MSD Oncology

KEYTRUDA® (pembrolizumab) in the adjuvant treatment of patients with Stage IIB and IIC 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.

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.

GB-OOC-00946 | Date of preparation: April 2025

KEYTRUDA® (pembrolizumab)

KEYTRUDA melanoma indications[1]

- 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 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 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 dosing[1]

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.

bw, bodyweight; **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 IIB/IIC melanoma?

- Stages of melanoma
- 5- and 10-year survival rates
- Relapse rate and distant metastasis rate
- Time to relapse

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

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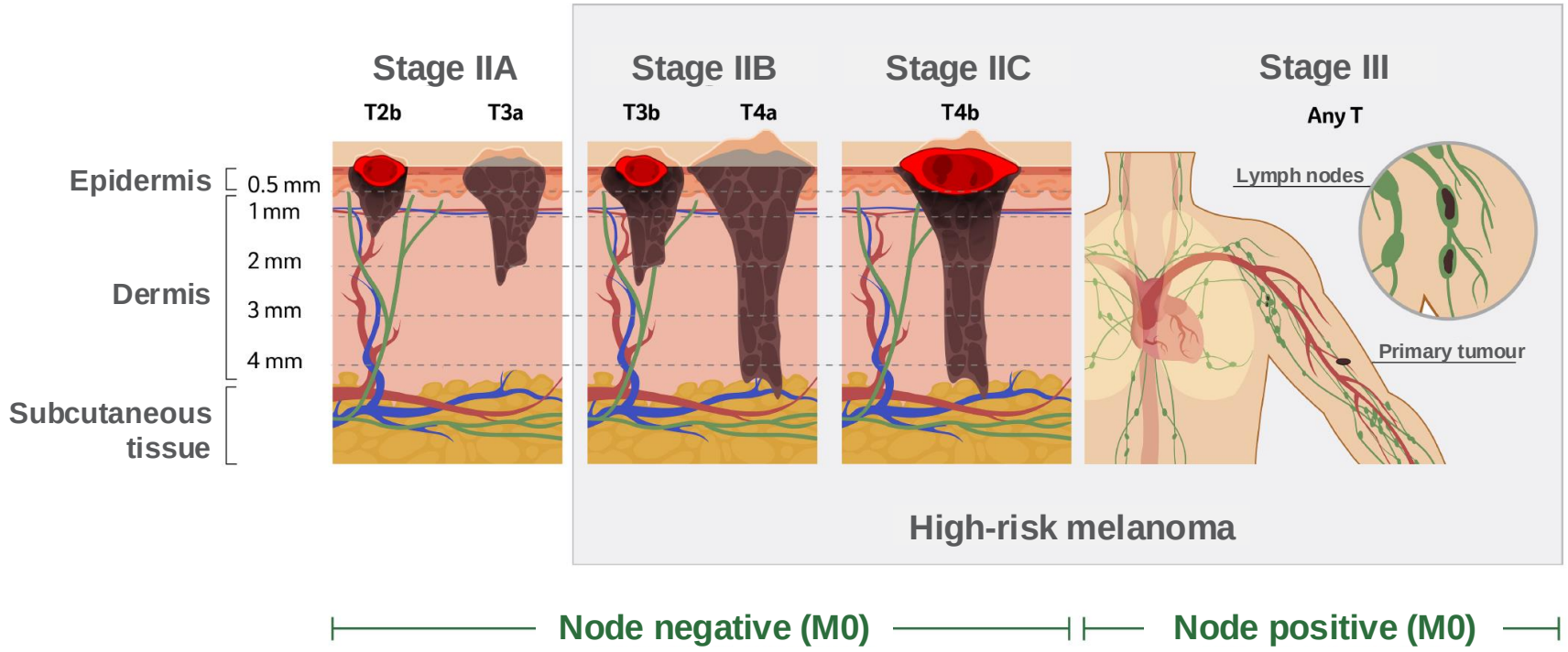
Patients with melanoma Stage IIB or higher are at risk of recurrence following resection*[1–3]

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; **M0,** no evidence of distant metastasis; **T,** tumour.
1. Mohr P, *et al. Melanoma Manag* 2019;6:MMT33. Supplementary appendix. **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.

