001*[1]

	Patients, n	Events	Median, (95% CI)
Treatment-naïve	151	81	38.6 (27.2–NR)
All patients	655	412	23.8 (20.2–30.4)



Adapted from Hamid, *et al.* 2019.[1]

In KEYNOTE-001, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-001 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Cut-off 1 September 2017. *Derived by the product limit (Kaplan-Meier) method of censored data. OS and PFS were secondary endpoints.[1]
CI, confidence interval; NR, not reached; OS, overall survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.
1. Hamid O, *et al. Ann Oncol* 2019;30:582–588; **2**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

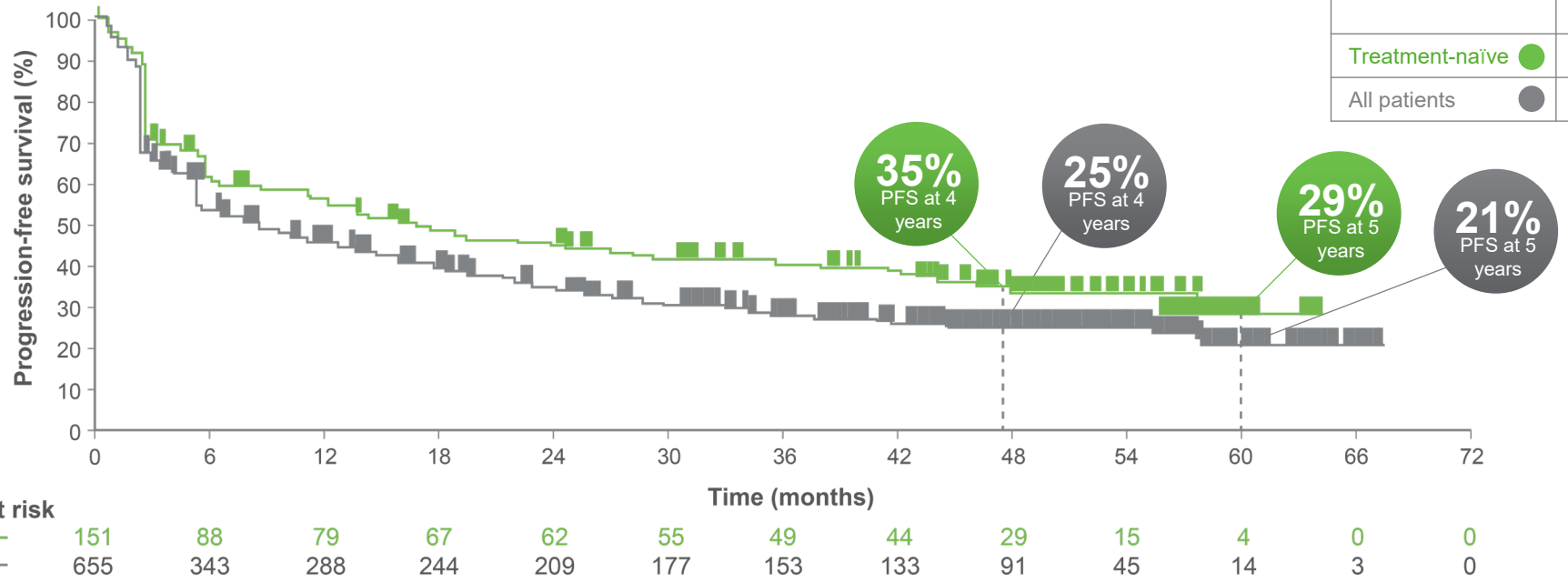
KEYTRUDA® (pembrolizumab)

Return to data selection | Overall response | GB PI | NI PI

PFS After 5 Years In All Patients And In Treatment-naïve Patients With KEYTRUDA[1]

Median duration of follow-up was 55 months[1]

Kaplan-Meier estimate of PFS per irRC by investigator in KEYNOTE-001*[1]



	Patients, n	Events	Median, (95% CI)
Treatment-naïve	151	94	16.9 (9.3–35.5)
All patients	655	479	8.3 (5.8–11.1)

Adapted from Hamid, *et al.* 2019.[1]

In KEYNOTE-001, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-001 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Cut-off 1 September 2017. *Derived by the product limit (Kaplan-Meier) method of censored data. OS and PFS were secondary endpoints.[1]
CI, confidence interval; irRC, immune-related response criteria; NR, not reached; PFS, progression-free survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.
1. Hamid O, *et al. Ann Oncol* 2019;30:582–588; **2**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Overall Response To KEYTRUDA In All Patients And In Treatment-Naïve Patients[1]

Median duration of follow-up was 55 months[1]

Best overall response per irRC by investigator in KEYNOTE-001*[1]

	All patients N=655 % (95% CI)	Treatment-naïve n=151 % (95% CI)
Overall response	41 (37–45)	52 (43–60)
Complete response	16 (13–19)	25 (19–33)
Partial response	25 (22–28)	27 (20–34)
Stable disease	24 (21–27)	20 (14–27)
Progressive disease	25 (22–29)	21 (15–29)
No assessment	10 (8–13)	7 (4–13)

Adapted from Hamid, *et al.* 2019.[1]

In KEYNOTE-001, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-001 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Cut-off 1 September 2017. *Analysis based on patients with a best overall response as confirmed complete or partial response.
CI, confidence interval; irRC, immune-related response criteria; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.
1. Hamid O, *et al. Ann Oncol* 2019;30:582–588; **2**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

