

MSD Oncology

KEYTRUDA[®]
(pembrolizumab)
in the adjuvant treatment
of patients with Stage III
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 (Tel: 020 8154 8000). **By clicking the above link, you will leave the MSD website and be taken to the MHRA website.**

Please refer to the full KEYTRUDA Summary of Product Characteristics and Risk Minimisation Materials for Patients before prescribing KEYTRUDA. These slides are provided to UK healthcare professionals as a resource for data for your personal education. To ensure compliance with all relevant codes and regulations, these slides must not be amended.



IIIA
melanoma



IIIB
melanoma



IIIC
melanoma



IIID
melanoma

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

UK prescribing information can be found at <https://www.emcpi.com/pi/33162>. Full indications can be found on Slide 2.

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GB-OOC-00947 | Date of preparation: April 2025

KEYTRUDA melanoma indications¹

- KEYTRUDA as monotherapy is indicated for the treatment of adults and 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 information¹

- 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 the 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
- A link to the prescribing information for KEYTRUDA can be found at the top of each slide in this presentation
- For any queries, please contact your local MSD contact at msdukoncology@msd.com

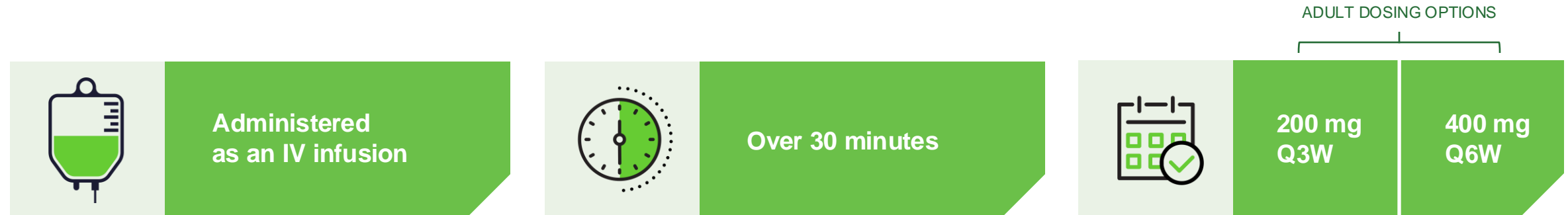
MSD does not recommend the use of products outside their licensed indications. Please refer to the Summary of Product Characteristics and risk minimisation materials available on the EMC website before prescribing.

EMC, electronic medicines compendium.

1. KEYTRUDA Summary of Product Characteristics. United Kingdom. Available at: <https://www.medicines.org.uk/emc/product/2498> Accessed: March 2025.

KEYTRUDA[®]
(pembrolizumab)

KEYTRUDA offers flexibility of dosing¹



Assessment of regimens

The 200 mg Q3W (once every 3 weeks) regimen has been assessed in Phase II and 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 Q6W (once every 6 weeks) dosing for monotherapy and combination therapy.

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.

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.

IV, intravenous; Q3W, every three weeks; Q6W, every six weeks.

1. KEYTRUDA Summary of Product Characteristics. United Kingdom. Available at: <https://www.medicines.org.uk/emc/product/2498> Accessed: March 2025.

KEYTRUDA
(pembrolizumab)

What are the associated risks for patients with resected Stage III melanoma?

[Stages of melanoma >](#)[5- and 10-year survival rates >](#)[Relapse rate and distant metastasis rate >](#)[Time to relapse >](#)

IIIA
melanoma



IIIB
melanoma



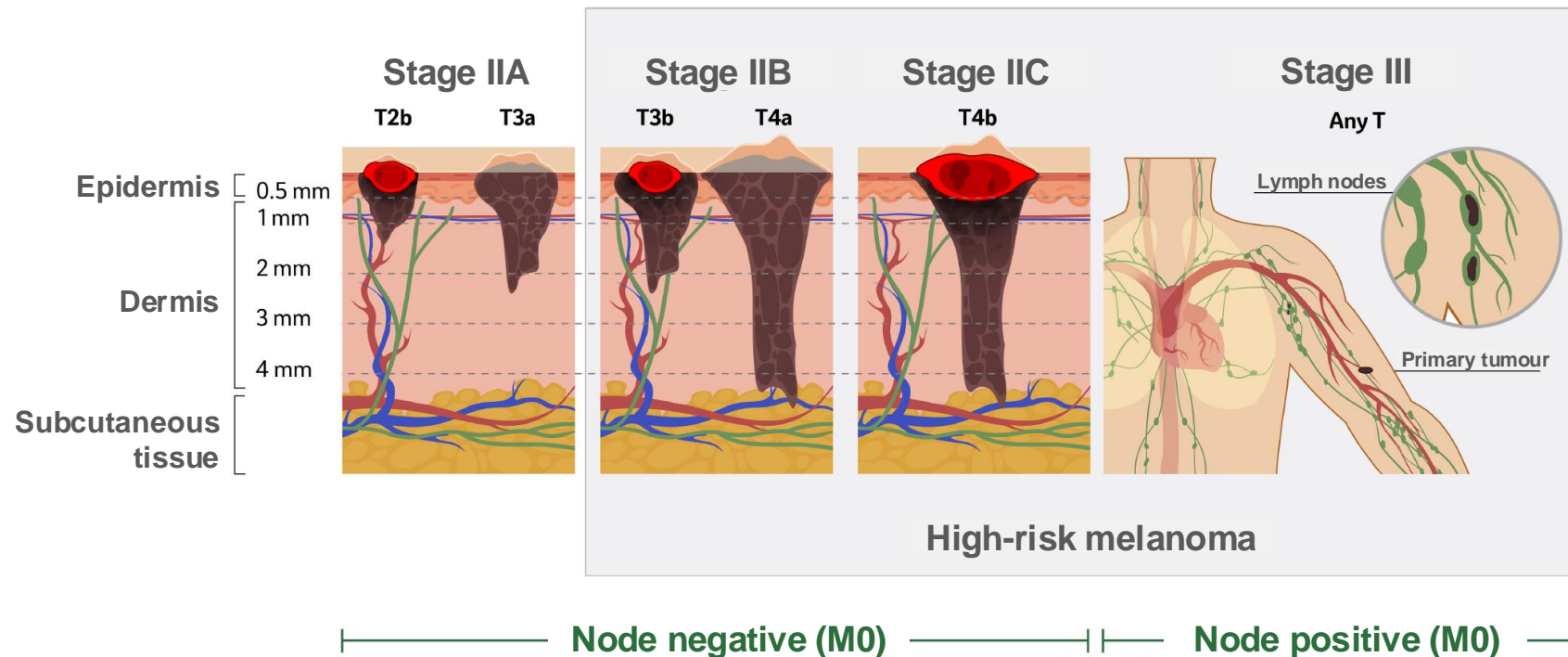
IIIC
melanoma



IIID
melanoma

Patients with melanoma Stage IIB or higher are at risk of recurrence following resection^{*1–3}

Stages of melanoma (based on the AJCC 8th edition clinical staging criteria for melanoma)^{*4}



Adapted from Gershenwald JE, et al. *CA Cancer J Clin*. 2017.⁴

*Stage IV melanoma that is resectable is also high risk but is not discussed here.

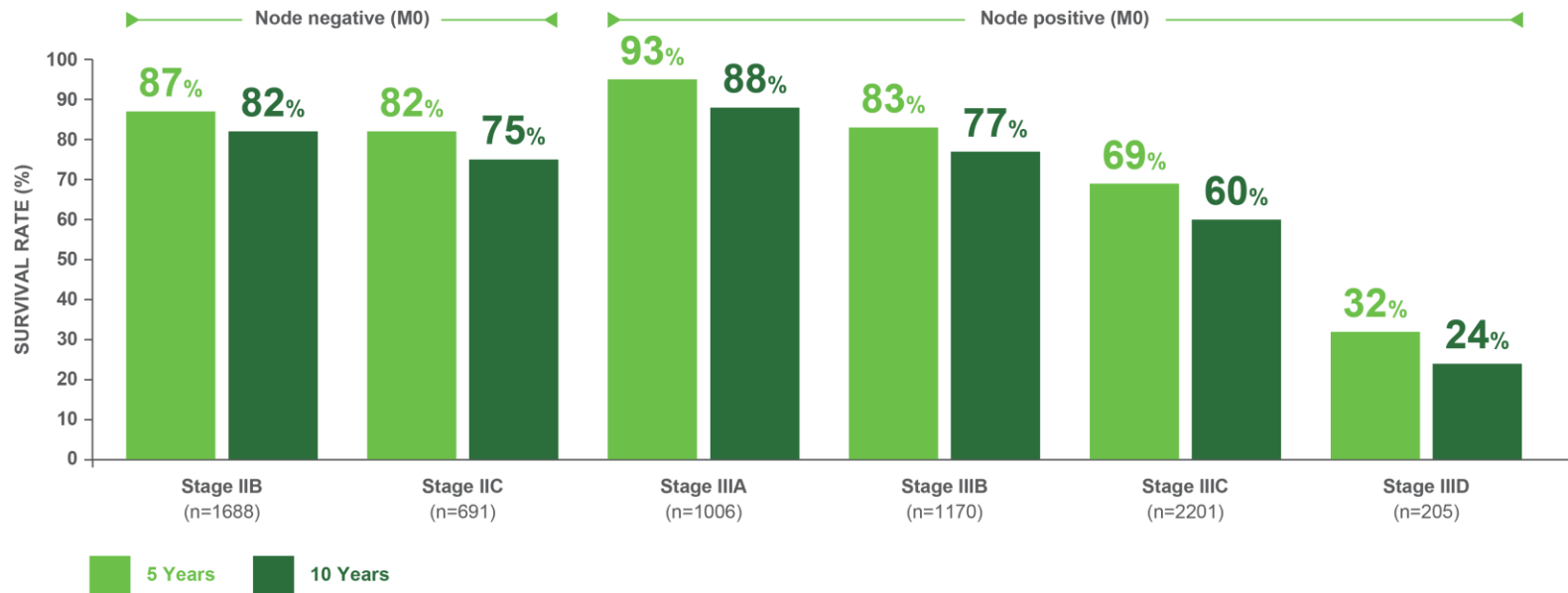
AJCC, American Joint Committee on Cancer.

1. Mohr P, et al. *Melanoma Manag* 2019;6:MMT33. 2. Yushak M, et al. *Am Soc Clin Oncol Educ Book* 2019;39:e207–e211. 3. Lee AY, et al. *Ann Surg Oncol* 2017;24:939–946.

4. Gershenwald JE, et al. *CA Cancer J Clin* 2017;67:472–492.

KEYTRUDA
(pembrolizumab)

Melanoma-specific survival rates at 5 and 10 years according to AJCC 8th Edition pathologic staging criteria for melanoma¹



Survival data generated using IMDPP database, containing records of >46,000 patients with melanoma (n=43,792 qualified for analysis).

Included patient records from 10 institutions in the US, Europe and Australia with melanoma at Stage I–III at initial diagnosis and had received treatment since 1998.

Were you aware of the difference in survival rates across Stage III melanoma?

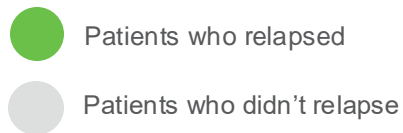
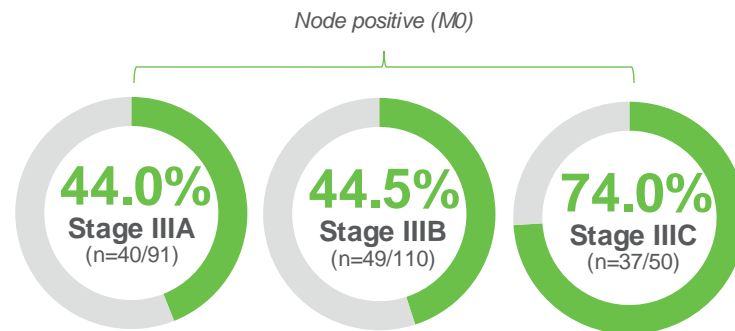
Adapted from Gershenwald JE, et al. *CA Cancer J Clin*. 2017.¹

Data based on Kaplan-Meier estimates of melanoma-specific survival as reported by the AJCC melanoma expert panel.¹
AJCC, American Joint Committee on Cancer; **IMDPP**, International Melanoma Database and Discovery Platform.
 1. Gershenwald JE, et al. *CA Cancer J Clin* 2017;67:472–492.

KEYTRUDA
 (pembrolizumab)

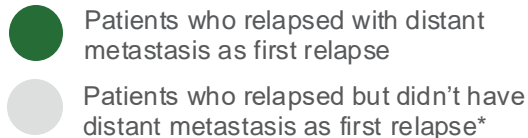
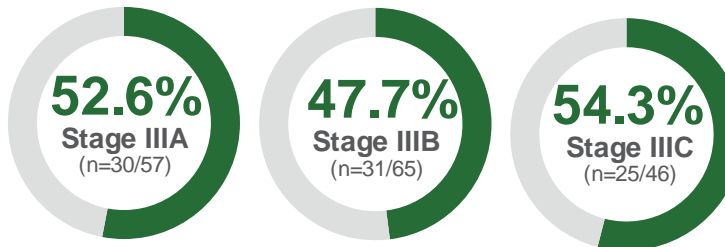
Relapse rates in patients with Stage III melanoma are 44.0%, 44.5% and 74.0% for Stages IIIA, IIIB and IIIC, respectively¹

Stage III relapse rates in patients who received watch-and-wait post-surgery¹



Stage III patients who relapsed with distant metastasis*¹

Percentage of patients who relapsed with unresectable or distant metastasis as first relapse*



A retrospective chart review of 251 patients from 2011–2016 with Stage III resected melanoma (AJCC 7th ed.) followed by watch-and-wait. Patients included in this study were from North America, South America and Europe.

- > Relapse-free survival (RFS) was measured from the date of initial surgery for Stage III melanoma to the earliest among the date of first relapse (event), date of death (event) or end of follow-up (i.e. end of care for the patient or date of data collection; censoring) among patients with known information on time of relapse/death²
- > Median follow-up was 3.1 years²

Were you aware of the rate of distant relapses across Stage III melanoma?

*The remainder of patients experienced a locoregional relapse or a secondary primary melanoma relapse.
AJCC, American Joint Committee on Cancer.

1. Mohr P, et al. *Melanoma Manag* 2019;6:MMT33. Supplementary appendix. 2. Mohr P, et al. *Melanoma Manag* 2019;6:MMT33.

The median time to relapse from resection is 5.2 months at Stage IIIC and less than 1.5 years at Stage IIIA¹

Median time to relapse in Stage III¹



Stage IIIA
(n=40/91)



Stage IIIB
(n=49/110)



Stage IIIC
(n=37/50)

A retrospective chart review of 251 patients from 2011–2016 with Stage III resected melanoma (AJCC 7th ed.) followed by watch-and-wait. Patients included in this study were from North America, South America and Europe.

- Median follow-up was 3.1 years²
- RFS was measured from the date of initial surgery for Stage III melanoma to the earliest among the date of first relapse (event), date of death (event) or end of follow-up (i.e. end of care for the patient or date of data collection; censoring) among patients with known information on time of relapse/death

Would you treat patients with Stage IIIA melanoma differently to those with Stage IIIB melanoma?

Summary

- Patients with Stage III are at risk of relapse following resection*†1,2
- 5- and 10-year estimated survival rates **decrease** in patients with **more advanced** Stage III melanoma‡3
- **Over 44%** of patients with melanoma in Stages IIIA and beyond will recur*†1
- When patients with Stage III melanoma relapse, **approximately 50%** present with distant metastases*†1

The median time to relapse in patients with Stage IIIA melanoma is less than 1.5 years and as low as 5.2 months in Stage IIIC patients*†1

Patients with Stage III melanoma could be considered at risk of disease recurrence

*According to AJCC 7th edition pathologic staging criteria for melanoma. †A retrospective chart review of 251 patients from 2011–2016 with Stage III resected melanoma followed by watch-and-wait. Patients included in this study were from North America, South America and Europe. ‡Based on the AJCC 8th edition clinical staging criteria for melanoma. **AJCC**, American Joint Committee on Cancer.

1. Mohr P, et al. *Melanoma Manag* 2019;6:MMT33. 2. Yushak M, et al. *Am Soc Clin Oncol Educ Book* 2019;39:e207–e211. 3. Gershenwald JE, et al. *CA Cancer J Clin* 2017;67:472–492.

KEYTRUDA: bringing immunotherapy to Stage IIB–IV melanoma

This deck covers KEYNOTE-054 and patients with Stage III melanoma.

To find out more about KEYTRUDA in Stage II and IV melanoma, contact your local MSD representative or [visit MSD Connect](#).



KEYNOTE-716
Over 4 years of data

KEYNOTE-054
Over 7 years of data

KEYNOTE-006
Over 10 years
of data

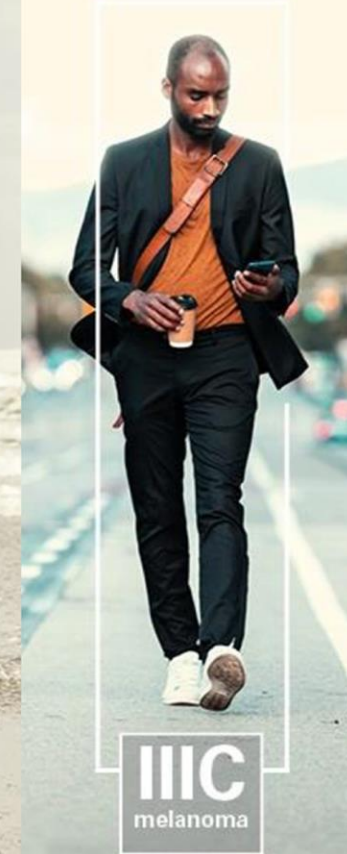
Images are illustrative of the range of patients diagnosed with melanoma.

KEYTRUDA as monotherapy is indicated for the treatment of adults and adolescents aged 12 years and older with advanced (unresectable or metastatic) melanoma.¹
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1. KEYTRUDA Summary of Product Characteristics. United Kingdom. Available at: <https://www.medicines.org.uk/emc/product/2498> Accessed: March 2025.

KEYTRUDA
(pembrolizumab)

How can KEYTRUDA support patients with Stage III melanoma in the adjuvant setting?



Meet Suzie and Claire*

Name: Suzie
Age: 31

Medical history:

- Non-smoker with a fit and active lifestyle
- Saw her doctor after a new mole appeared on her thigh
- A biopsy revealed invasive melanoma and surgery was scheduled
- Underwent a wide local excision to remove the tumour (<2 mm thickness) and conducted a sentinel node biopsy
- Review confirmed that a microscopic tumour had spread to one nearby lymph node, which was removed



Name: Claire
Age: 64

Medical history:

- Retired nurse who enjoys outdoor activities
- Had ignored a mole on her calf for years until one day it was raised and bleeding
- Consulted her GP and was referred to a dermatologist who conducted a biopsy, which identified melanoma
- Sentinel node biopsy confirmed the tumour (3 mm thickness) had spread to one nearby lymph node
- The tumour was removed along with the lymph node involved

Would you consider Suzie and Claire to be at risk of disease relapse?