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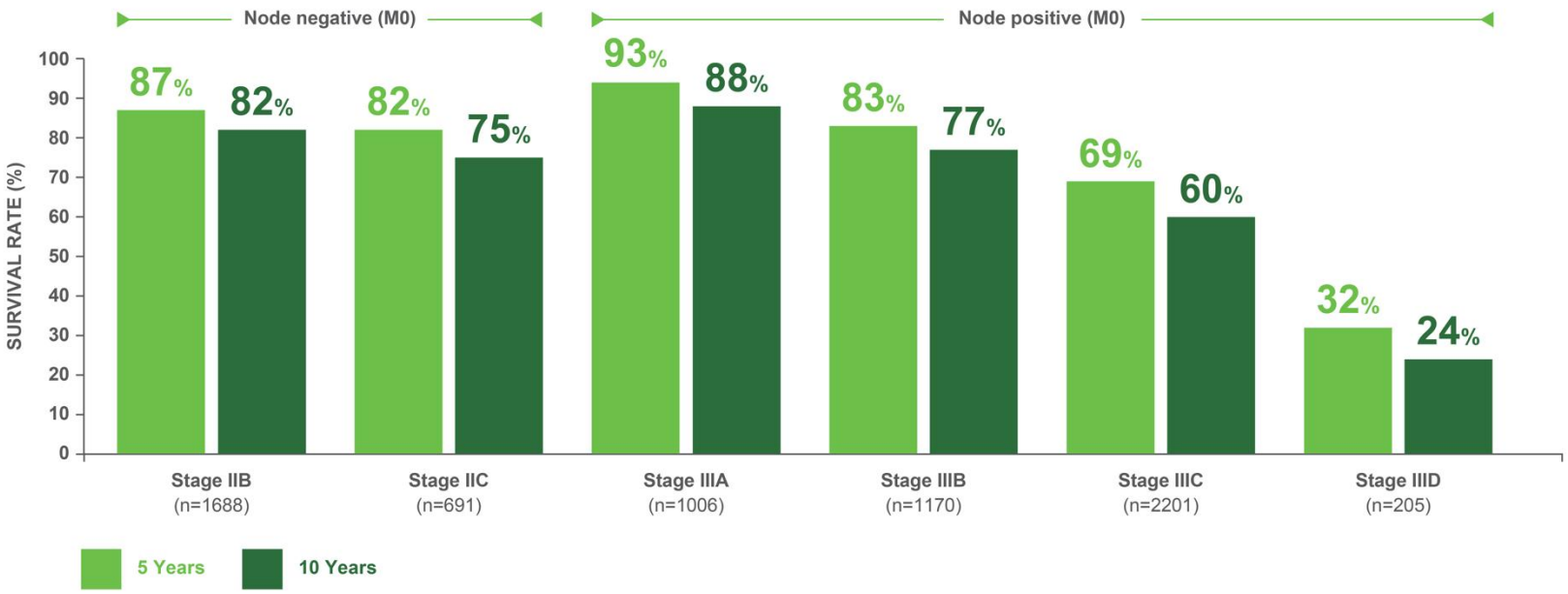
Melanoma-specific survival rates at 5- and 10-years according to AJCC 8th Edition pathologic staging criteria for melanoma[1]



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

- These data 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

Based on this survival data, how would your opinion on treating patients with Stage II melanoma change?

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.