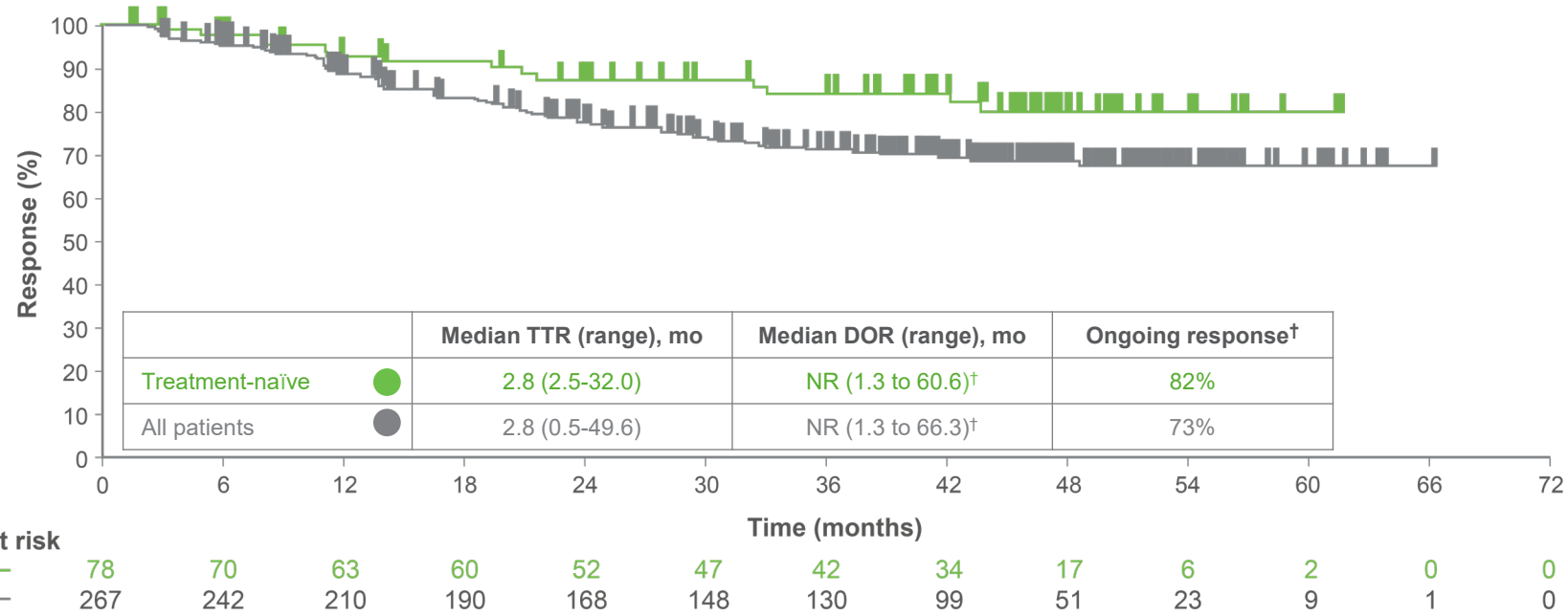
KEYTRUDA® (pembrolizumab)

Return to data selection
GB PI
NI PI

Objective Response Duration In All Patients And In Treatment-Naïve Patients With KEYTRUDA[1]

Median duration of follow-up was 55 months[1]

Duration of response per irRC by investigator in KEYNOTE-001*[1]



	Median TTR (range), mo	Median DOR (range), mo	Ongoing response†
Treatment-naïve	2.8 (2.5-32.0)	NR (1.3 to 60.6)†	82%
All patients	2.8 (0.5-49.6)	NR (1.3 to 66.3)†	73%

Number at risk

78	70	63	60	52	47	42	34	17	6	2	0	0
267	242	210	190	168	148	130	99	51	23	9	1	0

Adapted from Hamid, *et al.* 2019.[1]

In KEYNOTE-001, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[3] Data from KEYNOTE-001 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[3]

Analysis based on patients with a best overall response as confirmed complete or partial response. *Cut-off 1 September 2017.[2] †Indicates non-progressive disease at the last assessment (censored) for the patient with the minimum and maximum response duration within the treatment group. ‡Derived by the Kaplan-Meier method of censored data.[1]
DOR, duration of response; irRC, immune-related response criteria; mo, months; NR, not reached; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; TTR, time to response.

1. Hamid O, et al. *Ann Oncol* 2019;30:582–588. Supplementary appendix; **2.** Hamid O, *et al. Ann Oncol* 2019;30:582–588; **3.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