*These hypothetical patients have Stage IIIA and IIIB melanoma that has been completely resected.
GP, general practitioner.

Meet Aaron and Tony*

Name: Aaron
Age: 34

Medical history:

- > At 25, he had a dark spot on his face removed as it was new and had an irregular shape. It was defined as Stage I melanoma
- > 9 years later, he noticed an enlarged lymph node under his chin, which following a biopsy was identified as melanoma
- > Investigations found the tumour had spread to two further nearby lymph nodes, which were removed



Name: Tony
Age: 58

Medical history:

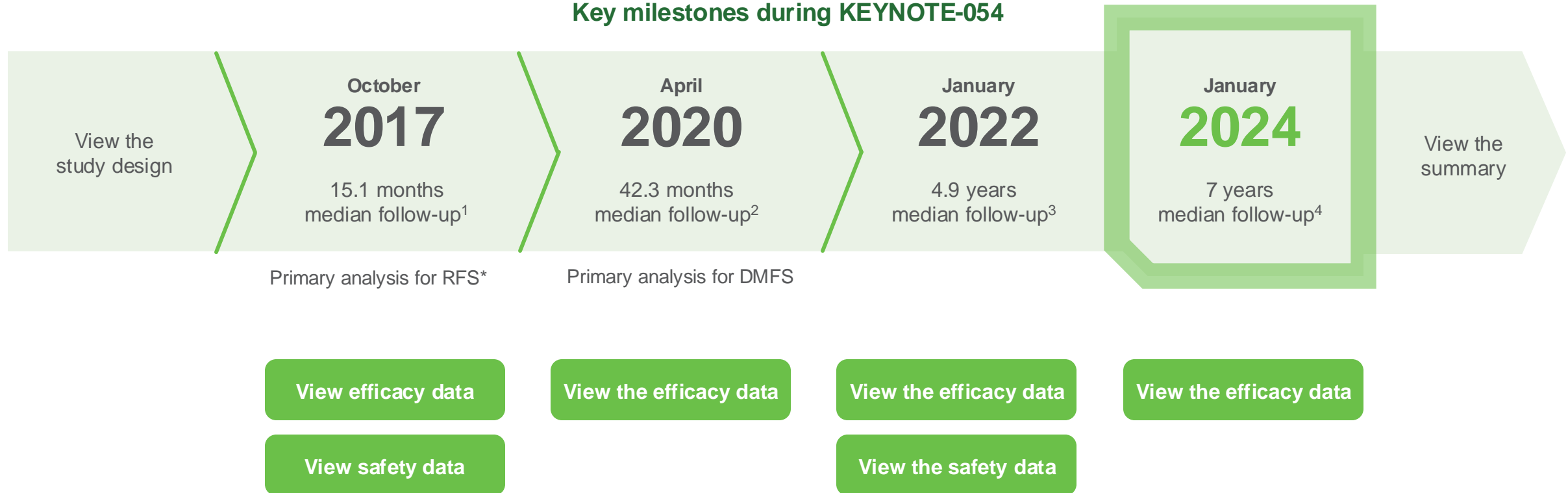
- > A retired builder who enjoys hiking
- > His partner noticed a large mole on his back, which had grown rapidly in recent weeks and was dry and bleeding if rubbed
- > The mole was biopsied and excised once identified as melanoma
- > The tumour was deep (>4 mm) and ulcerated with a high mitotic rate. Investigations identified melanoma in four nearby lymph nodes, which were removed
- > No distant metastases were found

Would you consider Aaron and Tony to be at risk of disease relapse?

*These hypothetical patients have Stage IIIC and IIID melanoma that has been completely resected.

KEYNOTE-054: a randomised, double-blind, placebo-controlled Phase III trial in patients with high-risk, resected Stage III melanoma

Key milestones during KEYNOTE-054



*RFS was defined as the time from randomisation until the date of first recurrence (local, regional or distant metastasis) or death from any cause.¹

DMFS, distant metastasis-free survival; **RFS**, recurrence-free survival.

1. Eggermont AMM, *et al. N Engl J Med* 2018;378:1789–1801. 2. Eggermont AMM, *et al. Lancet Oncol* 2021;22:643–654. 3. Eggermont AMM, *et al. N Engl J Med Evid* 2022;22:1:EVIDo2200214.

4. Eggermont AMM, *et al. Eur J Cancer* 2024;211:114237.

KEYNOTE-054:

Study design



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

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KEYNOTE-054 study design: randomised, double-blind, Phase III trial in collaboration with EORTC^{1,2}

High-risk, resected, Stage III cutaneous melanoma

- Aged ≥18 years
- No prior systemic therapy for melanoma
- No autoimmune disease or uncontrolled infections
- ECOG PS 0–1
- Excluding mucosal or ocular melanoma
- No prior therapy for melanoma, other than surgery or interferon for thick primary melanomas without evidence of lymph node involvement

Stratification factors:

- Stage: IIIA (>1 mm metastasis) vs IIIB vs IIIC 1–3 positive lymph nodes vs IIIC ≥4 positive lymph nodes
- Region: 17 regions, each formed by 1–3 countries

PART 1: ADJUVANT THERAPY^{1,2}

R 1:1
(N=1019)

Within 13 weeks of surgery

KEYTRUDA (n=514)

200 mg IV Q3W
Total of 18 doses; approximately 1 year*

Placebo (n=505)

IV Q3W
Total of 18 doses; approximately 1 year*

Primary endpoint:

- Investigator-assessed RFS

Secondary endpoints:

- DMFS and OS
- Safety and tolerability

[View baseline patient characteristics](#)

PART 2: POST-RECURRENCE¹

(investigations are ongoing and include non-reimbursed, non-licensed indications)

Recurrence >6 months

Recurrence

Crossover and unblinding

KEYTRUDA 200 mg IV Q3W until progression or recurrence, up to 2 years

Data from the treatment crossover will allow comparison of KEYTRUDA adjuvant therapy vs KEYTRUDA to treat relapses



Please note that the post-recurrence part of KEYNOTE-054 is not covered in this presentation as this is outside the licensed indication for KEYTRUDA

Adapted from Eggermont AMM, et al. *N Engl J Med* 2022.¹

Refer to the Supplementary Appendix for the list of inclusion and exclusion criteria.²

*KEYNOTE-054 enrolled patients per AJCC 7th edition. Stage IIIA melanoma according to the AJCC 8th edition identifies a patient population with a better prognosis compared to Stage IIIA according to AJCC 7th edition.^{1,3} **AJCC**, American Joint Committee on Cancer; **DMFS**, distant metastasis-free survival; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **EORTC**, European Organisation for Research and Treatment of Cancer; **OS**, overall survival; **PD-1**, programmed death protein 1; **RFS**, recurrence-free survival.

1. Eggermont AMM, et al. *N Engl J Med* 2018;378:1789–1801. 2. Eggermont AMM, et al. *N Engl J Med* 2018;378:1789–1801. Protocol. 3. Keung EZ & Gershenwald JE. *Expert Rev Anticancer Ther* 2018;18:775–784.

KEYTRUDA
(pembrolizumab)

KEYNOTE-054: key trial endpoints¹

The efficacy analysis was done in the ITT population, which included all patients randomly assigned to treatment. Safety was assessed in the group of patients who started their randomly assigned trial regimen.

Primary efficacy endpoint:

Investigator-assessed, recurrence-free survival (RFS)* in the whole population and in the population with PD-L1-positive tumours[†]

- At the clinical cut-off date (2 October 2017), 351 events (recurrences or deaths) had been reported in the ITT population

Secondary endpoints:

Distant metastasis-free survival (DMFS)[‡] and overall survival (OS) in the whole population; adverse event profile

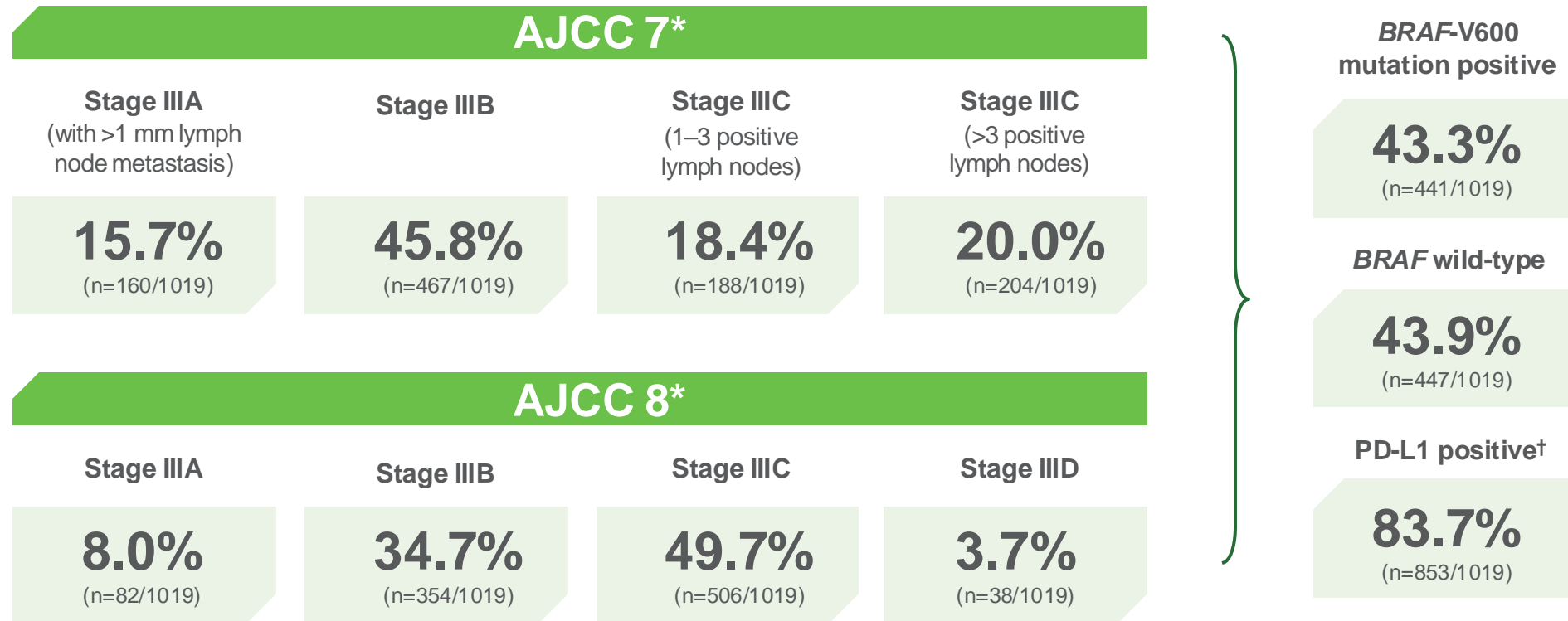
- DMFS was a secondary endpoint, and data were only available after the 42.3-month analysis²
- The OS analysis is planned after 380 deaths or 10 years from the randomisation of the last patient, whichever occurs first³

*RFS was defined as the time from randomisation until the date of first recurrence (local, regional or distant metastasis) or death from any cause.¹ †PD-L1 expression was tested retrospectively by immunohistochemistry assay with the 22C3 anti-PD-L1 antibody.¹ ‡DMFS was defined as the time from randomisation until first distant metastasis or death from any cause.³

DMFS, distant metastasis-free survival; ITT, intent-to-treat; OS, overall survival; PD-L1, programmed death-ligand 1; RFS, recurrence-free survival.

1. Eggermont AMM, et al. *N Engl J Med* 2018;378:1789–1801. 2. Eggermont AMM, et al. *Lancet Oncol* 2021;22:643–654. 3. Eggermont AMM, et al. *Eur J Cancer* 2024;211:114327.

Patients in KEYNOTE-054 were representative of the Stage III melanoma population^{*1,2}



*AJCC 7 population characteristics are based on randomisation; AJCC 8 population characteristics are based on case report forms.² †PD-L1 positivity defined as staining on >1% of tumour cells according to an investigational immunohistochemistry assay.^{1,2} **AJCC**, American Joint Committee on Cancer; **PD-L1**, programmed death-ligand 1.
1. Eggermont AMM, et al. *N Engl J Med* 2018;378:1789–1801. 2. Eggermont AMM, et al. *Eur J Cancer* 2019;116:148–157.

KEYNOTE-054:

Efficacy data from the initial analysis of RFS (IA1)

View the 42.3-month data >

View the 5-year data >

View the latest data at 7 years >

IIIA
melanoma

IIIB
melanoma

IIIC
melanoma

IIID
melanoma

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

KEYTRUDA®
(pembrolizumab)

RFS following treatment with adjuvant KEYTRUDA versus placebo¹

PRIMARY ENDPOINT (median follow-up: 15.1 months)

RFS in the ITT population

- > Patients with events: 26.3% (n=135/514) vs 42.8% (n=216/505)
- > HR: 0.57; 95% CI: 0.43–0.74; p<0.001
 - The interim analysis (IA1) was performed at a one-sided alpha level of 0.8% (two-sided alpha level: 1.6%)
- > 12-month RFS rate: 75.4% vs 61.0%

43%

relative reduction
in risk of disease
recurrence with
KEYTRUDA
vs placebo

RFS in the PD-L1-positive population

- > Patients with events: 23.8% (n=102/428) vs 41.4% (n=176/425)
- > HR: 0.54; 95% CI: 0.42–0.69; p<0.001
- > 12-month RFS rate: 77.1% vs 62.6%

46%

relative reduction
in risk of disease
recurrence with
KEYTRUDA
vs placebo

In December 2017, the independent data and safety monitoring committee reviewed the unblinded results and recommended the reporting of the primary endpoints and safety. Because the results were positive in the ITT population, **the interim analysis of RFS became the final analysis.**

See RFS KM curve
in ITT population

View RFS KM curve
in PD-L1+ population

View RFS data
by AJCC classification

View RFS data
by *BRAF* status

View relapse rates

IA1 data cut-off: 2 October 2017.¹

CI, confidence interval; HR, hazard ratio; IA, interim analysis; ITT, intent-to-treat; PD-L1, programmed death-ligand 1; RFS, recurrence-free survival.

1. Eggermont AMM, et al. *N Eng J Med* 2018;378:1789–1801.

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KEYNOTE-054:

Safety data from the initial analysis (IA1)

Safety data at the initial analyses >

Treatment-related adverse events >

Immune-mediated adverse events >

Safety data at 5 years >

IIIA
melanoma

IIIB
melanoma

IIIC
melanoma

IIID
melanoma

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

KEYTRUDA[®]
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Summary of adverse events during KEYNOTE-054¹

Median follow-up: 15.1 months. Safety data includes patients who received at least one dose of study treatment.

Adverse event, n (%)	KEYTRUDA (n=509)	Placebo (n=502)
Any	475 (93.3)	453 (90.2)
Treatment-related*	396 (77.8)	332 (66.1)
Grade 3–4	75 (14.7)	17 (3.4)
Led to discontinuation	70 (13.8)	11 (2.2)
Immune-mediated and infusion reactions	190 (37.3)	45 (9.0)
Grade 3–4	36 (7.1)	3 (0.6)

- Similar proportions of patients in both study arms completed treatment (n=509 for KEYTRUDA, n=502 for placebo)
- The safety profile of KEYTRUDA among the patients with resected melanoma enrolled in KEYNOTE-054 was consistent with previous analyses
- There was one KEYTRUDA-related death due to myositis

Adapted from Eggermont AMM, et al. *N Eng J Med* 2018.¹

Refer to the SmPC and Risk Management Materials for further details on AEs before prescribing.

IA1 data cut-off: 2 October 2017.¹ All adverse events correspond to part 1 of the trial (the 1-year adjuvant-therapy period) and not to part 2 (in which patients with disease recurrence were eligible to cross over or receive repeat treatment with KEYTRUDA). *The investigators determined whether adverse events were related to a trial agent.

AE, adverse event; **IA**, interim analysis; **SmPC**, Summary of Product Characteristics.

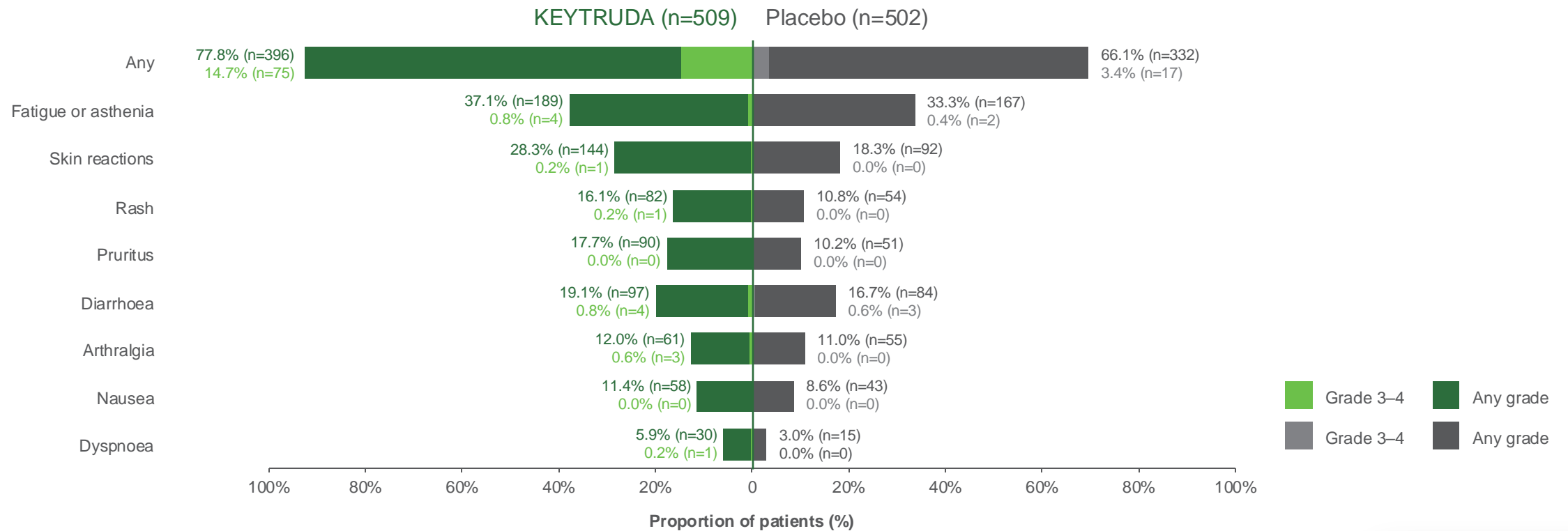
1. Eggermont AMM, et al. *N Engl J Med* 2018;378:1789–1801.

KEYTRUDA[®]
(pembrolizumab)

Summary of TRAEs during KEYNOTE-054¹

Safety data includes patients who received at least one dose of study treatment.

TRAEs reported by 15.1-month median follow-up*



Adapted from Eggermont AMM, *et al. N Eng J Med* 2018.¹

Refer to the SmPC and Risk Management Materials for further details on AEs before prescribing.

IA1 data cut-off: 2 October 2017.¹

*The investigators determined whether adverse events were related to a trial agent.

AE, adverse event; IA, interim analysis; SmPC, Summary of Product Characteristics; TRAE, treatment-related adverse event.