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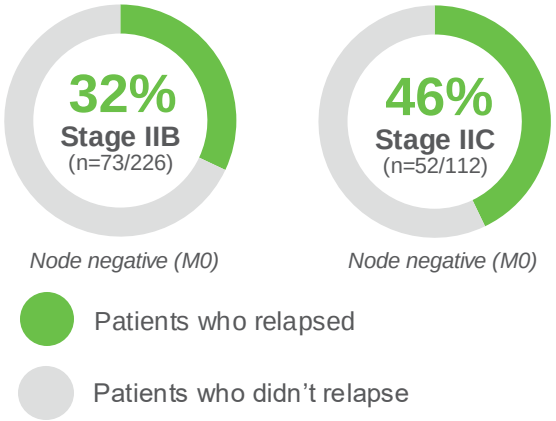
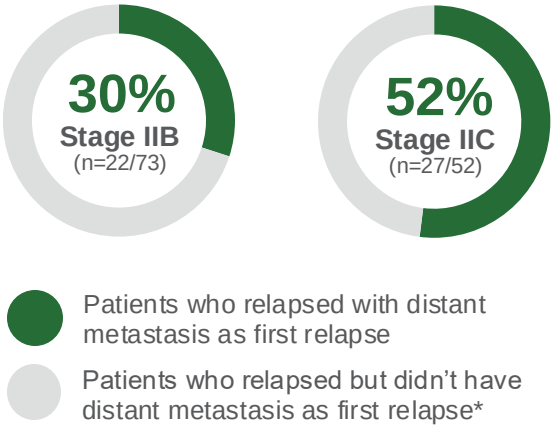
Relapse rates in patients with Stage IIB melanoma are 32%, increasing to 46% in Stage IIC melanoma[1]

Stage IIB and Stage IIC relapse rates[1]



Stage IIB and Stage IIC patients who relapsed with distant metastasis*[1]



Data based on a retrospective review of 738 adult patients from a prospectively maintained, single-institution database, with resected pathologic Stage II primary cutaneous melanoma (AJCC 7th ed.)[1]

- All patients were treated at Memorial Sloan Kettering Cancer Center, USA, between January 1993 and December 2013
- Patients underwent pathological nodal staging by sentinel lymph node biopsy or elective lymph node dissection
- Synchronous initial relapses were scored by the most advanced site. Secondary primary melanomas were not recorded as relapses
- Median follow-up of all patients was 4.3 years (50.2 and 46.2 months for Stage IIB and Stage IIC melanoma, respectively)

View relapse rates in Stage III

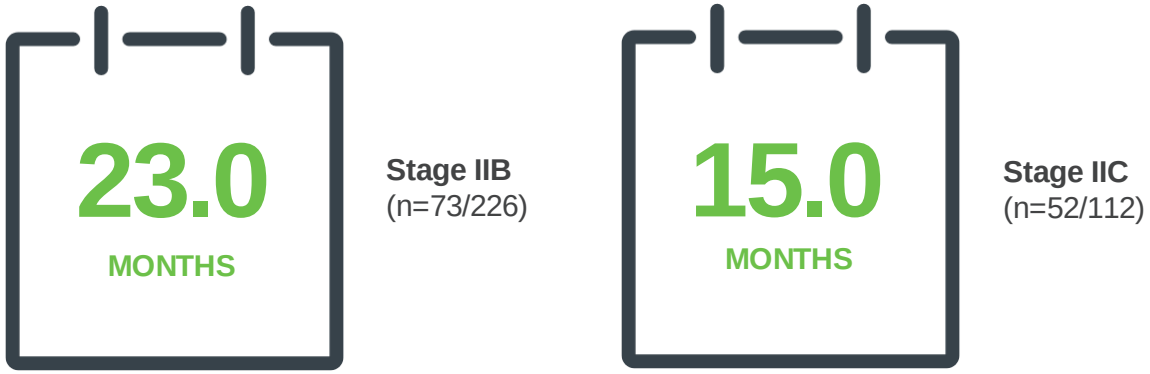
Were you aware of the rate of distant relapses across Stages IIB and IIC melanoma?

*The remainder of patients experienced a local/in-transit or regional nodal relapse.
AJCC, American Joint Committee on Cancer; **IMDPP**, International Melanoma Database and Discovery Platform.
1. Lee AY, *et al. Ann Surg Oncol* 2017;24:939–946.