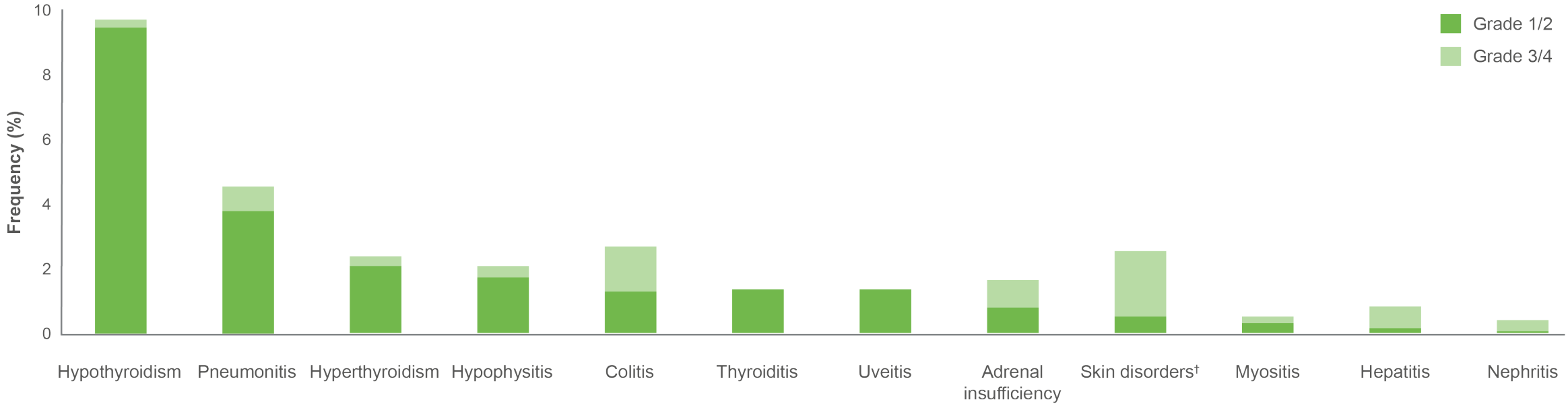
Immune-Mediated Adverse Events With KEYTRUDA[1]

Return to safety overview

GB PI | NI PI

Median duration of follow-up was 55 months[1]

Immune-mediated adverse events in KEYNOTE-001 that occurred in >2 patients*[1]



Adapted from Hamid, *et al.* 2019.[1]

In KEYNOTE-001, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-001 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Cut-off 1 September 2017. *Based on a list determined by the sponsor and regardless of attribution by the investigator.[1] †Includes bullous dermatitis, exfoliative dermatitis, erythema multiforme, exfoliative rash, pemphigoid, pruritus, rash, erythematous rash, generalised rash, maculopapular rash and pruritic rash.[1]
Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Hamid O, *et al. Ann Oncol* 2019;30:582–588. Supplementary appendix; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Patient Baseline Characteristics (1/2)[1]

Return to study design
GB PI
NI PI

	KEYTRUDA 2 mg/kg (n=180)	KEYTRUDA 10 mg/kg (n=181)	Chemotherapy control (n=179)
Median age (years)	62 (15–87)	60 (27–89)	63 (27–87)
Male, n (%)	58	60	64
Race, n (%)			
White	176 (98)	179 (99)	172 (96)
Other	4 (2)	2 (1)	6 (3)
Missing	0	0	1 (<1)
ECOG PS, n (%)			
0	98 (54)	98 (54)	99 (55)
1	80 (44)	83 (46)	80 (45)
Missing	2 (1)	0	0
BRAF V600-mutation status, n (%)			
Mutant	44 (24)	40 (22)	41 (23)
Wild-type	136 (76)	141 (78)	138 (77)

Adapted from Ribas A, *et al.* 2015.[1]

In KEYNOTE-002, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-002 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Due to rounding, some sections may not add up to 100%. Data are median (range) or n (%).
ECOG PS, Eastern Cooperative Oncology Group performance status; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.
1. Ribas A, *et al. Lancet Oncol* 2015;16:908–918; **2**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Patient Baseline Characteristics (2/2)[1]

Return to study design
GB PI
NI PI

	KEYTRUDA 2 mg/kg (n=180)	KEYTRUDA 10 mg/kg (n=181)	Chemotherapy control (n=179)
LDH, n (%)			
Normal	99 (55)	105 (58)	107 (60)
Raised	77 (43)	73 (40)	68 (38)
Unknown	4 (2)	3 (2)	4 (2)
M category, n (%)			
M0	1 (<1)	1 (<1)	2 (1)
M1a	9 (5)	13 (7)	15 (8)
M1b	22 (12)	17 (9)	15 (8)
M1c	148 (82)	150 (83)	147 (82)
Number of lines of previous systemic therapies, n (%)			
0*	1 (<1)	0	0
1	40 (22)	56 (31)	47 (26)
2	79 (44)	66 (36)	78 (44)
≥3	60 (33)	59 (33)	54 (30)

Adapted from Ribas A, *et al.* 2015.[1]

In KEYNOTE-002, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-002 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Due to rounding, some sections may not add up to 100%. *Patients with no previous systemic therapies received neoadjuvant or adjuvant therapy only.
LDH, lactate dehydrogenase; M, metastasis; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Ribas A, *et al. Lancet Oncol* 2015;16:908–918; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Return to safety design

GB PI | NI PI

Treatment-Related Adverse Events With Incidence Occurring In ≥5% Of Patients In Any Treatment Group[1]

Median time on treatment was 112.5 days (range: 1.0–988.0) and 145.0 days (range: 1.0–967.0) for patients receiving KEYTRUDA 2 mg/kg and 10 mg/kg, respectively