1. Eggermont AMM, *et al. N Engl J Med* 2018;378:1789–1801.

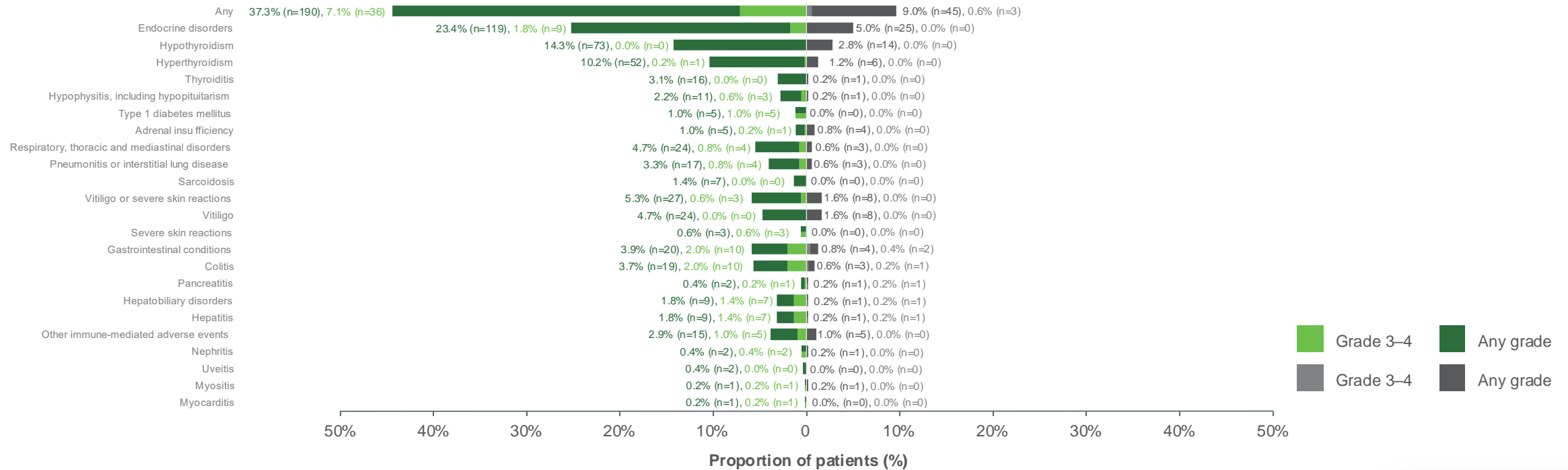
KEYTRUDA
(pembrolizumab)

Summary of IMAEs during KEYNOTE-054¹

Safety data includes patients who received at least one dose of study treatment.

IMAEs reported by 15.1-month median follow-up

KEYTRUDA (n=509) Placebo (n=502)



Adapted from Eggermont AMM, *et al. N Eng J Med* 2018.¹

Refer to the SmPC and Risk Management Materials for further details on AEs before prescribing.

IA data cut-off: 2 October 2017.¹

AE, adverse event; IA, interim analysis; IMAE, immune-mediated adverse event; SmPC, Summary of Product Characteristics.

1. Eggermont AMM, *et al. N Engl J Med* 2018;378:1789–1801.

KEYTRUDA
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At 5-year follow-up, serious TRAEs were reported in nine patients receiving KEYTRUDA and one patient receiving placebo*¹

Median follow-up: 4.9 years. Safety data includes patients who received at least one dose of study treatment.

Treatment-related serious AEs reported during follow-up treatment with KEYTRUDA²

Adverse event	Grade	Number of patients
Allergic oedema	3	1
Diarrhoea	3	2
Enteritis	3	1
Immune thrombocytopenia	4	1
Immune-mediated enterocolitis	4	1
Myositis	5	1
Plasmacytoma	3	1
Pneumonitis	3	1

Adapted from Eggermont AMM, *et al. N Engl J Med Evid* 2022.²

Refer to the SmPC and Risk Management Materials for further details on AEs before prescribing.

Data cut-off: 17 January 2022.¹

*Only serious treatment-related AEs were requested to be reported during the follow-up period starting 90 days after treatment administration.¹

AE, adverse event; SmPC, Summary of Product Characteristics; TRAE, treatment-related adverse event.

1. Eggermont AMM, *et al. N Engl J Med Evid* 2022;22:1:EVIDo2200214; 2. Eggermont AMM, *et al. N Engl J Med Evid* 2022;22:1:EVIDo2200214. Supplementary appendix.

KEYTRUDA[®]
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KEYNOTE-054:

Efficacy data from the initial analyses of DMFS

View the 15.1-month data



View the 5-year data



View the latest data at 7 years



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

KEYTRUDA[®]
(pembrolizumab)

DMFS was significantly higher in patients treated with adjuvant KEYTRUDA vs placebo after 3 years¹

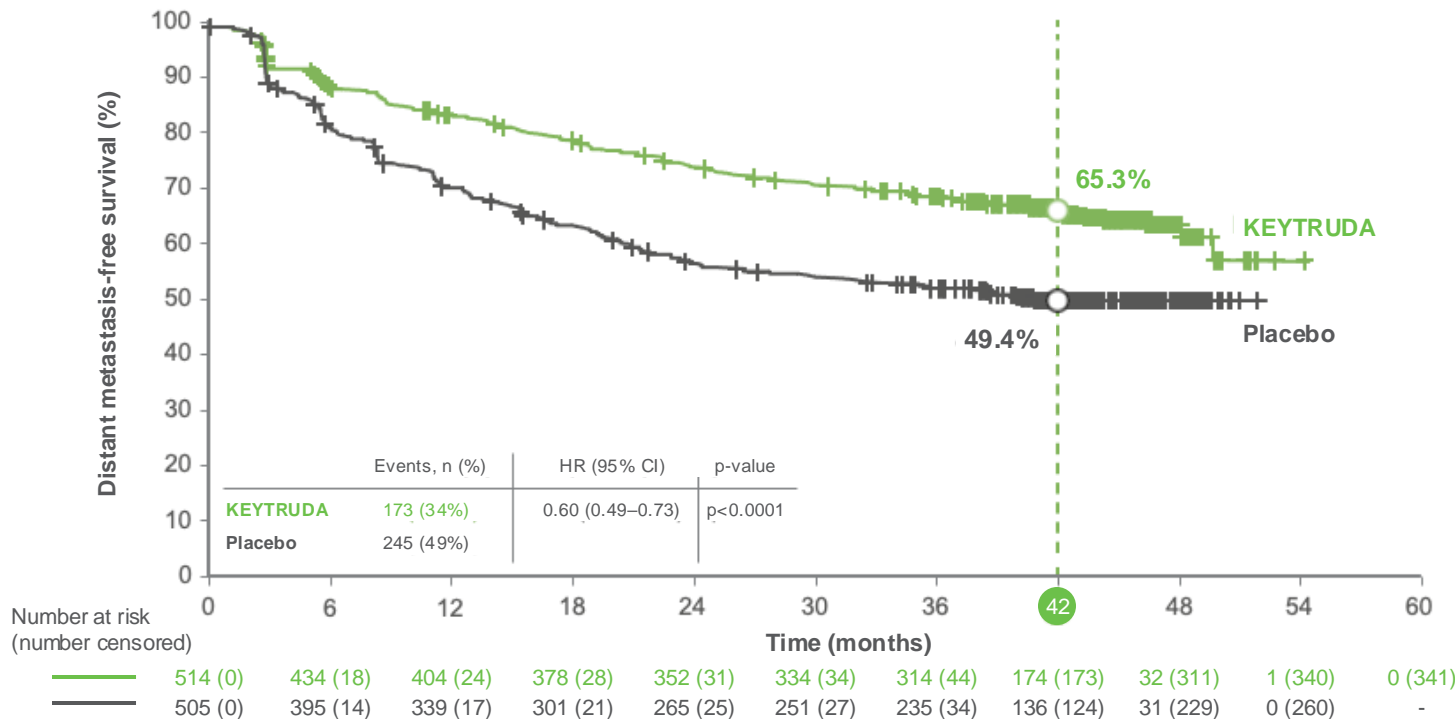
3 years

Kaplan-Meier estimates of DMFS in ITT population

40%
relative risk
reduction

Median follow-up: 42.3 months. DMFS was a secondary endpoint and data were only available at this analysis.¹

- After 3 years, KEYTRUDA demonstrated a **40% relative risk reduction** in distant metastasis versus placebo
- Patients with events: 34% (n=173/514) vs 49% (n=245/505)
- HR: 0.60; 95% CI: 0.49–0.73; p<0.0001



Adapted from Eggermont AMM, et al. *Lancet Oncol* 2021.¹

Data cut-off: 3 April 2020.¹ RFS was the primary endpoint.

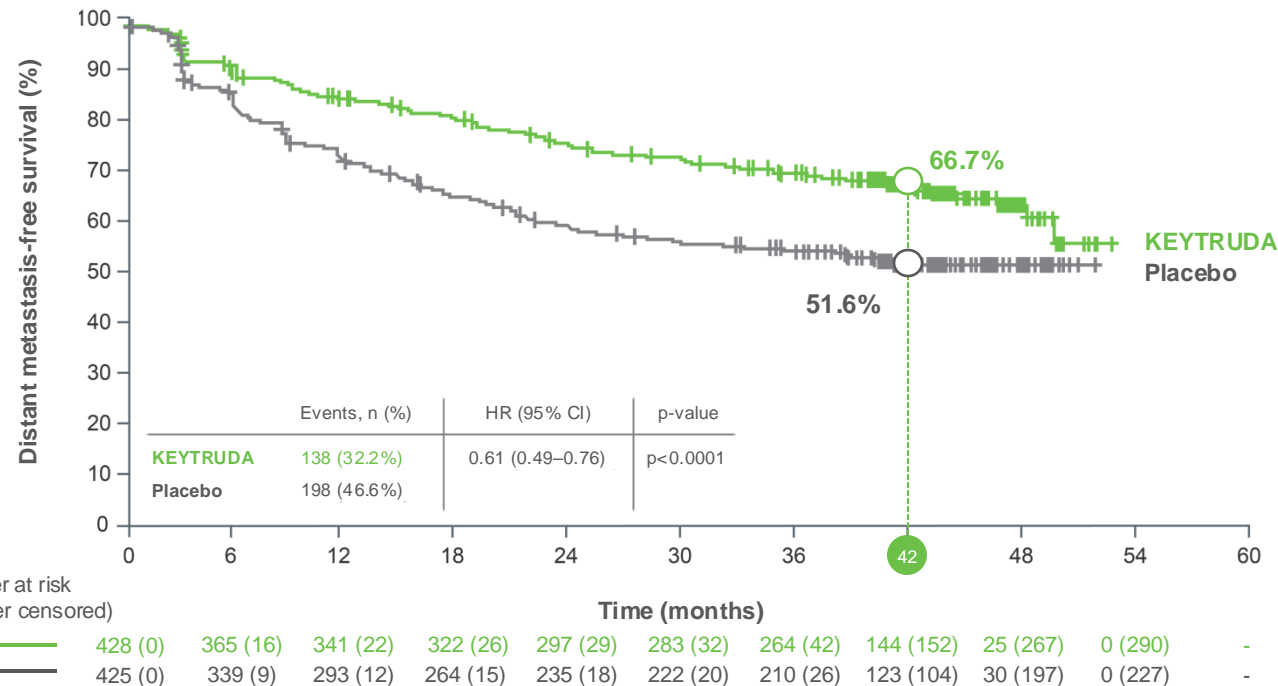
CI, confidence interval; **DMFS**, distant metastasis-free survival; **HR**, hazard ratio; **ITT**, intent-to-treat; **RFS**, recurrence-free survival.

¹. Eggermont AMM, et al. *Lancet Oncol* 2021;22:643–654.

KEYTRUDA
(pembrolizumab)

Significant increases in DMFS were also seen in patients with PD-L1-positive tumours treated with adjuvant KEYTRUDA vs placebo¹

3 years Kaplan-Meier estimates of DMFS in the PD-L1-positive population



Median follow-up: 42.3 months. DMFS was a secondary endpoint and data were only available at this analysis.¹

39%
relative risk
reduction

> In the PD-L1-positive population, KEYTRUDA demonstrated a **39% relative risk reduction** in distant metastasis versus placebo¹

- Patients with events: 32.2% (n=138/514) vs 46.6% (n=198/505)
- HR: 0.61; 95% CI: 0.49–0.76; p<0.0001

Adapted from Eggermont AMM, et al. *Lancet Oncol* 2021.¹

Data cut-off: 3 April 2020.¹ RFS was the primary endpoint.

CI, confidence interval; **DMFS**, distant metastasis-free survival; **HR**, hazard ratio; **ITT**, intent-to-treat; **RFS**, recurrence-free survival.

1. Eggermont AMM, et al. *Lancet Oncol* 2021;22:643–654.

KEYTRUDA
(pembrolizumab)

KEYNOTE-054:

Efficacy data from the 5-year analysis

[View the 15.1-month data >](#)

[View the 42.3-month data >](#)

[View the latest data
at 7 years >](#)



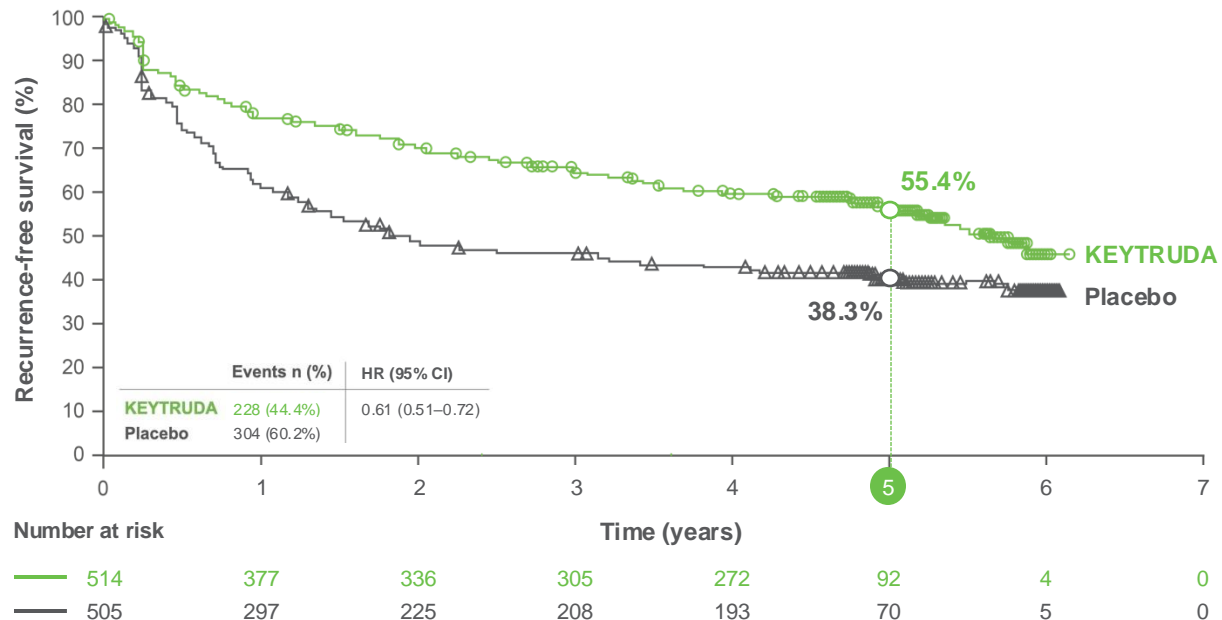
Images are illustrative of the range of patients diagnosed with melanoma.

KEYTRUDA®
(pembrolizumab)

Patients treated with adjuvant KEYTRUDA showed higher RFS vs placebo after 5 years¹

Median follow-up: 4.9 years. Exploratory long-term analysis; statistical significance was met in the initial analysis; significance was not tested at this timepoint and no statistical conclusions can be drawn from this analysis.

5 years Kaplan-Meier estimates of RFS in the ITT population



39%
relative risk
reduction

➤ After 5 years, KEYTRUDA demonstrated a **39% relative risk reduction** in disease recurrence versus placebo¹

- Patients with events: 44.4% (n=228/514) vs 60.2% (n=304/505)
- HR: 0.61; 95% CI: 0.51–0.72*

[View RFS data in the PD-L1-positive population](#)

[View RFS data in the PD-L1-negative population](#)

Adapted from Eggermont AMM, et al. *N Engl J Med* 2022.¹

Data cut-off: 17 January 2022.¹

*The HR and its CI were estimated using the Cox proportional hazards model stratified by Stage provided at randomisation.¹ CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; RFS, recurrence-free survival.

1. Eggermont AMM, et al. *N Engl J Med* 2022;22:1:EVIDo2200214.

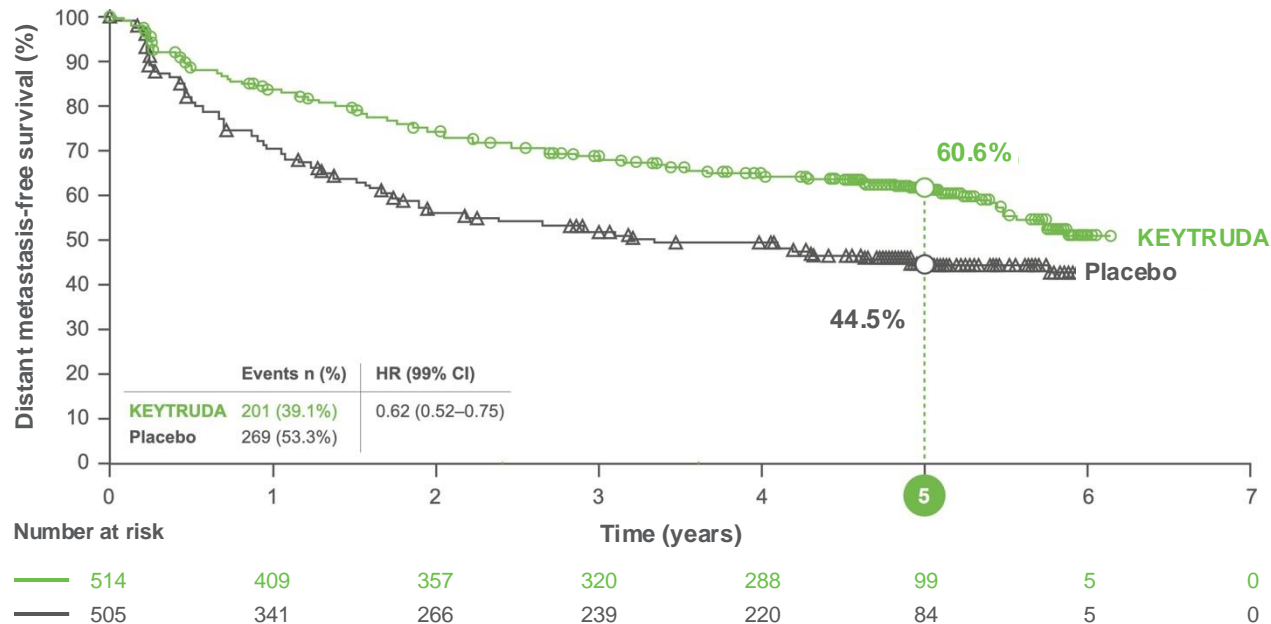
KEYTRUDA
(pembrolizumab)

DMFS was higher in patients treated with adjuvant KEYTRUDA vs placebo after 5 years¹

Median follow-up: 4.9 years. Exploratory long-term analysis; statistical significance was met in the initial analysis; significance was not tested at this timepoint and no statistical conclusions can be drawn from this analysis.