KEYTRUDA® (pembrolizumab)

The median time to relapse from resection is under 2 years for Stage IIB and under 1.5 years for Stage IIC[1]

Median time to relapse in Stage IIB and Stage IIC[1]



View time to relapse in Stage III

Data based on a retrospective review of 738 adult patients from a prospectively maintained, single-institution database, with resected pathologic Stage II primary cutaneous melanoma (AJCC 7th ed.)[1]

- All patients were treated at Memorial Sloan Kettering Cancer Center, USA, between January 1993 and December 2013
- Patients underwent pathological nodal staging by sentinel lymph node biopsy or elective lymph node dissection.
- Synchronous initial relapses were scored by the most advanced site. Secondary primary melanomas were not recorded as relapses
- Median follow-up of all patients was 4.3 years (50.2 and 46.2 months for Stage IIB and Stage IIC melanoma, respectively)

Is there more that can be done for patients – beyond observation – to reduce their risk of relapse?

AJCC, American Joint Committee on Cancer.

1. Lee AY, *et al. Ann Surg Oncol* 2017;24:939–946.

KEYTRUDA® (pembrolizumab)

Summary

Patients with Stage IIB and IIC melanoma* have 10-year estimated survival rates of 82% and 75%, respectively.[1]

Patients with Stage IIB melanoma† or higher are at risk of relapse following resection:[2–4]

- Relapse rates in patients with Stage IIB and IIC melanoma are 32% and 46%, respectively[2]
- 30% and 52% of patients with Stage IIB and IIC melanoma relapse with distant metastasis, respectively[2]

Patients with Stage IIB and IIC melanoma† are still at risk of relapse, with half of all Stage IIB and IIC relapses occurring within 2 years[2]

Patients with Stage IIB/C melanoma could be considered at risk of disease recurrence

*According to AJCC 8th edition Pathological Staging Criteria for Melanoma.[1] †According to AJCC 7th edition Pathologic Staging Criteria for Melanoma.[2]
AJCC, American Joint Committee on Cancer.

1. Gershenwald JE, *et al. CA Cancer J Clin* 2017;67:472–492. **2.** Lee AY, *et al. Ann Surg Oncol* 2017;24:939–946. **3.** Yushak M, *et al. Am Soc Clin Oncol Educ Book* 2019;39:e207–e211.
4. Mohr P, *et al. Melanoma Manag* 2019;6:MMT33. Supplementary appendix.

KEYTRUDA® (pembrolizumab)

KEYTRUDA: bringing immunotherapy to Stage IIB–IV melanoma

This deck covers KEYNOTE-716 and patients with Stage II melanoma. To find out more about KEYTRUDA in Stage III 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