Summary	Pembrolizumab 2 mg/kg n=178			Pembrolizumab 10 mg/kg n=179			Chemotherapy n=171		
Events, n (%)	Grade 1–2	Grade 3–4	Grade 5	Grade 1–2	Grade 3–4	Grade 5	Grade 1–2	Grade 3–4	Grade 5
Fatigue	42 (23.5)	2 (1.1)	0	55 (30.7)	2 (1.1)	0	53 (30.9)	8 (4.6)	0
Pruritus	39 (21.9)	0	0	45 (25.1)	0	0	6 (3.5)	0	0
Nausea	11 (6.2)	0	0	17 (9.5)	1 (<1)	0	55 (32.2)	4 (2.3)	0
Decreased appetite	11 (6.2)	0	0	15 (8.3)	0	0	26 (15.2)	0	0
Anaemia	5 (2.8)	1 (<1)	0	7 (3.9)	0	0	26 (15.2)	9 (5.3)	0
Diarrhoea	18 (10.1)	0	0	18 (10.0)	4 (2.2)	0	11 (6.5)	3 (1.8)	0
Rash	23 (12.9)	0	0	23 (12.8)	0	0	8 (4.7)	0	0
Alopecia	6 (3.4)	0	0	1 (<1)	0	0	36 (21.1)	0	0
Vomiting	3 (1.7)	1 (<1)	0	10 (5.6)	1 (<1)	0	22 (12.8)	4 (2.3)	0
Arthralgia	14 (7.9)	1 (<1)	0	13 (7.2)	1 (<1)	0	8 (4.6)	1 (<1)	0
Constipation	5 (2.8)	0	0	10 (5.6)	0	0	14 (8.2)	0	0
Myalgia	8 (4.5)	2 (1.1)	0	6 (3.4)	0	0	9 (5.2)	1 (<1)	0
Asthenia	6 (3.3)	1 (<1)	0	8 (4.4)	1 (<1)	0	9 (5.2)	1 (<1)	0
Hypothyroidism	14 (7.9)	0	0	13 (7.2)	0	0	0	0	0
Vitiligo	13 (7.3)	0	0	14 (7.8)	0	0	2 (1.2)	0	0
Dry skin	12 (6.7)	0	0	11 (6.1)	0	0	3 (1.8)	0	0
Thrombocytopenia	2 (1.1)	0	0	1 (<1)	1 (<1)	0	12 (7.0)	4 (2.3)	0
Neutropenia	1 (<1)	0	0	0	0	0	9 (5.3)	6 (3.5)	0
Peripheral neuropathy	2 (1.1)	0	0	1 (<1)	0	0	12 (6.0)	2 (1.1)	0
Maculopapular rash	6 (3.3)	1 (<1)	0	12 (6.7)	1 (<1)	0	0	0	0
Leukopenia	0	0	0	1 (<1)	0	0	8 (4.7)	7 (4.0)	0
Paraesthesia	1 (<1)	0	0	2 (1.2)	0	0	10 (5.8)	0	0
Platelet count decreased	0	0	0	1 (<1)	0	0	7 (4.1)	5 (3.0)	0

Adapted from Hamid O, *et al.* 2017.[1]

In KEYNOTE-002, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-002 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Cut-off 16 November 2015. Due to rounding, some sections may not add up to 100%. Safety was assessed in all patients who received ≥1 dose of study treatment.
Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Hamid O, *et al. Eur J Cancer* 2017;86:37–45; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Immune-Mediated Adverse Events At Final Analysis[1]

Return to safety design
GB PI
NI PI

Median time on treatment was 112.5 days (range: 1.0–988.0) and 145.0 days (range: 1.0–967.0) for patients receiving KEYTRUDA 2 mg/kg and 10 mg/kg, respectively

Events, n (%)	KEYTRUDA 2 mg/kg (n=178)		KEYTRUDA 10 mg/kg (n=179)		Chemotherapy control (n=171)	
All events	32 (18)		38 (21)		3 (2)	
	Grade 1–2	**Grade 3–5**	**Grade 1–2**	**Grade 3–5**	**Grade 1–2**	**Grade 3–5**
Hypothyroidism	16 (9)	0	15 (8)	0	1 (<1)	0
Hyperthyroidism	7 (4)	0	2 (1)	0	0	0
Hepatitis*	1 (<1)	0	0	2 (1)	0	0
Colitis	1 (<1)	0	2 (1)	3 (2)	0	1 (<1)
Pneumonitis	3 (2)	1 (<1)	2 (1)	3 (2)	0	0
Pancreatitis	1 (<1)	0	0	1 (<1)	0	0
Uveitis/Iritis	0	0	2 (1.1)	1 (<1)	0	0
Hypopituitarism	0	0	0	2 (1)	0	0
Hypophysitis	0	1 (<1)	1 (<1)	0	0	0

Adapted from Hamid O, *et al.* 2017.[1]

In KEYNOTE-002, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-002 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Cut-off 16 November 2015. Due to rounding, some sections may not add up to 100%. *Includes autoimmune hepatitis.
Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Hamid O, *et al. Eur J Cancer* 2017;86:37–45; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Patient Baseline Characteristics In The Original Trial[1] (1/2)

Return to study design

GB PI | NI PI

	KEYTRUDA 10 mg/kg Q2W* (n=279)	KEYTRUDA 10 mg/kg Q3W (n=277)	Ipilimumab 3 mg/kg Q3W (n=278)
Median age, years	61 (18–89)	63 (22–89)	62 (18–88)
Male, n (%)	161 (57.7)	174 (62.8)	162 (58.3)
ECOG PS			
0, n (%)	196 (70.3)	189 (68.2)	188 (67.6)
1, n (%)	83 (29.7)	88 (31.8)	90 (32.4)
Elevated LDH level, n (%)	81 (29.0)	98 (35.4)	91 (32.7)
M stage			
M0	9 (3.2)	9 (3.2)	14 (5.0)
M1	6 (2.2)	4 (1.4)	5 (1.8)
M1a	21 (7.5)	34 (12.3)	30 (10.8)
M1b	64 (22.9)	41 (14.8)	52 (18.7)
M1c	179 (64.2)	189 (68.2)	177 (63.7)

Adapted from Robert C, *et al.* 2015.[1]

***These are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes. Data from KEYNOTE-001, 002 and 006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]**

ECOG PS, European Cooperative Oncology Group performance status; LDH, lactose dehydrogenase; M, metastasis; Q2W, every 2 weeks; Q3W, every 3 weeks.