5 years

Kaplan-Meier estimates of DMFS in the ITT population



38%
relative risk
reduction

> After 5 years, KEYTRUDA demonstrated a **38% relative risk reduction** in distant metastasis versus placebo

- Patients with events: 39.1% (n=201/514) vs 53.3% (n=269/505)
- HR: 0.62; 99% CI: 0.52–0.75

[View DMFS data in the PD-L1-positive population](#)

[View DMFS data by AJCC classification](#)

[View DMFS data by *BRAF* status](#)

Adapted from Eggermont AMM, et al. *N Engl J Med* Evid 2022.¹

Data cut-off: 17 January 2022.¹

CI, confidence interval; DMFS, distant metastasis-free survival; HR, hazard ratio; ITT, intent-to-treat; RFS, recurrence-free survival.

1. Eggermont AMM, et al. *N Engl J Med* Evid 2022;22:1:EVIDo2200214.

KEYTRUDA
(pembrolizumab)

DMFS and RFS over the full study period¹

Median follow-up: 4.9 years.

Distant metastasis-free survival status, n (%)

	KEYTRUDA (n=514)	Placebo (n=505)
No event	313 (60.9)	236 (46.7)
Event	201 (39.1)	269 (53.3)
Distant metastasis*	187 (36.4)	264 (52.3)
Lymph node	65 (12.6)	91 (18.0)
Lung	68 (13.2)	108 (21.4)
Liver	40 (7.8)	57 (11.3)
Bone	21 (4.1)	35 (6.9)
Brain	29 (5.6)	38 (7.5)
Skin	14 (2.7)	25 (5.0)
Other soft tissues	28 (5.4)	43 (8.5)
Other site	24 (4.7)	40 (7.9)
Death not due to melanoma [†]	9 (1.8)	3 (0.6)
Death due to melanoma, no distant metastasis reported	5 (1.0)	2 (0.4)

Recurrence-free survival status, n (%)

	KEYTRUDA (n=514)	Placebo (n=505)
No event	286 (55.6)	201 (39.8)
Event	228 (44.4)	304 (60.2)
Recurrence		
Locoregional recurrence only	74 (14.4)	96 (19.0)
Distant metastasis only	133 (25.9)	174 (34.5)
Both, diagnosed within 30 days of each other	10 (1.9)	32 (6.3)
Death not due to melanoma, including unknown type or recurrence [†]	9 (1.8)	2 (0.4)
Death due to melanoma, no recurrence reported	2 (0.4)	0

Data cut-off: 17 January 2022.²

*Distant metastasis occurring as first type of recurrence or after a locoregional recurrence; the different types of sites involved are indicated; one patient might have several sites involved.¹

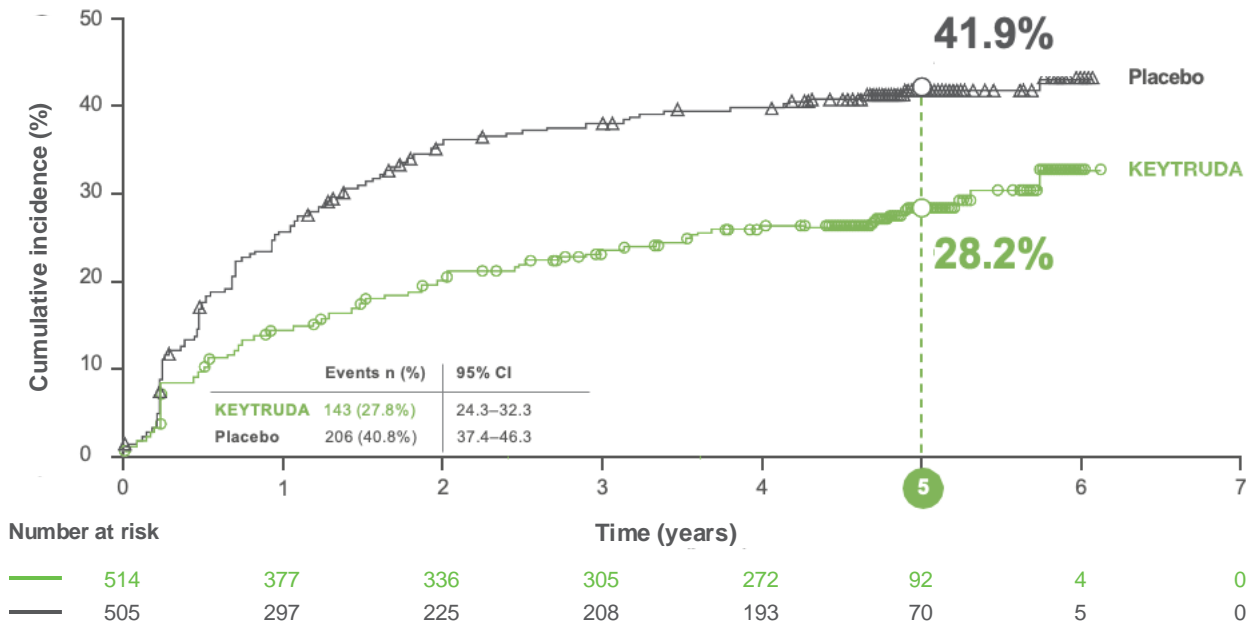
[†]One patient (<1%) died due to myositis in the KEYTRUDA group; all others died due to causes of death unrelated to treatment allocated by randomisation.¹

DMFS, distant metastasis-free survival; RFS, recurrence-free survival.

1. Eggermont AMM, et al. *N Engl J Med Evid* 2022;22:1:EVIDoa2200214. Supplementary appendix. 2. Eggermont AMM, et al. *N Engl J Med Evid* 2022;22:1:EVIDoa2200214.

Patients treated with adjuvant KEYTRUDA showed a lower cumulative incidence of distant metastases as first type of recurrence vs placebo^{1,2}

5 years Cumulative incidence of distant metastasis as first type of recurrence



Adapted from Eggermont AMM, et al. *N Engl J Med* 2022.^{1,2}

Data cut-off: 17 January 2022²

*5-year cumulative incidence of distant metastasis as the first type of recurrence. Adjuvant KEYTRUDA group: 28.2% (95% CI: 24.3–32.3); 41.9% (95% CI: 37.4–46.3).²
CI, confidence interval.

1. Eggermont AMM, et al. *N Engl J Med* 2022;22:1:EVIDoa2200214. Supplementary appendix. 2. Eggermont AMM, et al. *N Engl J Med* 2022;22:1:EVIDoa2200214.

- Positive treatment effect was seen for both locoregional recurrences and distant metastases²
- The 5-year cumulative incidence of distant metastasis as first type was 28.2% and 41.9% in the KEYTRUDA and placebo groups, respectively*²

KEYNOTE-054:

Efficacy data from the 7-year analysis

View the 15.1-month
data



View the 42.3-month data



View the 5-year data



IIIA
melanoma



IIIB
melanoma



IIIC
melanoma



IIID
melanoma

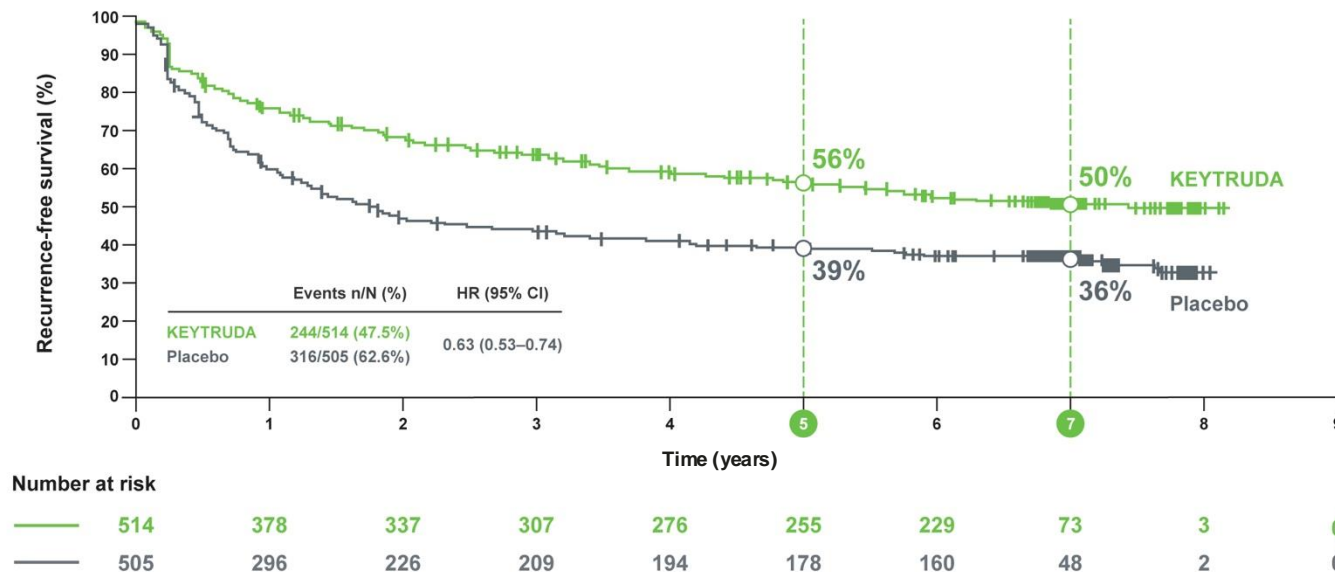
Images are illustrative of the range of patients diagnosed with melanoma.

KEYTRUDA®
(pembrolizumab)

Patients treated with adjuvant KEYTRUDA showed higher RFS vs placebo after 7 years¹

Exploratory long-term analysis; statistical significance was met in the initial analysis; significance was not tested at this timepoint and no statistical conclusions can be drawn from this analysis.

7 years Kaplan-Meier estimates of RFS in ITT population



37%
relative risk
reduction

> After 7 years, KEYTRUDA demonstrated a **37% relative risk reduction** in disease recurrence versus placebo¹

- Patients with events: 47.5% (n=244/514) vs 62.6% (n=316/505)
- HR: 0.63; 95% CI: 0.53–0.74*

Adjuvant KEYTRUDA continued to provide long-term, sustained benefit in RFS compared with placebo after a median follow-up of 7 years¹

Adapted from Eggermont AMM, et al. Eur J Cancer 2024.¹

Data cut-off: 3 January 2024.¹

*The estimate of the hazard ratio was based on a Cox model stratified according to disease stage at randomisation.

CI, confidence interval; HR, hazard ratio; RFS, recurrence-free survival; ITT, intent-to-treat; n, number of events; N, number of patients.

1. Eggermont AMM, et al. Eur J Cancer 2024;211:114327.

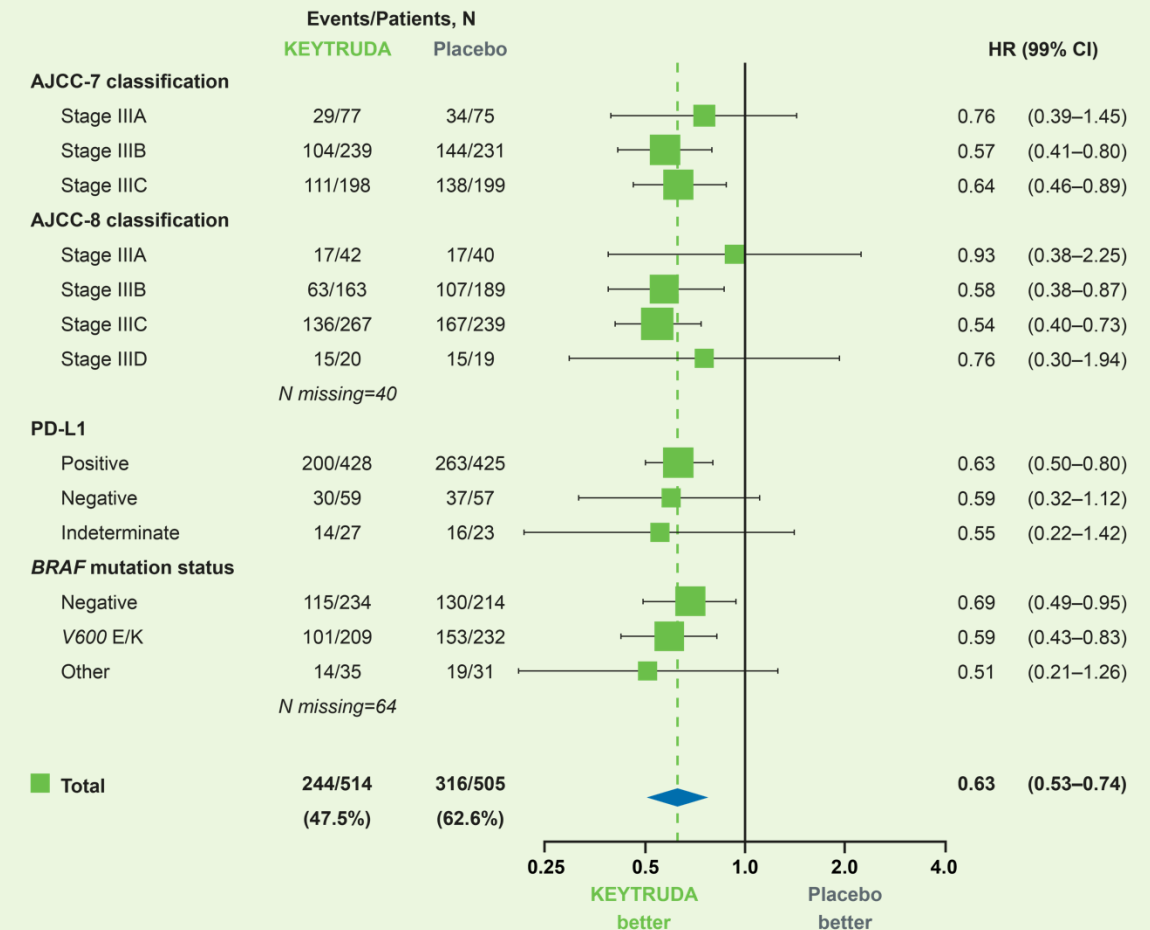
KEYTRUDA
(pembrolizumab)

KEYTRUDA showed consistent RFS across subgroups after 7 years¹

Exploratory long-term analysis; statistical significance was met in the initial analysis; significance was not tested at this timepoint and no statistical conclusions can be drawn from this analysis.

- Improvements vs placebo across AJCC-7 and AJCC-8 classifications, consistent with previous reports, indicate that patients with microscopic minimal residual disease benefit equally, independent of sentinel node status¹
- Treatment effect was similar in both PD-L1-positive and PD-L1-negative patients¹

After 7 years, improvement in RFS with adjuvant KEYTRUDA was consistent across all subgroups and similar to previous analyses¹



Adapted from Eggermont AMM, et al. Eur J Cancer 2024.¹

Data cut-off: 3 January 2024.¹

In subgroups, 99% confidence intervals are displayed.

CI, confidence interval; HR, hazard ratio; RFS, recurrence-free survival; n, number of events; N, number of patients.

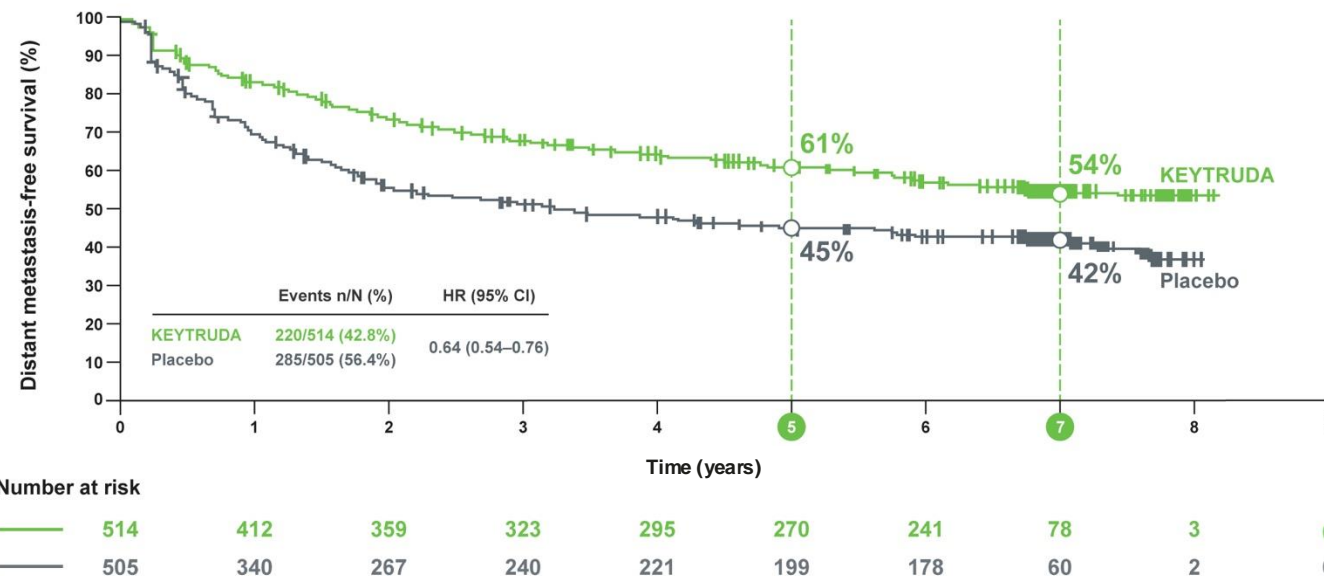
1. Eggermont AMM, et al. Eur J Cancer 2024;211:114327.

KEYTRUDA
(pembrolizumab)

Patients treated with adjuvant KEYTRUDA showed higher DMFS vs placebo after 7 years¹

Exploratory long-term analysis; statistical significance was met in the initial analysis; significance was not tested at this timepoint and no statistical conclusions can be drawn from this analysis.

7 years Kaplan-Meier estimates of DMFS in ITT population



36%
relative risk
reduction

> After 7 years, KEYTRUDA demonstrated a **36% relative risk reduction** in distant metastasis versus placebo¹

- Patients with events: 42.8% (n=220/514) vs 56.4% (n=285/505)
- HR: 0.64; 95% CI: 0.54–0.76

Adjuvant KEYTRUDA continued to provide long-term, sustained benefit in DMFS compared with placebo after a median follow-up of 7 years¹

Adapted from Eggermont AMM, et al. Eur J Cancer 2024.¹

Data cut-off: 3 January 2024.¹

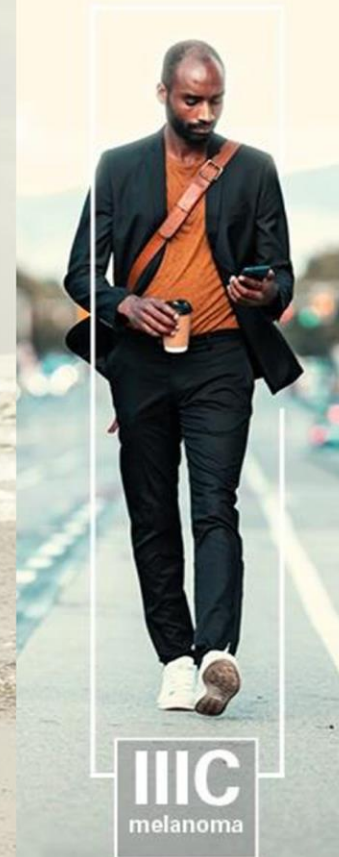
CI, confidence interval; DMFS, distant metastasis-free survival; HR, hazard ratio; ITT, intent-to-treat; n, number of events; N, number of patients.