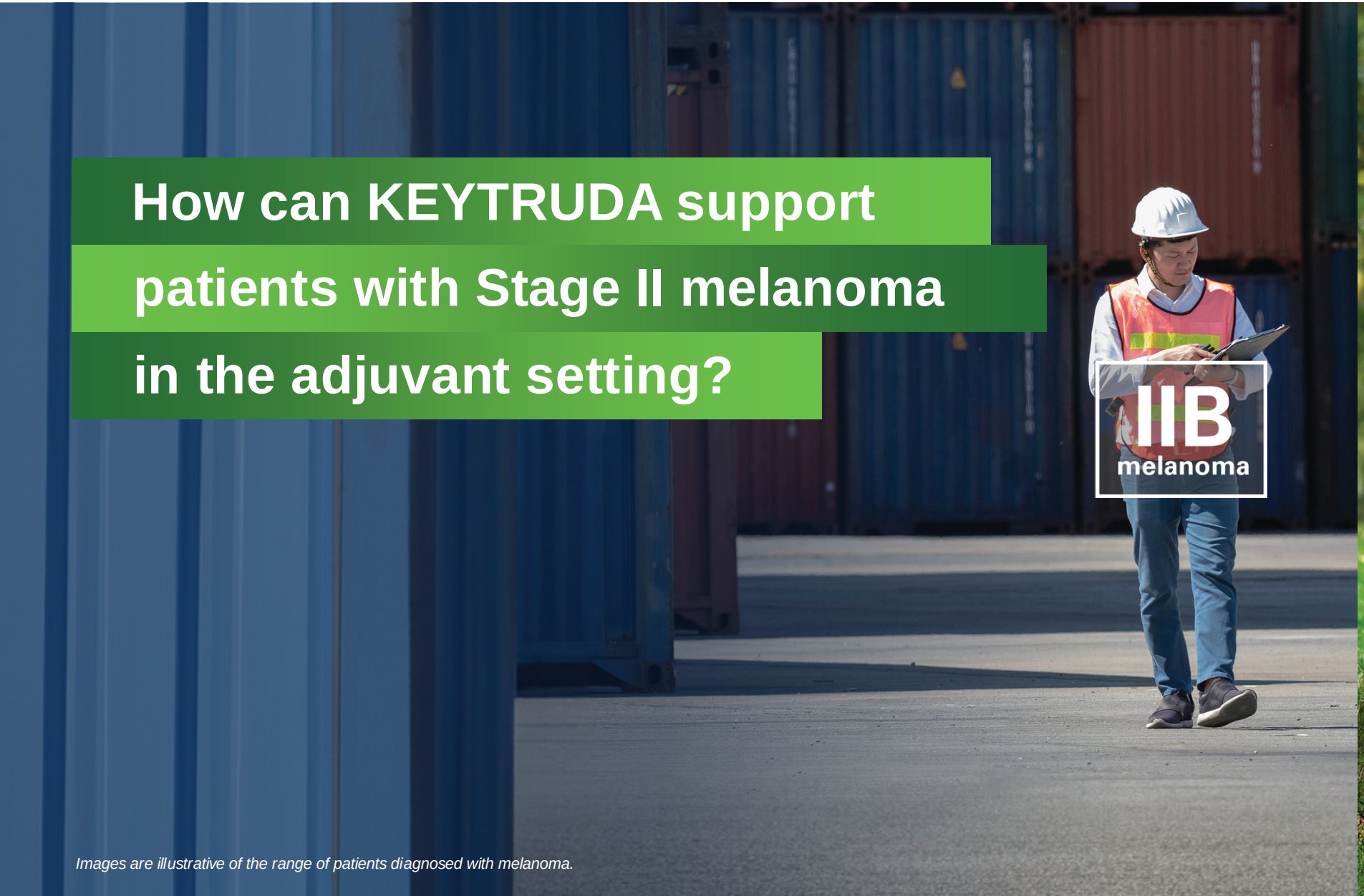
Images are illustrative of the range of patients diagnosed with melanoma.

KEYTRUDA as monotherapy is indicated for the treatment of adults and adolescents aged 12 years and older with advanced (unresectable or metastatic) melanoma.[1]
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.[1]

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 II melanoma in the adjuvant setting?



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

KEYTRUDA® (pembrolizumab)

Meet Mark and Tom*

Name: Mark
Age: 42

Medical history:

- Non-smoker with a fit and active lifestyle
- Saw his doctor after an increase in the size of an existing mole with an irregular border
- A biopsy diagnosed melanoma and the mole was excised
- Review confirmed the diagnosis of Stage IIB melanoma:
  - Ulcerated primary tumour (2–4 mm with ulceration)
  - No nodal involvement

Name: Tom
Age: 68

Medical history:

- Retired chemistry teacher with no history of cancer but has a family history of melanoma
- Saw his doctor about a dark spot on his back which would bleed when rubbed with a towel
- A biopsy diagnosed melanoma and the tumour was excised
- Review confirmed the diagnosis of Stage IIC melanoma:
  - Deep ulcerated primary tumour (>4 mm)
  - No nodal involvement
  - High mitotic rate
  - T4b Breslow tumour thickness

Would you consider Mark and Tom to be at risk of disease relapse?