1. Robert C, *et al. N Engl J Med* 2015;372:2521–2532; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Patient Baseline Characteristics In The Original Trial[1] (2/2)

Return to study design
GB PI
NI PI

	KEYTRUDA 10 mg/kg Q2W* (n=279)	KEYTRUDA 10 mg/kg Q3W (n=277)	Ipilimumab 3 mg/kg Q3W (n=278)
PD-L1 expression positive, n (%)	225 (80.6)	221 (79.8)	225 (80.9)
BRAF V600 mutation	98 (35.1)	97 (35.0)	107 (38.5)
Brain metastasis, n (%)	23 (8.2)	27 (9.7)	28 (10.1)
No. previous therapies, n (%)†			
0	183 (65.6)	185 (66.8)	181 (65.1)
1	96 (34.4)	91 (32.9)	97 (34.9)
Type of previous therapy, n (%)‡			
Chemotherapy	36 (12.9)	41 (14.8)	29 (10.4)
Immunotherapy	8 (2.9)	7 (2.5)	12 (4.3)
BRAF +/- *MEK* inhibitor	50 (17.9)	45 (16.2)	56 (20.1)

Adapted from Robert C, *et al.* 2015.[1]

***These are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes. Data from KEYNOTE-001, 002 and 006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[1]**

†One patient (0.4%) in the group receiving pembrolizumab every 3 weeks had received two previous systemic therapies.
‡Only therapy administered for advanced or metastatic disease is listed.
PD-L1, programmed cell death 1 ligand 1; Q2W, every 2 weeks; Q3W, every 3 weeks.

1. Robert C, *et al. N Engl J Med* 2015;372:2521–2532; **2**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

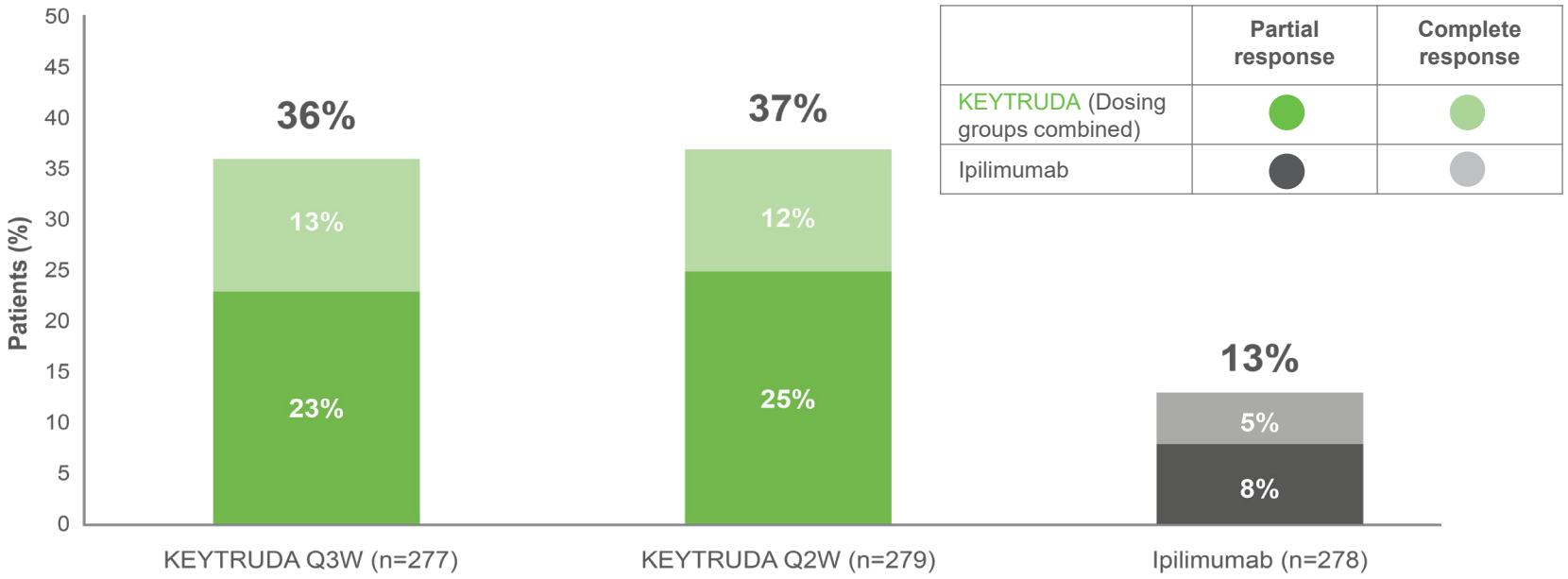
KEYTRUDA® (pembrolizumab)

ORRs In Patients With Advanced Melanoma On KEYTRUDA Or Ipilimumab[1,2]

Return to OS data
GB PI
NI PI

Minimum duration of follow-up was 21 months
The analysis shows pooled results from the 10 mg/kg Q2W and Q3W arms from KEYNOTE-006.