1. Eggermont AMM, et al. Eur J Cancer 2024;211:114327.

KEYTRUDA
(pembrolizumab)

KEYNOTE-054:

Summary



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

KEYTRUDA®
(pembrolizumab)

Patients with Stage III could benefit from adjuvant KEYTRUDA treatment, similar to patients in the KEYNOTE-054 trial

During KEYNOTE-054, in patients with Stage III melanoma, KEYTRUDA demonstrated vs placebo:

Significant extension of recurrence-free survival¹

15.1 months median follow-up:

- › ITT population: 43% RRR (HR: 0.57; 98.4% CI: 0.43–0.74; $p < 0.001$)
- › PD-L1+ population: 46% RRR (HR: 0.54; 95% CI: 0.42–0.69; $p < 0.001$)

Long term, sustained RFS benefit across 7 years of treatment²

7 years median follow-up:

- › ITT population: 37% RRR (HR: 0.63; 95% CI: 0.53–0.74)

Improvement in DMFS after 5 years across all subgroups³

4.9 years median follow-up:

- › ITT population: 38% RRR (HR: 0.62; 95% CI: 0.52–0.75)
- › Consistent benefit across subgroups, irrespective of AJCC-7/-8 staging, PD-L1 status or *BRAF* mutation status

A manageable safety profile, consistent with previous reports^{1,3,4}

At the initial analysis:

- › TRAEs occurred in 77.8% vs 66.1% of patients
- › IMAEs occurred in 37.3% vs 9.0% of patients
- › KEYTRUDA did not have a significant impact on long-term HRQoL⁵

AJCC, American Joint Committee on Cancer; CI, confidence interval; DMFS, distant metastasis-free survival; HR, hazard ratio; HRQoL, health-related quality of life; ITT, intent-to-treat; PD-L1, programmed death-ligand 1; RFS, recurrence-free survival; RRR, relative risk reduction.

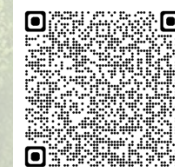
1. Eggermont AMM, et al. *N Engl J Med* 2018;378:1789–1801. 2. Eggermont AMM, et al. *Eur J Cancer* 2024;211:114327. 3. Eggermont AMM, et al. *N Engl J Med Evid* 2022;22:1:EVIDo2200214.

4. Eggermont AMM, et al. *Lancet Oncol* 2021;22:643–654. 5. Bührer E, et al. *Lancet Oncol* 2024;25:P1202–1212.



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



KEYNOTE-054:

Appendix



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

KEYTRUDA®
(pembrolizumab)

Baseline patient characteristics

		KEYTRUDA (n=514)	Placebo (n=505)
Median age, years		54	54
Aged ≥65 years, n (%)		125 (24.3)	126 (25.0)
Male, n (%)		324 (63.0)	304 (60.2)
Stage, n (%)*	IIIA	80 (15.6)	80 (15.8)
	IIIB	237 (46.1)	230 (45.5)
	IIIC w/ 1–3 positive LN	95 (18.5)	93 (18.4)
	IIIC w/ ≥4 positive LN	102 (19.8)	102 (20.2)
Ulceration, n (%)		208 (40.5)	197 (39.0)
1 vs 2–3 vs ≥4 positive LN, %		44.2 vs 34.4 vs 21.4	46.9 vs 32.9 vs 20.2
LN involvement, n (%)	Microscopic	187 (36.4)	161 (31.9)
	Macroscopic	327 (63.6)	344 (68.1)
PD-L1 status, n (%)†	Positive (MEL 2,3,4 or 5)	428 (83.3)	425 (84.2)
	Negative (MEL 0 or 1)	59 (11.5)	57 (11.3)
	Indeterminate	27 (5.3)	23 (4.6)
BRAF mutation status, n (%)	Wild type	233 (45.3)	214 (42.4)
	V600E/K mutant	210 (40.9)	231 (45.7)
	Other	35 (6.8)	31 (6.1)
	Unknown	36 (7.0)	29 (5.7)

- Baseline characteristics were similar between the two groups
- Out of 1019 patients randomised to KEYNOTE-054, 94% were ECOG PS 0 and 6% were ECOG PS 1²

Return to study design

Adapted from Eggermont AMM, *et al. N Engl J Med* 2018.¹

*According to AJCC 7th edition criteria. †PD-L1 expression was tested retrospectively by immunohistochemistry assay with the 22C3 anti-PD-L1 antibody. A positive score was defined as PD-L1 expression in ≥1% of tumour and tumour-associated immune cells relative to all viable tumour cells.¹ **AJCC**, American Joint Committee on Cancer; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **LN**, lymph node; **MEL**, melanoma; **PD-L1**, programmed death-ligand 1. 1. Eggermont AMM, *et al. N Engl J Med* 2018;378:1789–1801. 2. KEYTRUDA Summary of Product Characteristics. United Kingdom. Available at: <https://www.medicines.org.uk/emc/product/2498> Accessed: March 2025.

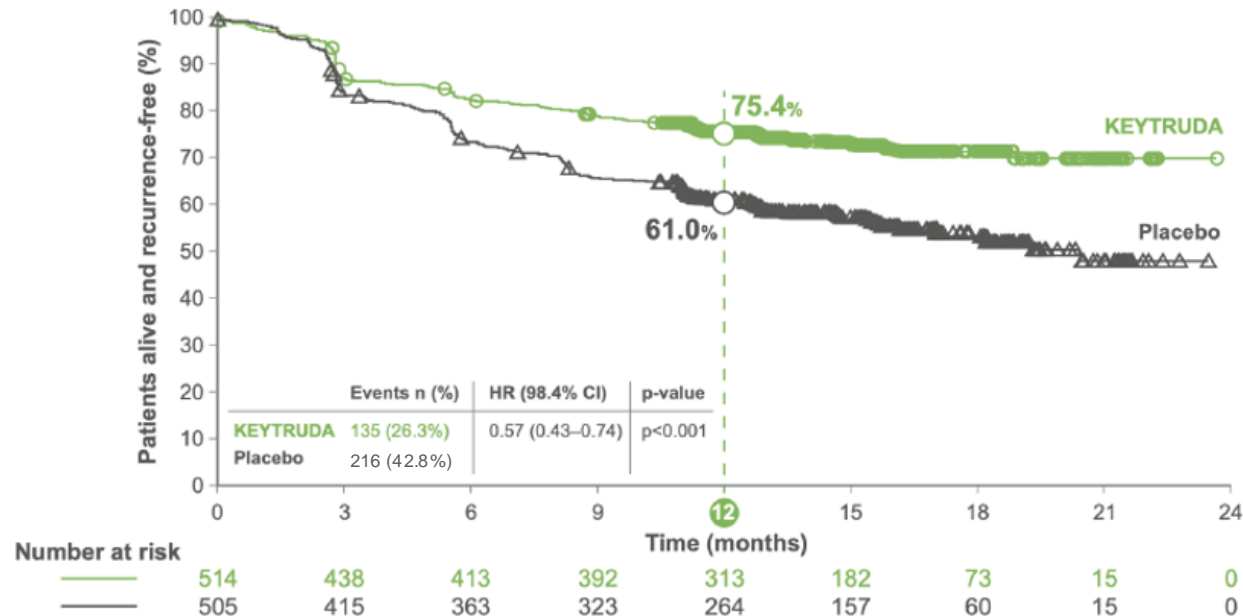
KEYTRUDA
(pembrolizumab)

KEYTRUDA treatment was associated with a significant improvement in RFS vs placebo in the overall population¹

Median follow-up: 15.1 months. RFS in the ITT population was a primary endpoint of KEYNOTE-054.

IA1

Kaplan-Meier estimates of RFS in the ITT population



Adapted from Eggermont AMM, et al. *N Engl J Med* 2018.¹

IA1 data cut-off: 2 October 2017.¹

Duration of treatment: Q3W for 18 doses (~1 year). Stratified by Stage given at randomisation.

CI, confidence interval; HR, hazard ratio; IA, interim analysis; ITT, intent-to-treat; n, number; Q3W, every three weeks.

1. Eggermont AMM, et al. *N Engl J Med* 2018;378:1789–1801.

43%
relative risk
reduction

During the initial analysis of RFS, adjuvant KEYTRUDA demonstrated a **43% relative risk reduction** in disease recurrence versus placebo¹

- Patients with events: 26.3% (n=135/514) vs 42.8% (n=216/505)
- HR: 0.57; 95% CI: 0.43–0.74; p<0.001

Benefit from adjuvant KEYTRUDA was maintained **beyond cessation** of treatment

[Return to RFS data](#)

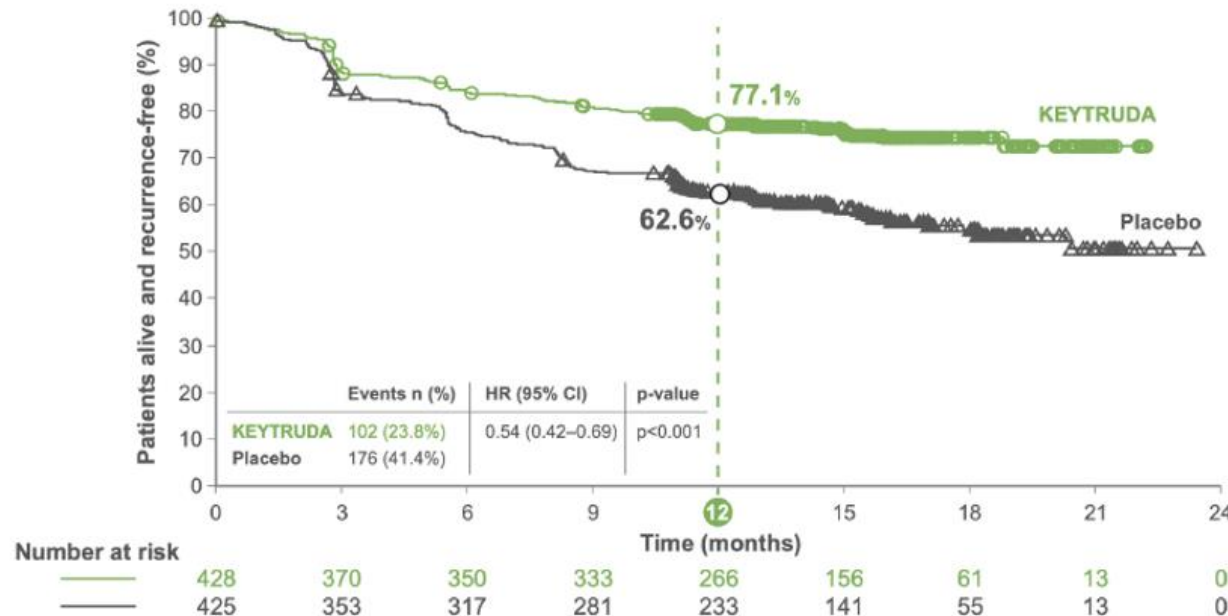
KEYTRUDA
(pembrolizumab)

PD-L1-positive patients also showed significant improvement in RFS with KEYTRUDA treatment vs placebo

Median follow-up: 15.1 months. RFS in the PD-L1+ population was a primary endpoint of KEYNOTE-054.

IA1

Kaplan-Meier estimates of RFS in the PD-L1-positive population



Adapted from Eggermont AMM, *et al. N Engl J Med* 2018.¹

46%
relative risk
reduction

➤ Within the PD-L1-positive population, adjuvant KEYTRUDA demonstrated a **46% relative risk reduction** in disease recurrence versus placebo¹

- Patients with events: 23.8% (n=102/428) vs 41.4% (n=176/425)
- HR: 0.54; 95% CI: 0.42–0.69; p<0.001

Both the PD-L1-positive and PD-L1-negative subgroups showed greater improvements in RFS with KEYTRUDA adjuvant therapy vs placebo¹

[Return to RFS data](#)

IA1 data cut-off: 2 October 2017.¹

Duration of treatment: Q3W for 18 doses (~1 year). Stratified by Stage given at randomisation.

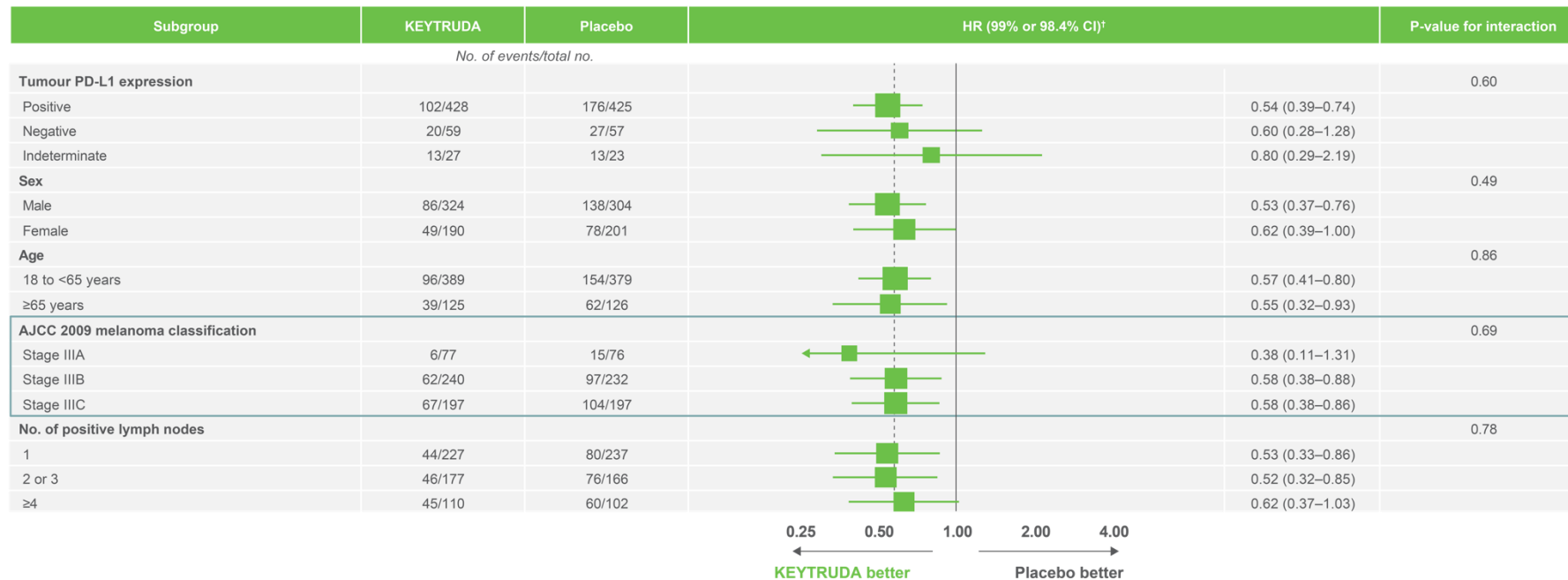
CI, confidence interval; HR, hazard ratio; IA, interim analysis; ITT, intent-to-treat; n, number; PD-L1, programmed death-ligand 1; Q3W, every three weeks.

1. Eggermont AMM, *et al. N Engl J Med* 2018;378:1789–1801.

KEYTRUDA
(pembrolizumab)

Adjuvant KEYTRUDA showed consistent RFS across AJCC staging classifications*¹

Median follow-up: 15.1 months. Subgroup analysis was pre-specified but not statistically powered for comparison, therefore results should be interpreted with caution.


[View RFS in Stage IIIA](#)
[View RFS in Stage IIIB](#)
[View RFS in Stage IIIC](#)
[Return to RFS data](#)

Adapted from Eggermont AMM, *et al. N Engl J Med* 2018.¹

IA1 data cut-off: 2 October 2017.¹ Staging was performed according to AJCC 7th edition pathologic staging criteria for melanoma.¹

*Small patient sample can be a limitation. [†]Unstratified HR. 98.4% CI covers the overall HR. 99% CI is presented for subgroup analysis.¹

AJCC, American Joint Committee on Cancer; **CI**, confidence interval; **HR**, hazard ratio; **IA**, interim analysis; **PD-L1**, programmed death-ligand 1; **Q3W**, every 3 weeks; **RFS**, recurrence-free survival.

1. Eggermont AMM, *et al. N Engl J Med* 2018;378:1789–1801.

KEYTRUDA
(pembrolizumab)

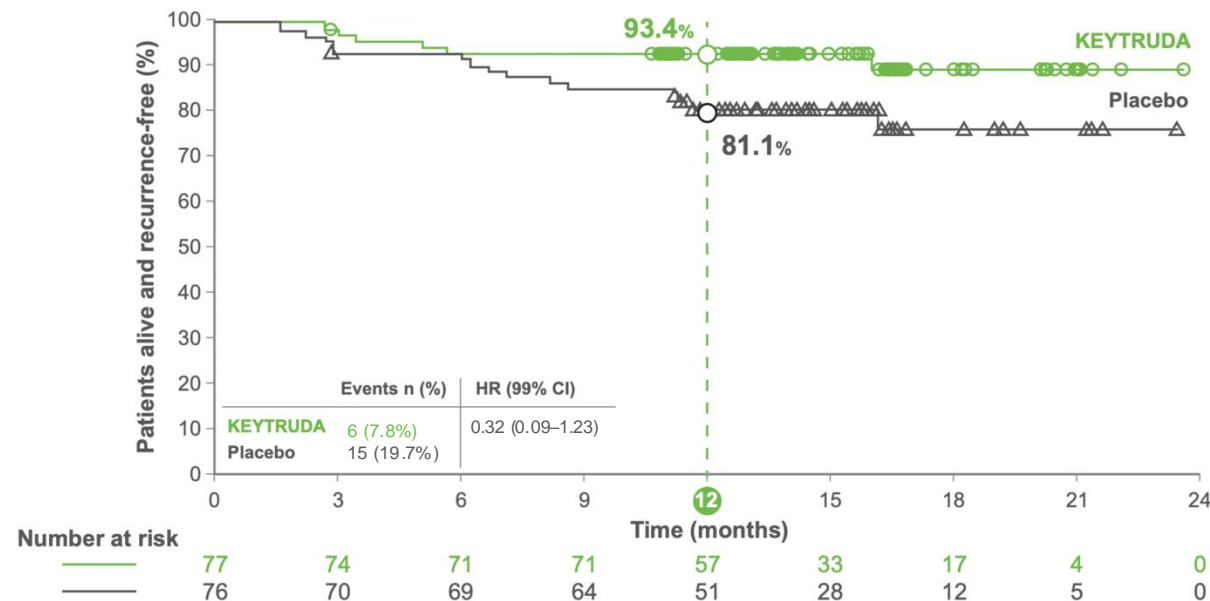
In Stage IIIA patients, adjuvant KEYTRUDA also showed a numerically higher RFS vs placebo¹

Median follow-up: 15.1 months.²

Subgroup analysis was pre-specified but not statistically powered for comparison.