*Hypothetical patient cases.

KEYTRUDA® (pembrolizumab)

KEYNOTE-716: a multicentre, randomised, double-blind, placebo-controlled Phase III trial in patients with completely resected Stage IIB or IIC melanoma

Key milestones during KEYNOTE-716

View the study design

December 2020
IA1
Initial analysis of RFS[1]

June 2022
EMA approval for adjuvant KEYTRUDA in Stage IIB–IIC melanoma*[2]

October 2022
IA3
Initial analysis of DMFS[3]

June 2023
IA4
Final analysis of DMFS[4]

October 2024
Median follow-up: 52.8 months
Pre-IA5
Latest analysis[5]

View the summary

View the efficacy data

**EMA approval in NI received in June 2022 and MHRA approval received in the rest of the UK in July 2022[2]*

View the efficacy data

View the efficacy data

View the safety data

View the efficacy data

IA1/2/3/4/5; first/second/third/fourth/fifth interim analysis; **DMFS,** distant metastasis-free survival; **EMA,** European Medicines Agency; **RFS,** recurrence-free survival.

1. Luke JJ, *et al. Lancet* 2022;399:1718–1729. **2.** KEYTRUDA. Procedural steps taken and scientific information after the authorisation. Available at: https://www.ema.europa.eu/en/documents/procedural-steps-after/keytruda-epar-procedural-steps-taken-scientific-information-after-authorisation_en.pdf Accessed: March 2025. **3.** Long GV, *et al. Lancet Oncol* 2022;23:1378–1388. **4.** Luke JJ, *et al. J Clin Oncol* 2024;42:1619–1624. **5.** Luke JJ, *et al.* Pembrolizumab vs Placebo as Adjuvant Therapy for High-Risk Stage II Melanoma: Long-Term Follow-Up, Rechallenge, and Crossover in KEYNOTE-716. ESMO. 13–17 September 2024. Barcelona, Spain. Oral presentation.

KEYTRUDA® (pembrolizumab)

KEYNOTE-716:

Study design

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

KEYTRUDA®
(pembrolizumab)

KEYNOTE-716 study design: randomised, double-blind, Phase III[1,2]

Newly diagnosed, completely resected, histologically confirmed Stage IIB or Stage IIC cutaneous melanoma without regional lymph node involvement

- Aged ≥12 years
- No prior systemic therapy for melanoma
- No autoimmune disease or uncontrolled infections
- No use of systemic glucocorticoids
- ECOG PS 0–1
- *EGFR/ALK*m permitted
- No prior therapy for melanoma other than surgery, including adjuvant radiation to the primary resection site

R 1:1
(N=976)

PART 1: ADJUVANT THERAPY

KEYTRUDA (n=487)
IV Q3W for up to 1 year or until disease recurrence or unacceptable toxicity.

Adult dose: 200 mg
Paediatric (≥12 years): 2 mg/kg (up to 200 mg)

Placebo (n=489)
IV Q3W for up to 1 year

PART 2: POST-RECURRENCE

Recurrence >6 months from Part 1
(after completion of 1 year of KEYTRUDA)

Recurrence
Crossover

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

UNBLINDED

Stratification factors:
- AJCC 8th edition T stage

Primary endpoint:
- Investigator assessed RFS in the ITT population

Secondary endpoints:
- DMFS and OS
- Safety and tolerability

Please note that the post-recurrence part of KEYNOTE-716 is not covered in this presentation as this is outside the licensed indication for KEYTRUDA.