Secondary efficacy outcome: ORR*



Adapted from Schachter J, *et al.* 2017.[1]

ORR was not a powered endpoint for this study and no statistical conclusions can be drawn from these results.[3]

In KEYNOTE-006, KEYTRUDA was dosed at 2 mg/kg Q3W or 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. To note, 2 mg/kg Q3W (up to a maximum of 200 mg) is licensed in paediatric patients aged 12 years and older with melanoma. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[5] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[5]

*Objective response rate was defined as the percentage of the participants with a best tumour response of complete response (disappearance of all target lesions with any pathological lymph nodes having a reduction in short axis to <10 mm) or partial response (≥30% decrease in the sum of diameters of target lesions).[1,4]
ORR, objective response rate; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Schachter J, *et al. Lancet* 2017;390:1853–1862 Supplementary appendix; **2.** Schachter J, *et al. Lancet* 2017;390:1853–1862; **3.** Robert C, *et al. N Engl J Med* 2015;372:2521–2532;
4. Eisenhauer EA, *et al. Eur J Cancer* 2009;45:228–247; **5.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Return to OS data

GB PI | NI PI

OS And ORR In Patients Stratified By *BRAF V600* Status Treated With KEYTRUDA vs Ipilimumab[1]

This is a subgroup analysis and no statistical conclusions can be drawn from these results.

The analysis shows pooled results from the 10mg/kg Q2W and Q3W arms from KEYNOTE-006.

Subgroup	*BRAF* wild type (n=525)		*BRAF V600* mutant without prior *BRAF* treatment (n=163)		*BRAF V600* mutant with prior treatment (n=139)	
Study arm	**KEYTRUDA**	**Ipilimumab (n=170)**	**KEYTRUDA**	**Ipilimumab (n=55)**	**KEYTRUDA**	**Ipilimumab (n=52)**
Median OS (95% CI) (months)	28.1 (21.1–42.7)	13.9 (10.7–24.8)	NR (36.1–NA)	26.2 (16.0–NR)	20.4 (12.8–35.6)	11.9 (6.0–17.8)
OS hazard ratio (95% CI)	0.73 (0.58–0.93)		0.70 (0.44–1.11)		0.71 (0.46–1.08)	
ORR	43%	16%	47%	18%	32%	13%

Adapted from Robert C, *et al.* 2019.[1]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Cut-off 3 December 2017.

CI, confidence interval; NA, not available; NR, not reported; ORR, objective response rate; OS, overall survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Robert C, et al. *Lancet Oncol* 2019;20:1239–1251; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

OS In Subgroups by Baseline Characteristics[1]

- This is a subgroup analysis and no statistical conclusions can be drawn from these results

	Deaths/no. (%)		7-year OS, %		OS, median (95% CI), months		
Characteristic	**Pembrolizumab**	**Ipilimumab**	**Pembrolizumab**	**Ipilimumab**	**Pembrolizumab**	**Ipilimumab**	**HR (95% CI)**
BRAF status							
Wild-type	216/355 (60.8)	112/170 (65.9)	36.5	25.7	28.1 (21.1 to 42.7)	13.9 (10.7 to 24.8)	0.71 (0.56 to 0.89)
Mutant (no prior BRAFi/MEKi)[a]	52/108 (48.1)	35/55 (63.6)	49.7	27.7	78.5 (36.1 to NE)	26.2 (16.0 to 64.0)	0.58 (0.38 to 0.89)
Mutant (prior BRAFi/MEKi)	61/87 (70.1)	36/52 (69.2)	28.3	20.0	20.4 (12.8 to 35.6)	11.9 (6.0 to 17.8)	0.72 (0.47 to 1.08)
LDH							
Normal	206/369 (55.8)	108/179 (60.3)	42.0	30.5	42.9 (34.5 to 53.5)	33.1 (20.1 to 49.2)	0.76 (0.60 to 0.96)
Elevated	122/179 (68.2)	70/91 (76.9)	28.9	14.7	14.7 (10.1 to 19.5)	6.0 (5.0 to 8.0)	0.59 (0.44 to 0.79)
Total tumour size, cm							
<10	165/292 (56.5)	91/152 (59.9)	40.7	30.7	42.7 (28.1 to 51.9)	22.4 (16.0 to 38.5)	0.74 (0.58 to 0.96)
≥10	76/106 (71.7)	41/51 (80.4)	26.1	15.9	9.5 (6.3 to 16.4)	5.9 (2.9 to 8.1)	0.67 (0.46 to 0.99)
Brain metastases							
Present	25/51 (49.0)	21/29 (72.4)	50.0	27.6	53.4 (16.6 to NE)	10.8 (4.8 to 27.0)	0.49 (0.27 to 0.87)
Absent	303/500 (60.6)	161/248 (64.9)	36.8	25.0	32.7 (24.5 to 41.2)	17.1 (13.6 to 23.5)	0.72 (0.59 to 0.87)

Adapted from Robert C, *et al.* 2023.[1]

Patients with *BRAF*-mutant melanoma with no prior *BRAF* inhibitor therapy were eligible for the study, provided they had normal LDH levels and had no clinically significant tumour-related symptoms.