IA1

Kaplan-Meier estimates of RFS in Stage IIIA (AJCC 7th edition)



68%
relative risk
reduction

> In patients with Stage IIIA melanoma, KEYTRUDA demonstrated a **68% relative risk reduction** in disease recurrence versus placebo

- Patients with events: 7.8% (n=6/77) vs 19.7% (n=15/76)
- HR: 0.32; 99% CI: 0.09–1.23
- Due to small patient numbers, results should be interpreted with caution

Return to RFS by AJCC classification

Adapted from Eggermont AMM, *et al.* AACR 2018.¹

IA1 data cut-off: 2 October 2017.¹

Stratified by stage given at randomisation. Staging per AJCC 7th edition.

Stage IIIA melanoma according to the AJCC 8th edition identifies a patient population with a better prognosis compared to Stage IIIA according to AJCC 7th edition.³

AJCC, American Joint Committee on Cancer; CI, confidence interval; HR, hazard ratio; IA, interim analysis; RFS, recurrence-free survival.

1. Eggermont A, *et al.* AACR Annual Meeting. 14–18 April 2018, Chicago, IL, USA. Abstract: LBA-10526. 2. Eggermont AMM, *et al.* *N Eng J Med* 2018;378:1789–1801. 3. Keung EZ & Gershenwald JE. *Expert Rev Anticancer Ther* 2018;18:775–784.

KEYTRUDA
(pembrolizumab)

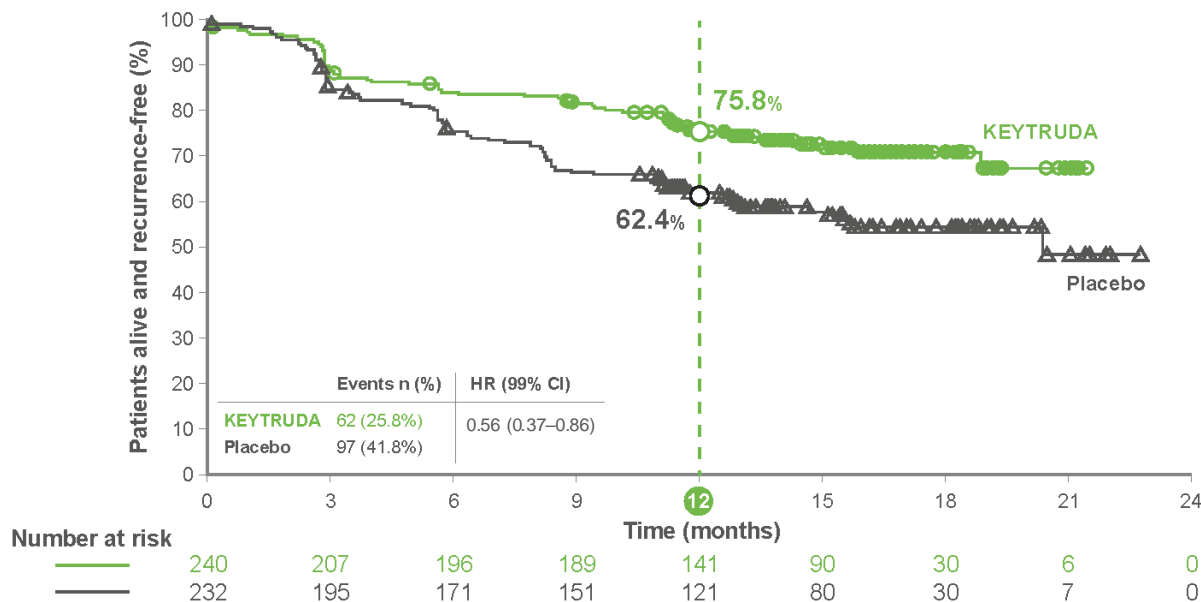
In Stage IIIB patients, adjuvant KEYTRUDA also showed a numerically higher RFS vs placebo¹

Median follow-up: 15.1 months.

Subgroup analysis was pre-specified but not statistically powered for comparison.

IA1

Kaplan-Meier estimates of RFS in Stage IIIB (AJCC 7th edition)



44%
relative risk
reduction

➤ In patients with Stage IIIB melanoma, KEYTRUDA demonstrated a **44% relative risk reduction** in disease recurrence versus placebo

- Patients with events: 25.8% (n=62/240) vs 41.8% (n=97/232)
- HR: 0.56; 99% CI: 0.37–0.86

Return to RFS by AJCC classification



Adapted from Eggermont AMM, *et al.* AACR 2018.¹

IA1 data cut-off: 2 October 2017.¹

Stratified by stage given at randomisation. Staging per AJCC 7th edition.

AJCC, American Joint Committee on Cancer; CI, confidence interval; HR, hazard ratio; IA, interim analysis; RFS, recurrence-free survival.

1. Eggermont A, *et al.* AACR Annual Meeting. 14–18 April 2018, Chicago, IL, USA. Abstract: LBA-10526.

KEYTRUDA
(pembrolizumab)

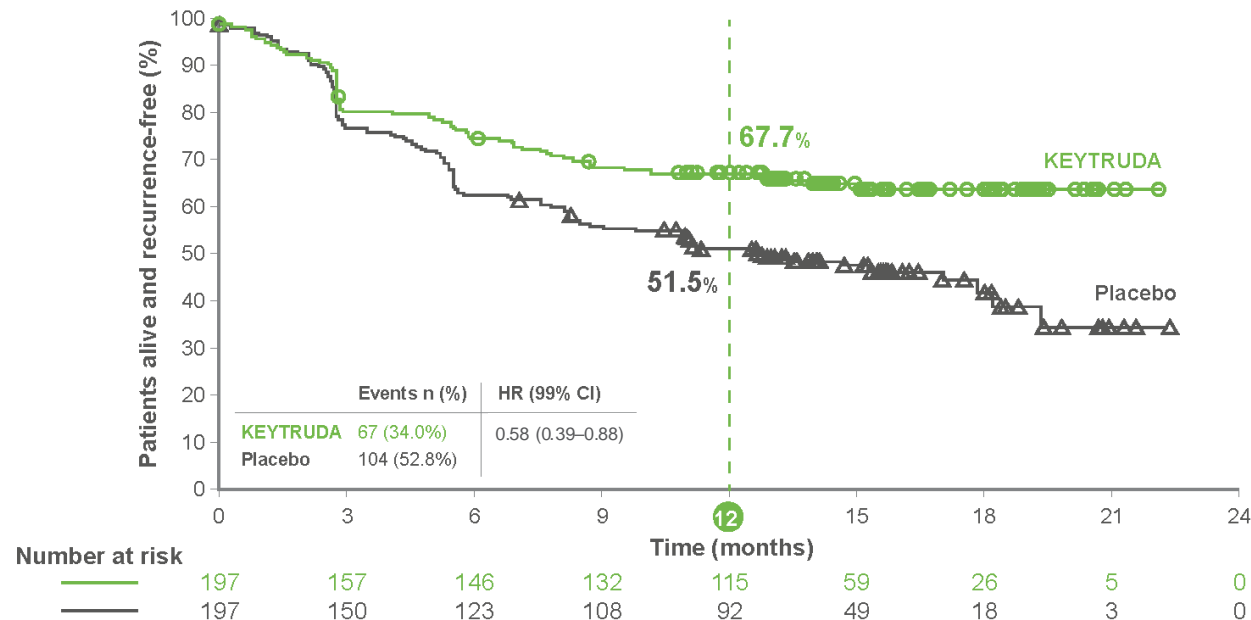
In Stage IIIC patients, adjuvant KEYTRUDA also showed a numerically higher RFS vs placebo¹

Median follow-up: 15.1 months.

Subgroup analysis was pre-specified but not statistically powered for comparison.

IA1

Kaplan-Meier estimates of RFS in Stage IIIC (AJCC 7th edition)



Adapted from Eggermont AMM, *et al.* AACR 2018.¹

42%
relative risk
reduction

> In patients with Stage IIIC melanoma, KEYTRUDA demonstrated a **42% relative risk reduction** in disease recurrence versus placebo

- Patients with events: 34.0% (n=67/197) vs 52.8% (n=104/197)
- HR: 0.58; 99% CI: 0.39–0.88

Return to RFS by AJCC classification



IA1 data cut-off: 2 October 2017.¹

Stratified by stage given at randomisation. Staging per AJCC 7th edition.

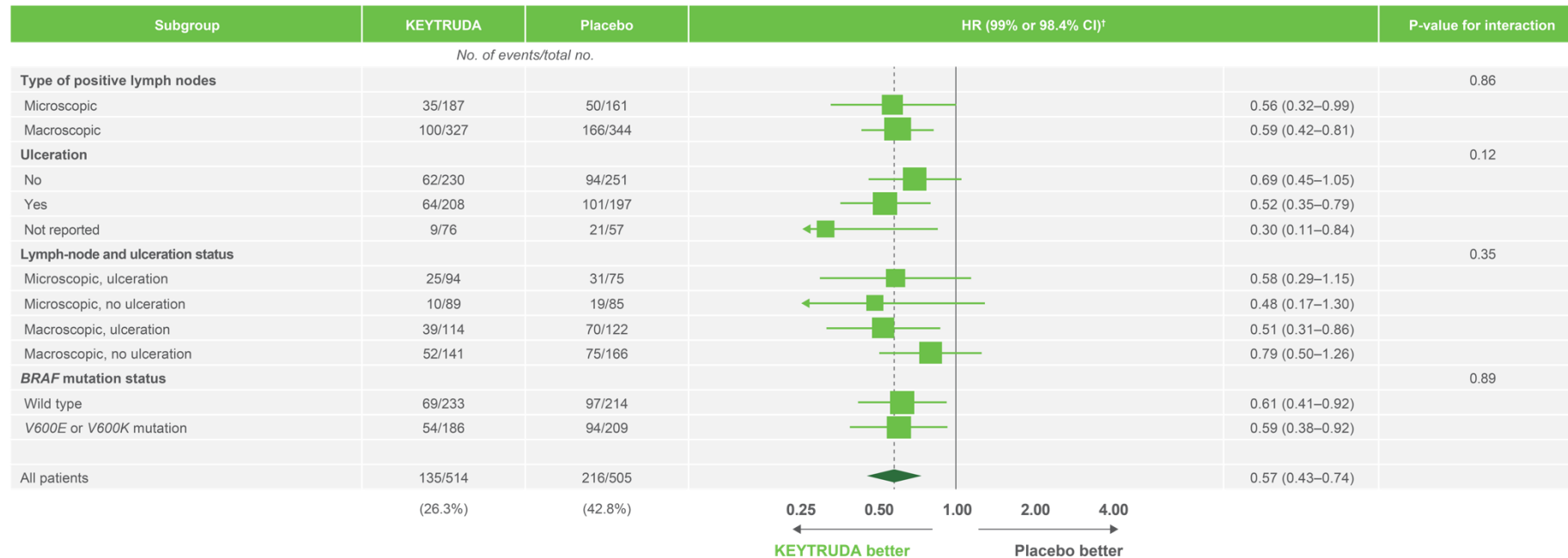
AJCC, American Joint Committee on Cancer; CI, confidence interval; HR, hazard ratio; IA, interim analysis; RFS, recurrence-free survival.

1. Eggermont A, *et al.* AACR Annual Meeting. 14–18 April 2018, Chicago, IL, USA. Abstract: LBA-10526.

KEYTRUDA
(pembrolizumab)

Adjuvant KEYTRUDA showed consistent RFS regardless of *BRAF* mutation status*1

Median follow-up: 15.1 months. Subgroup analysis was pre-specified but not statistically powered for comparison, therefore results should be interpreted with caution.



View RFS data by
BRAF V600E/K

View RFS data by *BRAF* WT

Return to RFS data

Adapted from Eggermont AMM, *et al. N Engl J Med* 2018.¹

IA1 data cut-off: 2 October 2017.¹

The green diamond is centred on the overall HR (dashed line) and covers its 98.4% CI.

*Small patient sample can be a limitation. †Unstratified HR. 98.4% CI covers the overall HR. 99% CI is presented for subgroup analysis.¹

CI, confidence interval; HR, hazard ratio; IA, interim analysis; Q3W, every 3 weeks; RFS, recurrence-free survival.

1. Eggermont AMM, *et al. N Engl J Med* 2018;378:1789–1801.

KEYTRUDA
(pembrolizumab)

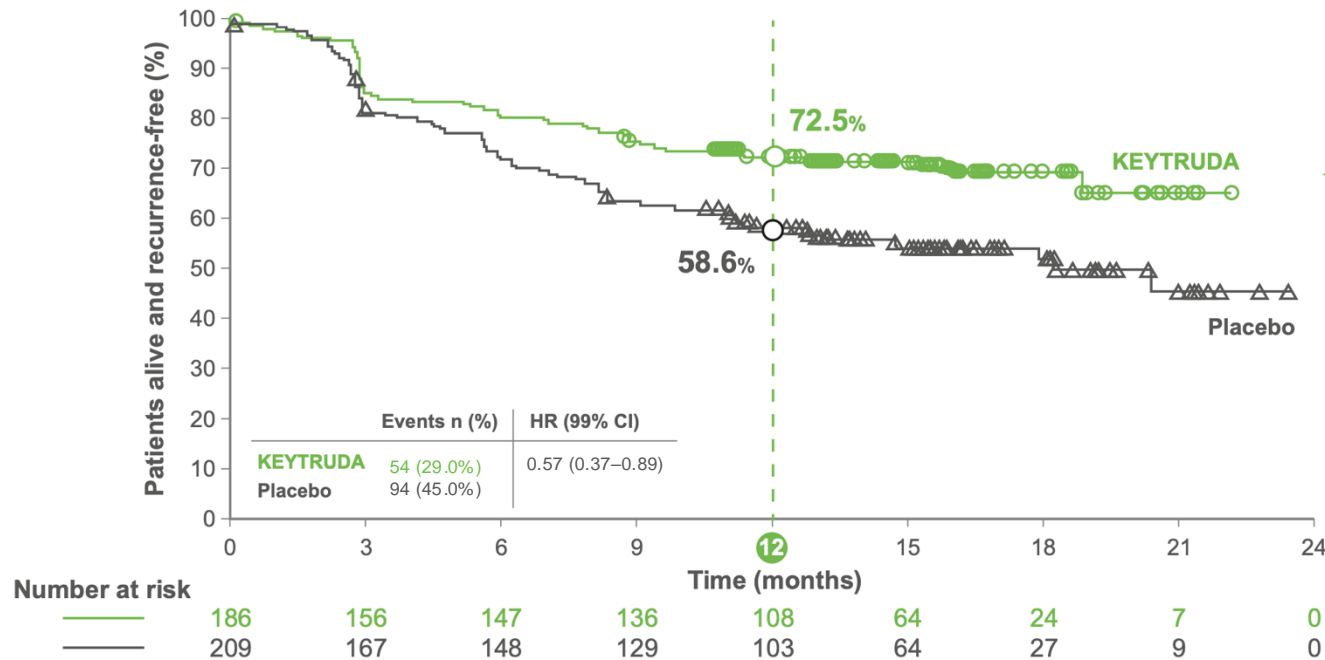
In patients with *BRAF*-V600E/K, adjuvant KEYTRUDA showed consistent RFS benefit vs placebo¹

Median follow-up: 15.1 months.

Subgroup analysis was pre-specified but not statistically powered for comparison.

IA1

Kaplan-Meier estimates of RFS in the *BRAF*-V600E/K population



Adapted from Eggermont AMM, *et al.* AACR 2018.¹

> In patients with a *BRAF*-V600E/K mutation, KEYTRUDA demonstrated a **43% relative risk reduction** in disease recurrence versus placebo

- Patients with events: 29.0% (n=54/186) vs 45.0% (n=94/209)
- HR: 0.57; 99% CI: 0.37–0.89

RFS results in *BRAF* subgroups were consistent with results in the ITT population¹

Return to RFS by *BRAF* status

IA1 data cut-off: 2 October 2017.¹

CI, confidence interval; HR, hazard ratio; IA, interim analysis; ITT, intent-to-treat; RFS, recurrence-free survival.

1. Eggermont A, *et al.* AACR Annual Meeting. 14–18 April 2018, Chicago, IL, USA. Abstract: LBA-10526.

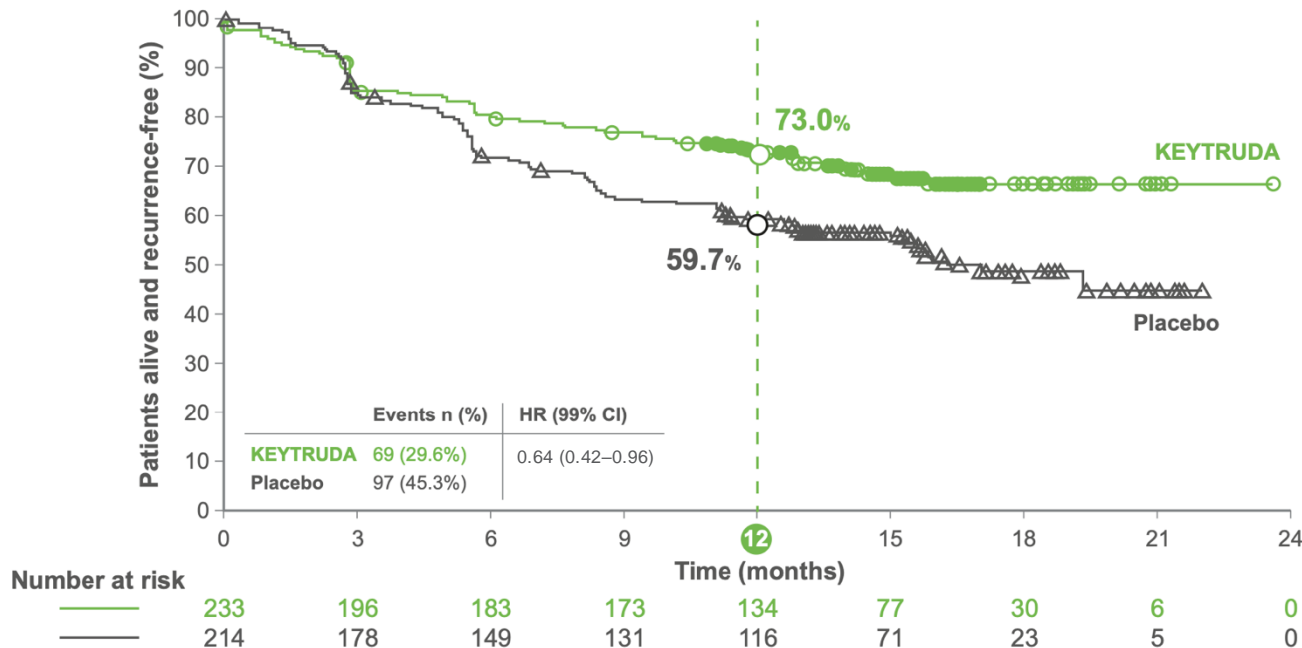
In patients with *BRAF*-WT, adjuvant KEYTRUDA showed a numerically higher RFS vs placebo¹

Median follow-up: 15.1 months.

Subgroup analysis was pre-specified but not statistically powered for comparison.