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

BRAFi, BRAF inhibitor; CI, confidence interval; HR, hazard ratio; LDH, lactate dehydrogenase; MEKi, MEK inhibitor; NE, not evaluable; OS, overall survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Robert C, *et al. J Clin Oncol* 2023;41:3998-4003; **2**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Overall Response To First- And Second-Course Pembrolizumab Among Patients Who Received Second-Course Pembrolizumab[1,2]

	Second-course best overall response, n-16			
First-course best overall response	Complete response	Partial response	Stable disease	Progressive disease
CR (n=7)	4	1	2	-
PR (n=7)	-	4	1	2
SD (n=2)	-	-	2	-

Adapted from Robert C, *et al.* 2023.[1]

Overall response was not a powered endpoint for this study and no statistical conclusions can be drawn from these results.[1]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[3] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[3]

*Objective response rate was defined as the percentage of the participants with a best tumour response of complete response (disappearance of all target lesions with any pathological lymph nodes having a reduction in short axis to <10 mm) or partial response (≥30% decrease in the sum of diameters of target lesions).[1,2]
CR, complete response; PR, partial response; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; SD, stable disease

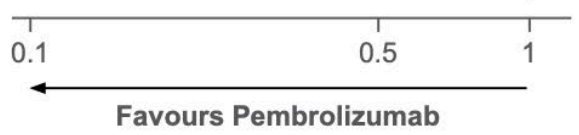
1. Robert C, *et al. J Clin Oncol* 2023; 41:3998-4003. **2.** Eisenhauer EA, *et al. Eur J Cancer* 2009;45:228–247; **3**. KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)

Subgroup Analysis of Overall Survival[1]

- This is a subgroup analysis and no statistical conclusions can be drawn from these results

Subgroup	Events/Participants	Hazard Ratio (95% CI)
Overall	516/834	0.69 (0.57 to 0.83)
BRAF subgroup		
BRAF-wildtype	328/525	0.71 (0.56 to 0.89)
BRAF-mutant no prior BRAFi/MEKi	87/163	0.58 (0.38 to 0.89)
BRAF-mutant prior BRAFi/MEKi	97/139	0.72 (0.47 to 1.08)
LDH level		
Normal	314/548	0.76 (0.60 to 0.96)
Elevated	192/270	0.59 (0.44 to 0.79)
Tumour size		
<10 cm	256/444	0.74 (0.58 to 0.96)
≥10 cm	117/157	0.67 (0.46 to 0.99)
Brain metastases		
Yes	46/80	0.49 (0.27 to 0.87)
No	464/748	0.72 (0.59 to 0.87)



Adapted from Robert C, *et al.* 2023.[1]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

BRAFi, BRAF inhibitor; CI, confidence interval; LDH, lactate dehydrogenase; MEKi, MEK inhibitor; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Robert C, *et al. J Clin Oncol* 2023;41:3998-4003; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

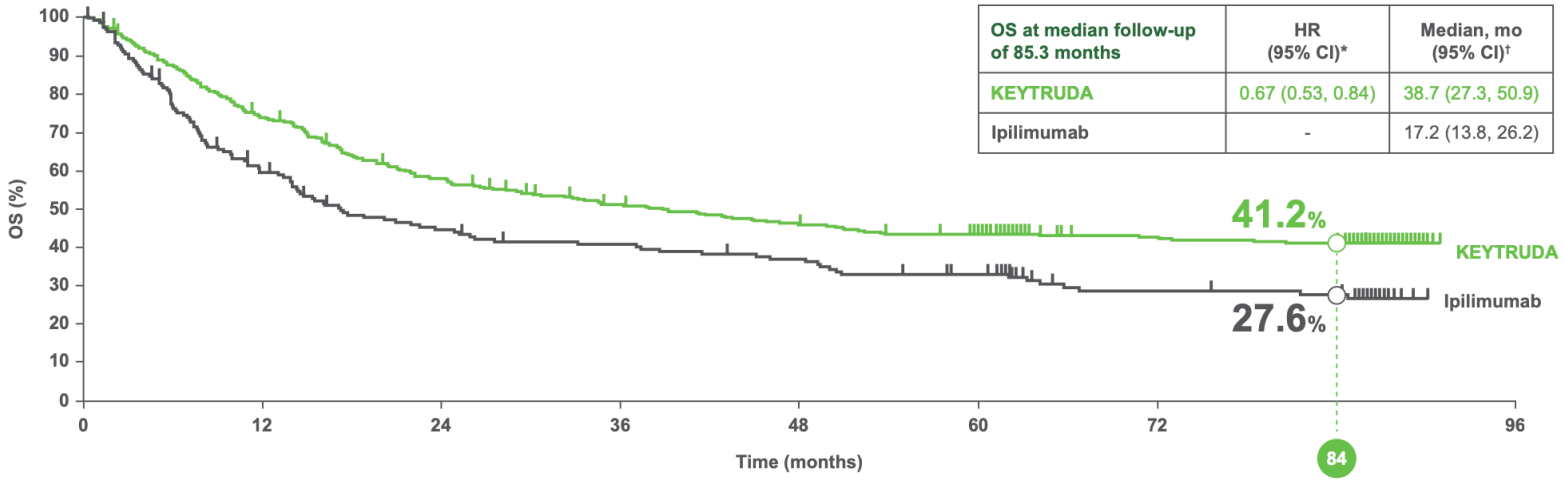
KEYTRUDA® (pembrolizumab)

OS In Patients Who Received Pembrolizumab Or Ipilimumab As First-line Therapy In KEYNOTE-006[1]

- This is a 7-year follow-up post hoc analysis and no statistical conclusions can be drawn from these results