IA1

Kaplan-Meier estimates of RFS in the *BRAF*-WT population



Adapted from Eggermont AMM, *et al.* AACR 2018.¹

36%
relative risk
reduction

> In patients with *BRAF*-WT, KEYTRUDA demonstrated a **36% relative risk reduction** in disease recurrence versus placebo

- Patients with events: 29.6% (n=69/233) vs 45.3% (n=97/214)
- HR: 0.64; 99% CI: 0.42-0.96

RFS results in *BRAF* subgroups were consistent with results in the ITT population¹

Return to RFS by *BRAF* status

IA1 data cut-off: 2 October 2017.¹

CI, confidence interval; HR, hazard ratio; IA, interim analysis; ITT, intent-to-treat; RFS, recurrence-free survival.

1. Eggermont A, *et al.* AACR Annual Meeting. 14-18 April 2018, Chicago, IL, USA. Abstract: LBA-10526.

KEYTRUDA
(pembrolizumab)

Patients receiving adjuvant KEYTRUDA had a lower relapse rate vs placebo¹

Median follow-up: 15.1 months. Exploratory analysis.

	KEYTRUDA (n=514)	Placebo (n=505)	
No RFS event, n (%)	379 (73.7)	289 (57.2)	
Locoregional recurrence only, n (%)	55 (10.7)	77 (15.2)	
Distant metastasis only, n (%)	69 (13.4)	114 (22.6)	Relapse rate 15.2% vs 27.4%
Both, diagnosed within 30 days of each other, n (%)	9 (1.8)	24 (4.8)	
Death without an RFS event, n (%)	2 (0.4)	1 (0.2)	

Adapted from Eggermont AMM, *et al.* ACCR 2018.¹

[Return to DMFS data](#)

DMFS, distant metastasis-free survival; RFS, recurrence-free survival.

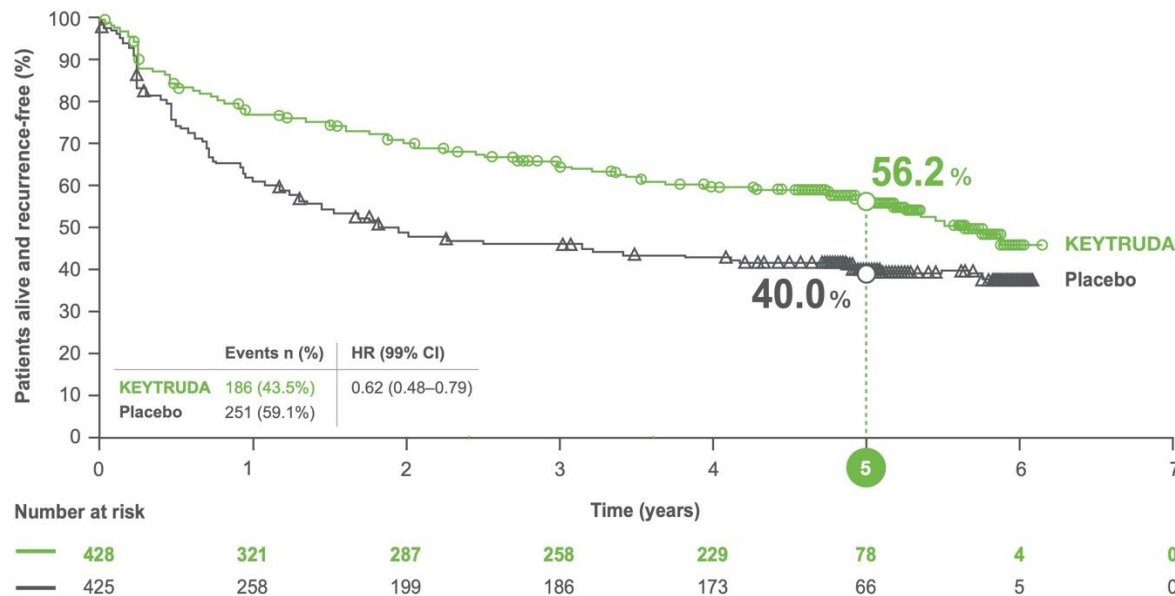
1. Eggermont A, *et al.* AACR Annual Meeting. 14–18 April 2018, Chicago, IL, USA. Abstract: LBA-10526.

KEYTRUDA
(pembrolizumab)

In patients with PD-L1-positive tumours, adjuvant KEYTRUDA resulted in higher RFS vs placebo after 5 years^{1,2}

Median follow-up: 4.9 years. Exploratory subgroup analysis was pre-specified but not statistically powered for comparison.

5 years Kaplan-Meier estimates of RFS in the PD-L1-positive population



Adapted from Eggermont AMM, et al. *N Engl J Med Evid* 2022.^{1,2}

38%
relative risk
reduction

> In the PD-L1-positive population, KEYTRUDA demonstrated a **38% relative risk reduction** distant metastasis versus placebo¹

- Patients with events:
43.5% (n=186/428) vs 59.1% (n=251/425)
- HR: 0.62; 99% CI: 0.48–0.79*

KEYTRUDA resulted in higher RFS in patients with PD-L1-positive and PD-L1-negative tumours vs placebo^{1,2}

[View RFS data in the PD-L1-negative population](#)

[Return to RFS data at 5 years](#)

Data cut-off: 17 January 2022.¹

*The HR and its CI were estimated using the Cox proportional hazards model stratified by Stage provided at randomisation.¹
CI, confidence interval; HR, hazard ratio; PD-L1, programmed death-ligand 1; RFS, recurrence-free survival.

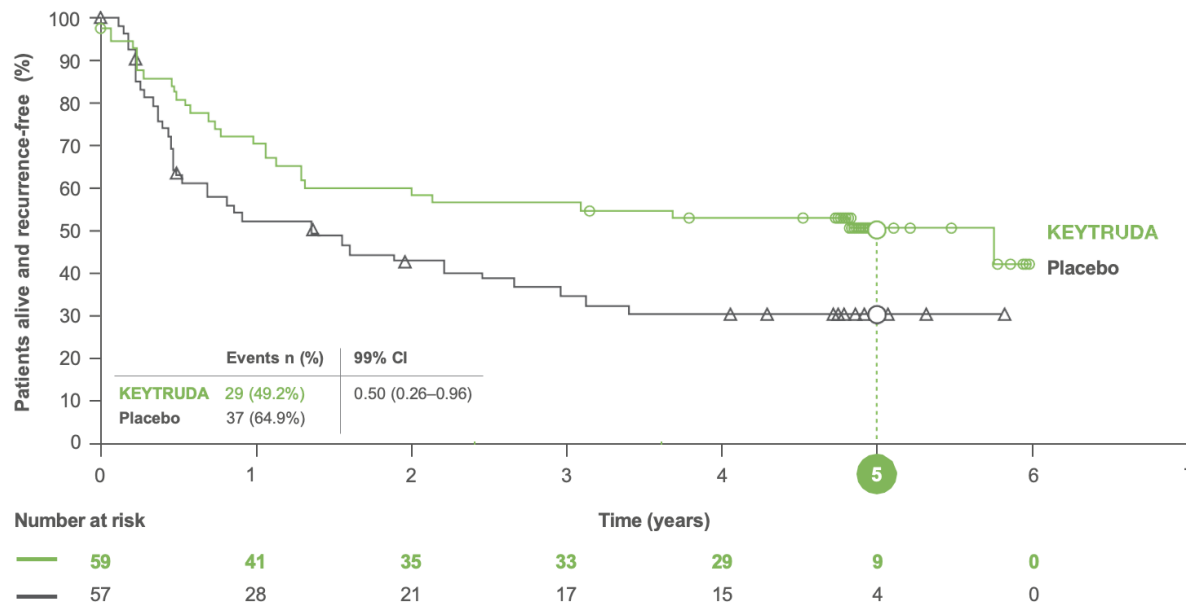
1. Eggermont AMM, et al. *N Engl J Med Evid* 2022;22:1:EVIDo2200214. 2. Eggermont AMM, et al. *N Engl J Med Evid* 2022;22:1:EVIDo2200214. Supplementary appendix.

KEYTRUDA®
(pembrolizumab)

In patients with PD-L1-negative tumours, adjuvant KEYTRUDA resulted in higher RFS vs placebo after 5 years^{1,2}

Median follow-up: 4.9 years. Exploratory subgroup analysis was pre-specified but not statistically powered for comparison.

5 years Kaplan-Meier estimates of RFS in the PD-L1-negative population



Adapted from Eggermont AMM, et al. *N Engl J Med Evid* 2022. Supplementary appendix.²

50%
relative risk
reduction

> In the PD-L1-negative population, KEYTRUDA demonstrated a **50% relative risk reduction** in distant metastasis versus placebo²

- Patients with events:
49.2% (n=29/59) vs 64.9% (n=37/57)
- HR: 0.50; 99% CI: 0.26–0.96*

KEYTRUDA resulted in higher RFS in patients with PD-L1-positive and PD-L1-negative tumours vs placebo^{1,2}

[View RFS data in the PD-L1-positive population](#)

[Return to RFS data at 5 years](#)

Data cut-off: 17 January 2022.¹

*The HR and its CI were estimated using the Cox proportional hazards model stratified by Stage provided at randomisation.¹

CI, confidence interval; HR, hazard ratio; PD-L1, programmed death-ligand 1; RFS, recurrence-free survival.

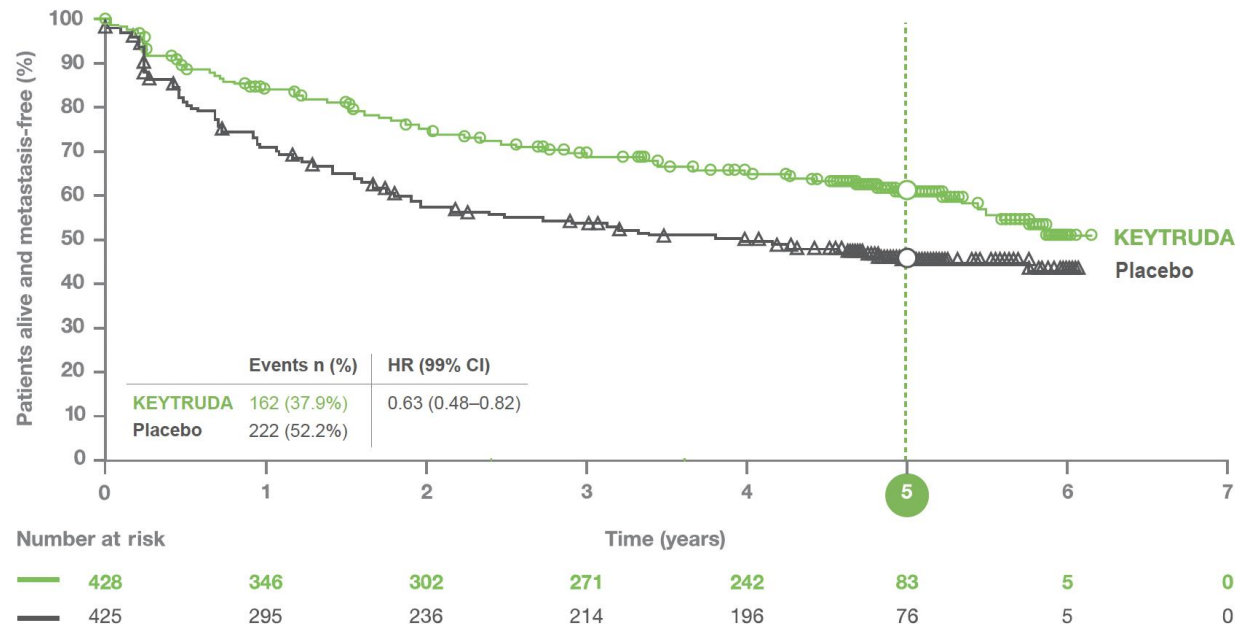
1. Eggermont AMM, et al. *N Engl J Med Evid* 2022;22:1:EVIDo2200214. 2. Eggermont AMM, et al. *N Engl J Med Evid* 2022;22:1:EVIDo2200214. Supplementary appendix.

KEYTRUDA®
(pembrolizumab)

In patients with PD-L1-positive tumours, adjuvant KEYTRUDA resulted in a higher DMFS vs placebo after 5 years^{1,2}

Median follow-up: 4.9 years. Exploratory subgroup analysis was pre-specified but not statistically powered for comparison.

5 years Kaplan-Meier estimates of DMFS in PD-L1-positive population



37%
relative risk
reduction

➤ In the PD-L1-positive population, KEYTRUDA demonstrated a **37% relative risk reduction** in distant metastasis versus placebo²

— Patients with events: 37.9% (n=162/428) vs 52.2% (n=222/425)

— HR: 0.63; 99% CI: 0.48–0.82*

Return to DMFS data at 5 years

Adapted from Eggermont AMM, et al. *N Engl J Med Evid* 2022. Supplementary appendix.²

Data cut-off: 17 January 2022.¹

*The HR and its CI were estimated using the Cox proportional hazards model stratified by Stage provided at randomisation.¹

CI, confidence interval; HR, hazard ratio; PD-L1, programmed death-ligand 1; RFS, recurrence-free survival.

1. Eggermont AMM, et al. *N Engl J Med Evid* 2022;22:1:EVIDoa2200214. 2. Eggermont AMM, et al. *N Engl J Med Evid* 2022;22:1:EVIDoa2200214. Supplementary appendix.

KEYTRUDA
(pembrolizumab)

Adjuvant KEYTRUDA showed consistent DMFS across staging classifications after 5 years^{1,2}



Adapted from Eggermont AMM, *et al. N Engl J Med Evid* 2022.¹

Data cut-off: 17 January 2022.²

*The overall HR is given with 95% CI. AJCC, American Joint Committee on Cancer; CI, confidence interval; DMFS, distant metastasis-free survival; HR, hazard ratio; ITT, intent-to-treat; n, number of events; N, number of patients; PD-L1, programmed death-ligand 1; RFS, recurrence-free survival.

1. Eggermont AMM, *et al. N Engl J Med Evid* 2022;22:1:EVIDo2200214. Supplementary appendix. 2. Eggermont AMM, *et al. N Engl J Med Evid* 2022;22:1:EVIDo2200214.

Median follow-up: 4.9 years. Exploratory subgroup analysis was pre-specified but not statistically powered for comparison

[View DMFS data in Stage IIIA](#)

[View DMFS data in Stage IIIB](#)

[View DMFS data in Stage IIIC](#)

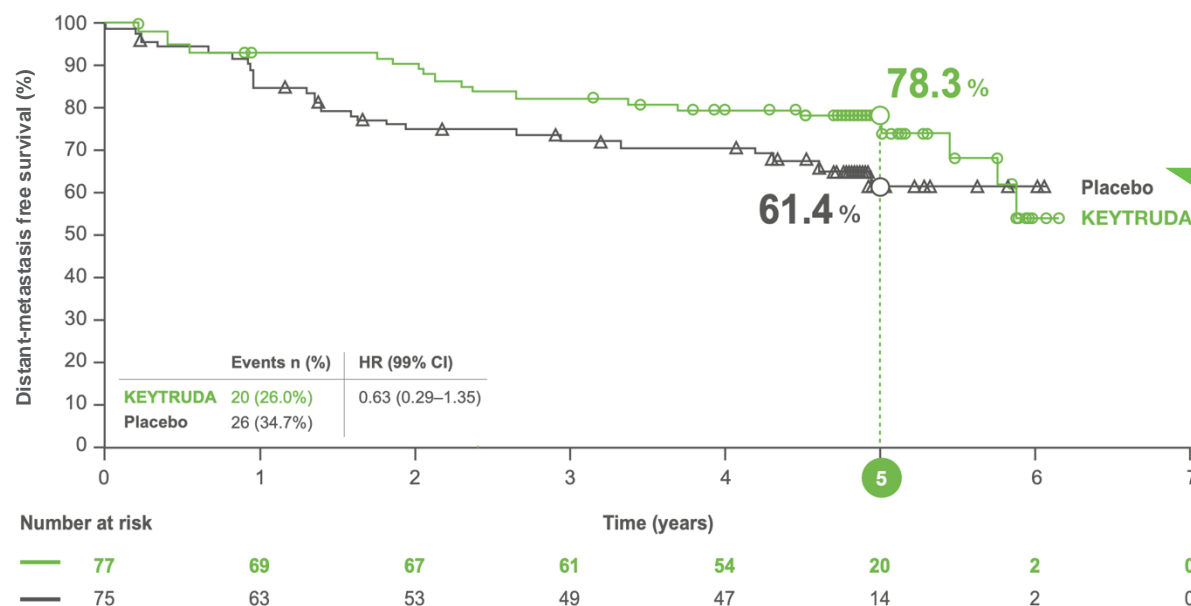
[Return to DMFS data at 5 years](#)

KEYTRUDA
(pembrolizumab)

In Stage IIIA patients, adjuvant KEYTRUDA showed higher DMFS vs placebo after 5 years¹

Median follow-up: 4.9 years. Exploratory subgroup analysis was pre-specified but not statistically powered for comparison.

5 years Kaplan-Meier estimates of DMFS in Stage IIIA (AJCC 7th edition)



Adapted from Eggermont AMM, et al. *N Engl J Med* 2022. Supplementary appendix.¹

> In patients with Stage IIIA melanoma, KEYTRUDA demonstrated a **37% relative risk reduction** in distant metastasis versus placebo¹

— Patients with events: 26.0% (n=20/77) vs 34.7% (n=26/75)

— HR: 0.63; 99% CI: 0.29–1.35*

After 5 years, DMFS in patients with Stage IIIA, IIIB and IIIC melanoma was higher for KEYTRUDA adjuvant therapy vs placebo, consistent with the ITT population¹

View DMFS
in Stage IIIB

Return to DMFS by
AJCC classification



Data cut-off: 17 January 2022.² *The HR and its CI were estimated using the Cox proportional hazards model stratified by Stage provided at randomisation.¹ RFS was the primary endpoint. DMFS was a secondary endpoint and data were only available at the 42.3-month and 4.9-year analyses.^{2,3}

Stratified by stage given at randomisation. Staging per AJCC 7th edition. Stage IIIA melanoma according to the AJCC 8th edition identifies a patient population with a better prognosis compared to Stage IIIA according to AJCC 7th edition.⁴ **AJCC**, American Joint Committee on Cancer; **CI**, confidence interval; **HR**, hazard ratio; **RFS**, recurrence-free survival.

1. Eggermont AMM, et al. *N Engl J Med* 2022;22:1:EVIDoa2200214. Supplementary appendix. 2. Eggermont AMM, et al. *N Engl J Med* 2022;22:1:EVIDoa2200214.