Median duration of follow-up of surviving patients was 85.3 months

Post hoc analysis: OS in patients who received pembrolizumab or ipilimumab as first-line therapy in KEYNOTE-006[1]



OS at median follow-up of 85.3 months	HR (95% CI)*	Median, mo (95% CI)†
KEYTRUDA	0.67 (0.53, 0.84)	38.7 (27.3, 50.9)
Ipilimumab	-	17.2 (13.8, 26.2)

Number at risk

KEYTRUDA	368	268	207	174	154	141	111	106	0
Ipilimumab	181	98	71	63	56	47	31	29	0

Adapted from Robert C, *et al.* 2023.[1]

- **Patients in KEYNOTE-006 who did not enrol in KEYNOTE-587 were censored at the date last known alive**
- **For OS, patients who had survival follow-up after the data cut-off date were censored at the time of data cut-off**

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Cut-off 19 April 2021. *On the basis of Cox regression model with the Efron method of tie handling with treatment as a covariate. †From product-limit (Kaplan-Meier) method for censored data.
CI, confidence interval; HR, hazard ratio; OS, overall survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.

1. Robert C, *et al. J Clin Oncol* 2023;41:3998-4003; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

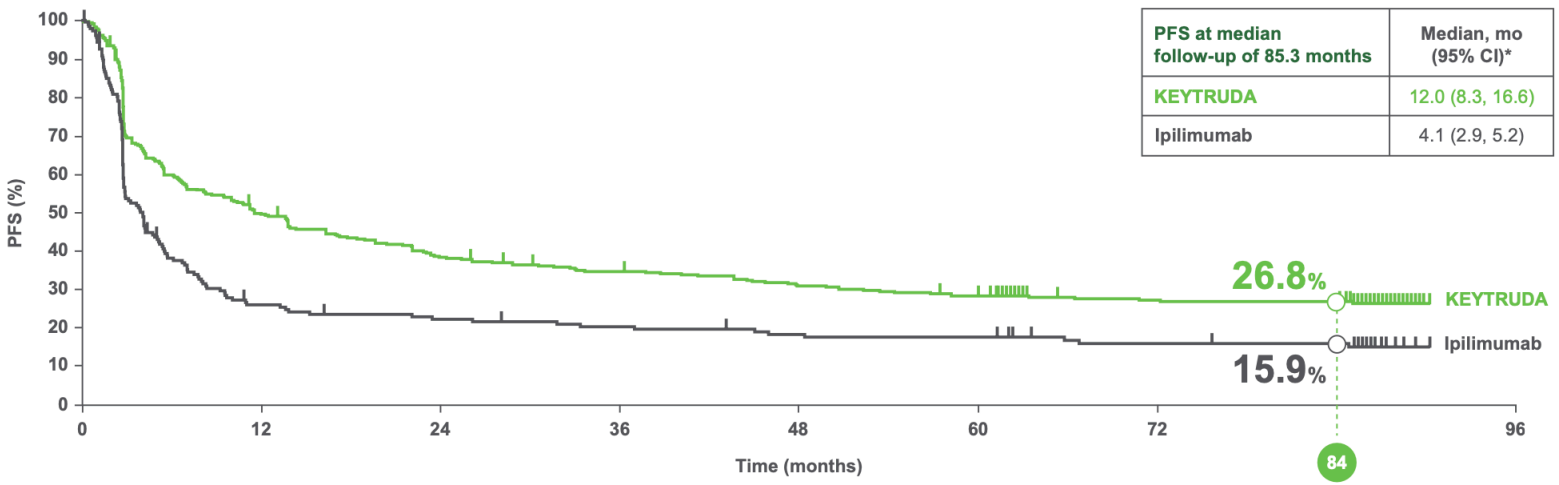
KEYTRUDA® (pembrolizumab)

PFS In Patients Who Received Pembrolizumab Or Ipilimumab As First-line Therapy In KEYNOTE-006[1]

- This is a 7-year follow-up post hoc analysis and no statistical conclusions can be drawn from these results

Median duration of follow-up of surviving patients was 85.3 months

Post hoc analysis: PFS in patients who received pembrolizumab or ipilimumab as first-line therapy in KEYNOTE-006[1]



PFS at median follow-up of 85.3 months	Median, mo (95% CI)*
KEYTRUDA	12.0 (8.3, 16.6)
Ipilimumab	4.1 (2.9, 5.2)

- **Patients in KEYNOTE-006 who did not enrol in KEYNOTE-587 were censored at the date last known alive**
- **For PFS, patients without progressive disease were censored at the date last known alive**

Adapted from Robert C, *et al.* 2023.[1]

In KEYNOTE-006, KEYTRUDA was dosed at 10 mg/kg Q2W or Q3W, which are unlicensed doses in adults. The licensed dose of KEYTRUDA in advanced melanoma in adults is either 200 mg Q3W or 400 mg Q6W administered intravenously over 30 minutes.[2] Data from KEYNOTE-006 was included as part of the regulatory submission for KEYTRUDA and appears in the Summary of Product Characteristics.[2]

Cut-off 19 April 2021. *From product-limit (Kaplan-Meier) method for censored data.
CI, confidence interval; HR, hazard ratio; PFS, progression-free survival; OS, overall survival; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks.
1. Robert C, *et al. J Clin Oncol* 2023;41:3998-4003; **2.** KEYTRUDA Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498/smpc Accessed April 2024.

KEYTRUDA® (pembrolizumab)