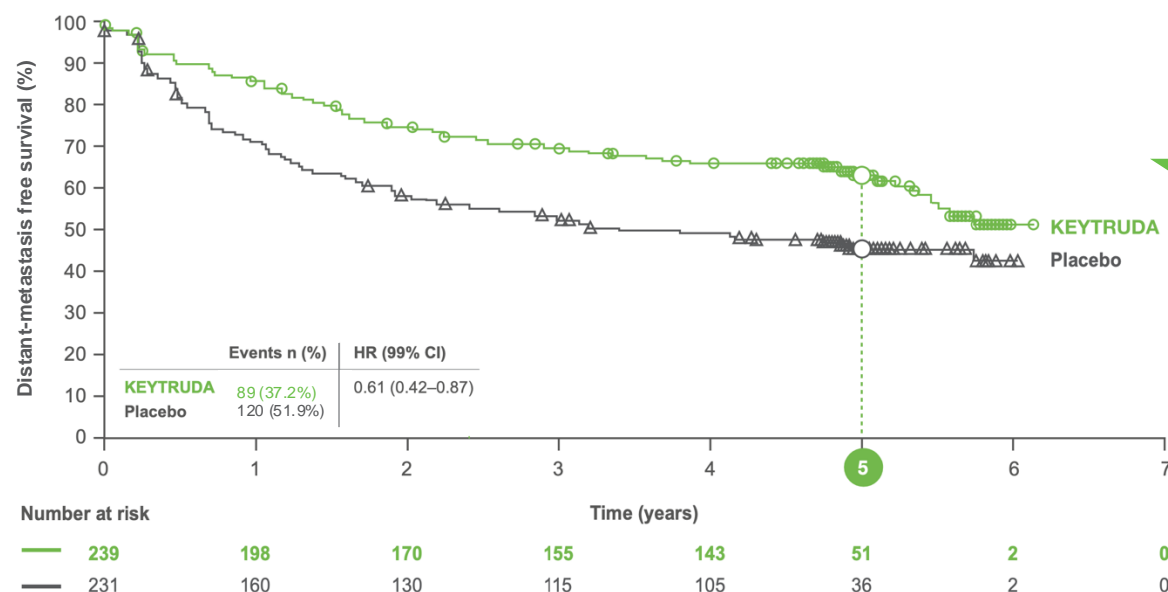
3. Eggermont AMM, et al. *Lancet Oncol* 2021;22:643–654. 4. Keung EZ & Gershenwald JE. *Expert Rev Anticancer Ther* 2018;18:775–784.

KEYTRUDA
(pembrolizumab)

In Stage IIIB patients, adjuvant KEYTRUDA also showed higher DMFS vs placebo at 5 years¹

Median follow-up: 4.9 years. Exploratory subgroup analysis was pre-specified but not statistically powered for comparison.

5 years Kaplan-Meier estimates of DMFS in Stage IIIB (AJCC 7th edition)



39%
relative risk
reduction

> In patients with Stage IIIB melanoma, KEYTRUDA demonstrated a **39% relative risk reduction** in distant metastasis versus placebo¹

— Patients with events: 37.2% (n=89/239) vs 51.9% (n=120/231)

— HR: 0.61; 99% CI: 0.42–0.87*

After 5 years, DMFS in patients with Stage IIIA, IIIB and IIIC melanoma was higher for KEYTRUDA adjuvant therapy vs placebo, consistent with the ITT population¹

View DMFS
in Stage IIIC

Return to DMFS by
AJCC classification



Adapted from Eggermont AMM, et al. *N Engl J Med* 2022; Supplementary appendix.¹

Data cut-off: 17 January 2022.² *The HR and its CI were estimated using the Cox proportional hazards model stratified by Stage provided at randomisation.¹ RFS was the primary endpoint. DMFS was a secondary endpoint and data were only available at the 42.3-month and 4.9-year analyses.^{2,3} Stratified by stage given at randomisation. Staging per AJCC 7th edition.

AJCC, American Joint Committee on Cancer; **CI**, confidence interval; **DMFS**, distant metastasis-free survival; **HR**, hazard ratio; **RFS**, recurrence-free survival.

1. Eggermont AMM, et al. *N Engl J Med* 2022;22:1:EVIDoa2200214. Supplementary appendix. 2. Eggermont AMM, et al. *N Engl J Med* 2022;22:1:EVIDoa2200214.

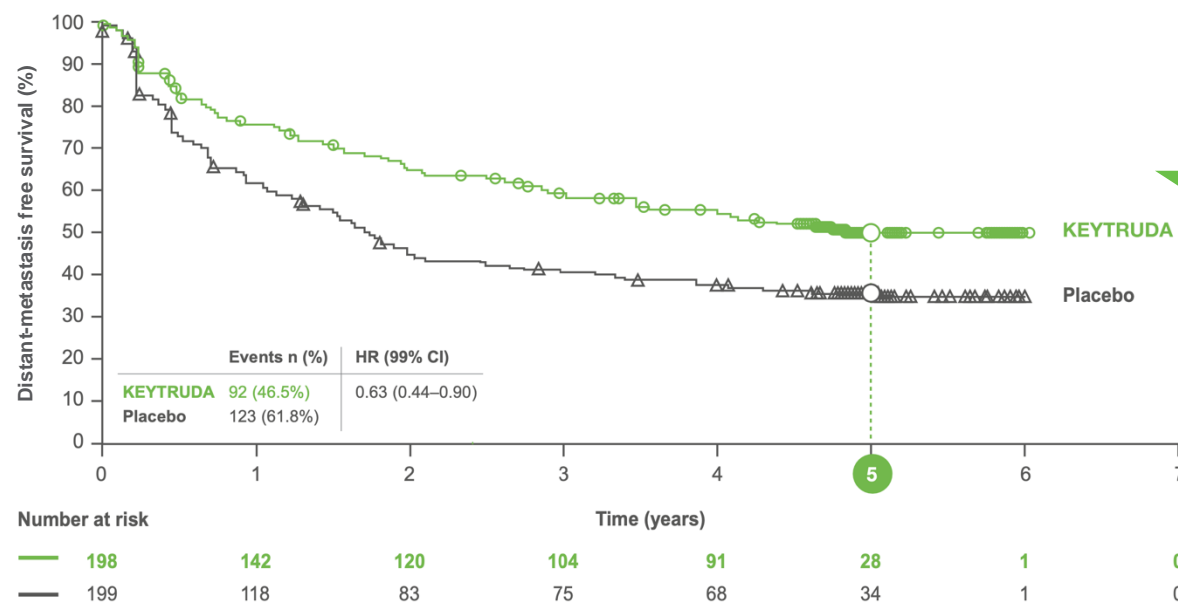
3. Eggermont AMM, et al. *Lancet Oncol* 2021;22:643–654.

KEYTRUDA
(pembrolizumab)

In Stage IIIC patients, adjuvant KEYTRUDA also showed higher DMFS vs placebo after 5 years¹

Median follow-up: 4.9 years. Exploratory subgroup analysis was pre-specified but not statistically powered for comparison.²

5 years Kaplan-Meier estimates of DMFS in Stage IIIC (AJCC 7th edition)



> In patients with Stage IIIC melanoma, KEYTRUDA demonstrated a **37% relative risk reduction** in distant metastasis versus placebo¹

— Patients with events: 46.5% (n=92/198) vs 61.8% (n=123/199)

— HR: 0.63; 99% CI: 0.44–0.90*

After 5 years, DMFS in patients with Stage IIIA, IIIB and IIIC melanoma was higher for KEYTRUDA adjuvant therapy vs placebo, consistent with the ITT population¹

Return to DMFS by AJCC classification



Adapted from Eggermont AMM, et al. *N Engl J Med Evid* 2022. Supplementary appendix.¹

Data cut-off: 17 January 2022.² *The HR and its CI were estimated using the Cox proportional hazards model stratified by Stage provided at randomisation.² RFS was the primary endpoint. DMFS was a secondary endpoint and data were only available at the 42.3-month and 4.9-year analyses.^{2,3} Stratified by stage given at randomisation. Staging per AJCC 7th edition.

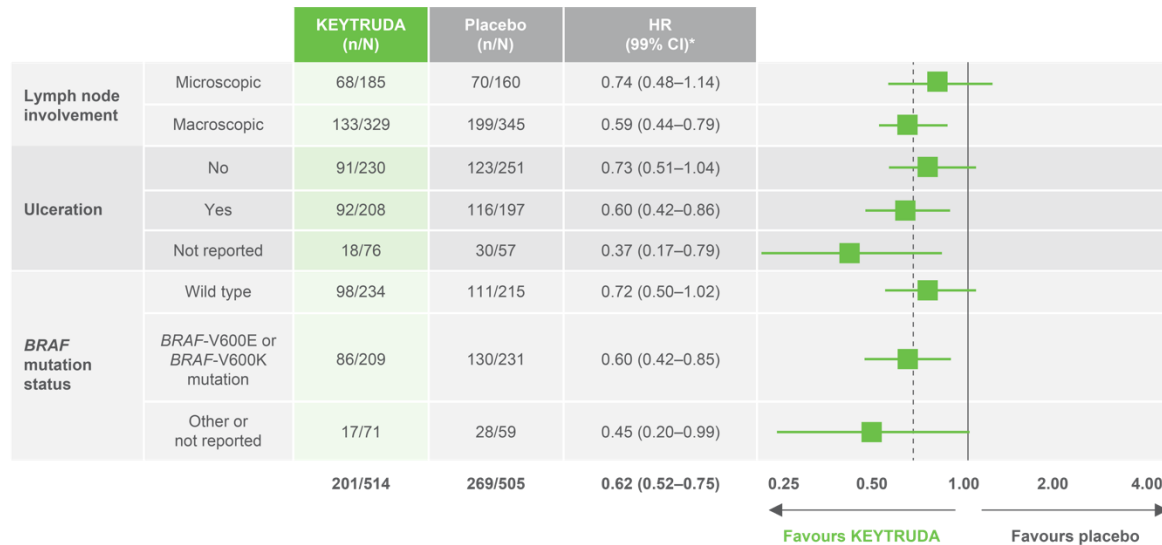
AJCC, American Joint Committee on Cancer; **CI**, confidence interval; **DMFS**, distant metastasis-free survival; **HR**, hazard ratio; **RFS**, recurrence-free survival.

1. Eggermont AMM, et al. *N Engl J Med Evid* 2022;22:1:EVIDoa2200214. Supplementary appendix. 2. Eggermont AMM, et al. *N Engl J Med Evid* 2022;22:1:EVIDoa2200214.

3. Eggermont AMM, et al. *Lancet Oncol* 2021;22:643–654.

KEYTRUDA
(pembrolizumab)

KEYTRUDA showed consistent DMFS across *BRAF* mutation status after 5 years¹



Median follow-up: 4.9 years. Exploratory subgroup analysis was pre-specified but not statistically powered for comparison

[View DMFS data in *BRAF*-V600E/K](#)

[View DMFS data in *BRAF*-WT](#)

[Return to DMFS data at 5 years](#)

Adapted from Eggermont AMM, et al. *N Engl J Med Evid* 2022. Supplementary appendix.¹

Data cut-off: 17 January 2022²

RFS was the primary endpoint. DMFS was a secondary endpoint and data were only available at the 42.3-month and 4.9-year analyses.^{2,3}

*The overall HR is given with 95% CI. CI, confidence interval; DMFS, distant metastasis-free survival; HR, hazard ratio; ITT, intent-to-treat; RFS, recurrence-free survival.

1. Eggermont AMM, et al. *N Engl J Med Evid* 2022;22:1:EVIDoa2200214. Supplementary appendix. 2. Eggermont AMM, et al. *N Engl J Med Evid* 2022;22:1:EVIDoa2200214.

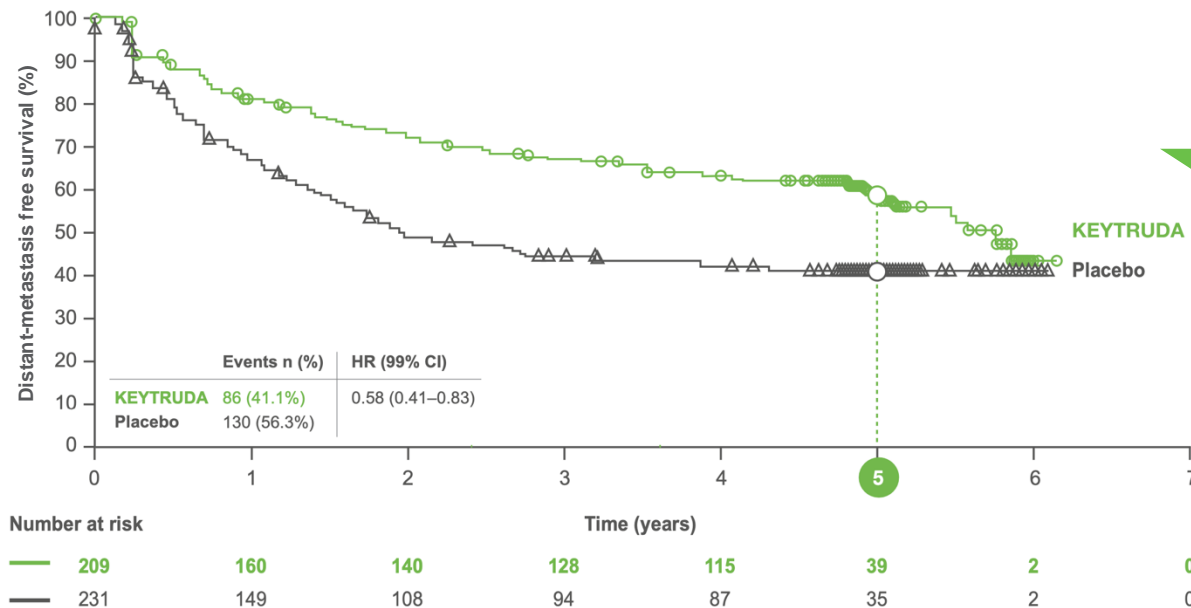
3. Eggermont AMM, et al. *Lancet Oncol* 2021;22:643–654.

KEYTRUDA[®]
(pembrolizumab)

In patients with *BRAF*-V600E/K, adjuvant KEYTRUDA showed improved DMFS vs placebo after 5 years¹

Median follow-up: 4.9 years. Exploratory subgroup analysis was pre-specified but not statistically powered for comparison.

5 years Kaplan-Meier estimates of DMFS in *BRAF*-V600E/K population



42%
relative risk
reduction

> In patients with *BRAF*-V600E/K, KEYTRUDA demonstrated a **42% relative risk reduction** in distant metastasis versus placebo²

- Patients with events: 41.1% (n=86/209) vs 56.3% (n=130/231)
- HR: 0.58; 99% CI: 0.41–0.83*

After 5 years, the *BRAF*-V600E/K mutation and *BRAF*-WT subgroups showed higher DMFS with adjuvant KEYTRUDA versus placebo, consistent with the ITT population^{1,2}

[Return to DMFS data by *BRAF* status](#)

Adapted from Eggermont AMM, et al. *N Engl J Med Evid*. 2022. Supplementary appendix.¹

Data cut-off: 17 January 2022.²

RFS was the primary endpoint. DMFS was a secondary endpoint and data were only available at the 42.3-month and 4.9-year analyses.^{2,3}

*The overall HR is given with 95% CI. CI, confidence interval; DMFS, distant metastasis-free survival; HR, hazard ratio; ITT, intent-to-treat; RFS, recurrence-free survival; WT, wild-type.

1. Eggermont AMM, et al. *N Engl J Med Evid* 2022;22:1:EVIDoA2200214. Supplementary appendix. 2. Eggermont AMM, et al. *N Engl J Med Evid* 2022;22:1:EVIDoA2200214.

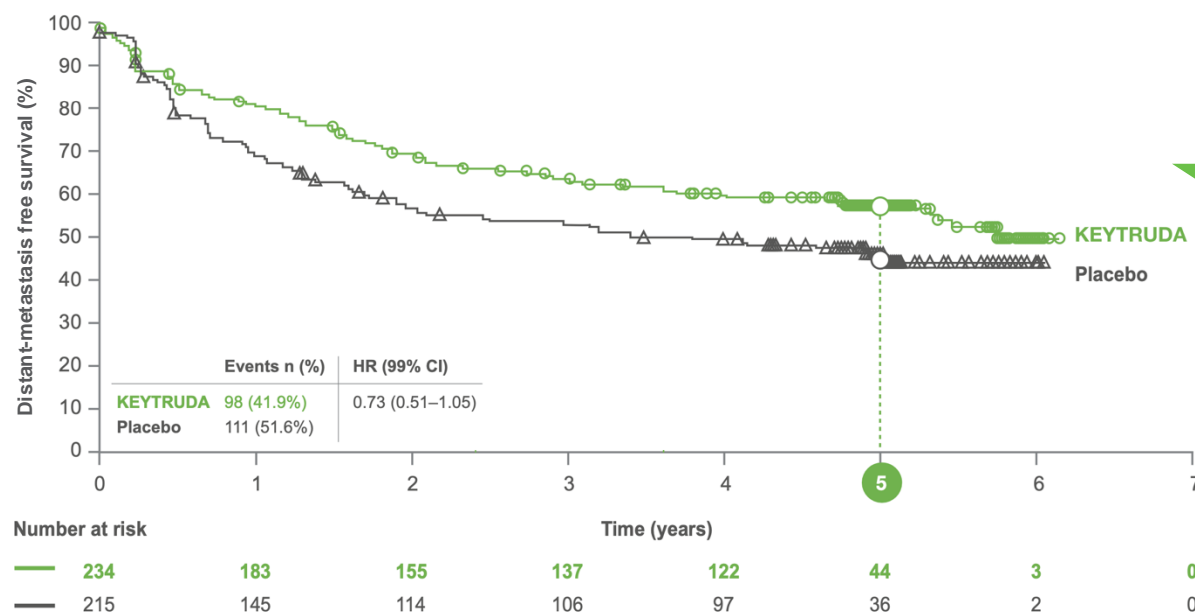
3. Eggermont AMM, et al. *Lancet Oncol* 2021;22:643–654.

KEYTRUDA
(pembrolizumab)

In patients with *BRAF*-WT, adjuvant KEYTRUDA showed improved DMFS vs placebo after 5 years¹

Median follow-up: 4.9 years. Exploratory subgroup analysis was pre-specified but not statistically powered for comparison.

5 years Kaplan-Meier estimates of DMFS in *BRAF*-WT population



27%
relative risk
reduction

> In patients with *BRAF*-WT, KEYTRUDA demonstrated a **27% relative risk reduction** in distant metastasis versus placebo²

- Patients with events: 41.9% (n=98/234) vs 51.6% (n=111/215)
- HR: 0.73; 99% CI: 0.51–1.05*

After 5 years, the *BRAF*-V600E/K mutation and *BRAF*-WT subgroups showed higher DMFS with adjuvant KEYTRUDA versus placebo, consistent with the ITT population^{1,2}

[Return to DMFS data by *BRAF* status](#)

Adapted from Eggermont AMM, et al. *N Engl J Med Evid* 2022. Supplementary appendix.¹

Data cut-off: 17 January 2022.²

RFS was the primary endpoint. DMFS was a secondary endpoint and data were only available at the 42.3-month and 4.9-year analyses.^{2,3}

*The overall HR is given with 95% CI. CI, confidence interval; DMFS, distant metastasis-free survival; HR, hazard ratio; ITT, intent-to-treat; RFS, recurrence-free survival; WT, wild-type.

1. Eggermont AMM, et al. *N Engl J Med Evid* 2022;22:1:EVIDo2200214. Supplementary appendix; 2. Eggermont AMM, et al. *N Engl J Med Evid* 2022;22:1:EVIDo2200214;

3. Eggermont AMM, et al. *Lancet Oncol* 2021;22:643–654.

KEYTRUDA
(pembrolizumab)