View baseline patient characteristics

Adapted from Luke JJ, *et al. Lancet* 2022.[1]

Refer to the Supplementary Appendix for a full list of inclusion and exclusion criteria.[2]
Patients underwent imaging at 6 months from the date of randomisation, then every 6 months from Years 2–4 after randomisation and then once in Year 5 from or until recurrence, whichever came first or as clinically indicated.[1] **AJCC,** American Joint Committee on Cancer; ***ALK*,** anaplastic lymphoma kinase gene; **DMFS,** distant metastasis-free survival; **ECOG PS,** Eastern Cooperative Oncology Group performance status; ***EGFR*,** epidermal growth factor receptor gene; **IV,** intravenous; **m,** mutation; **OS,** overall survival; **Q3W,** every three weeks; **RFS,** recurrence-free survival; **T,** tumour.

1. Luke JJ, *et al. Lancet* 2022;399:1718–1729. **2.** Luke JJ, *et al. Lancet* 2022;399:1718–1729. Supplementary appendix.

KEYTRUDA® (pembrolizumab)

KEYNOTE-716: key trial endpoints[1]

The efficacy analysis was done in the intent-to-treat (ITT) population, which included all patients randomly assigned to treatment. Safety was assessed in all patients randomly assigned to treatment who received at least one dose of study treatment.

Primary efficacy endpoint:

Investigator-assessed recurrence-free survival (RFS) (defined as the time between the date of randomisation and the date of first recurrence [local, regional or distant metastases] or death, whichever occurred first) in the ITT population

- The primary endpoint was met if RFS was significantly improved for KEYTRUDA versus placebo
- The overall type 1 error was controlled at a one-sided alpha of 2.5%
- The study met the prespecified RFS endpoint on the basis of results of the first interim analysis with 136 RFS events observed

Secondary endpoints:

Distant metastasis-free survival (DMFS) and overall survival (OS) in the ITT population; safety and tolerability of KEYTRUDA*

- As of November 2024, overall survival data is immature and is expected in a future analysis once a minimum of ~154 events have been observed[2]

*Data on adverse events were collected throughout the study through self-report by patient or reported by caregivers and reviewed by investigators during screening and then every 3 weeks from randomisation, and up to 30 days (90 days for serious adverse events) after treatment discontinuation and graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0.[1]

DMFS, distant metastasis-free survival; **ITT,** intent-to-treat; **OS,** overall survival; **RFS,** recurrence-free survival.

1. Luke JJ, *et al. Lancet* 2022;399:1718–1729. **2.** Luke JJ, *et al. Lancet* 2022;399:1718–1729. Supplementary appendix.

KEYTRUDA® (pembrolizumab)

KEYNOTE-716:

Efficacy data from initial analyses of RFS and DMFS (IA1 and IA3)

View the IA4 data ›

View the latest data ›

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

KEYTRUDA® (pembrolizumab)

RFS and DMFS following treatment with KEYTRUDA versus placebo at the first and third interim analyses[1–3]

PRIMARY ANALYSIS (IA1 at 14.4 MONTHS)

RFS

- Patients with events: 11% (54/487) vs 17% (82/489)
- HR: 0.65; 95% CI: 0.46–0.92; p=0.0066†
- 12-month RFS rate: 90% vs 83%

View the KM curve

35%

relative reduction in risk of recurrence or death with KEYTRUDA vs placebo in the ITT population*

SECONDARY ANALYSIS (IA3 at 27.4 MONTHS)

DMFS

- Patients with events: 13% (63/487) vs 19% (95/489)
- HR: 0.64; 95% CI: 0.47–0.88
- 24-month DMFS rate: 88% vs 82%

View the KM curve

36%

relative reduction in risk of distant metastasis with KEYTRUDA vs placebo in the ITT population‡

RFS benefit was sustained at 27.4 months median follow-up (IA3) for KEYTRUDA vs placebo (HR: 0.64; 95% CI: 0.50–0.84)

Statistical superiority of KEYTRUDA versus placebo for RFS was not tested at IA3

IA1 analysis cut-off date: 4 December 2020.[1] IA3 analysis cut-off date: 4 January 2022.[2]

*RFS was defined as time from randomisation to the date of first recurrence of melanoma at any site (local, in-transit or regional lymph nodes or distant recurrence) or death due to any cause, whichever occurred first. †Based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by melanoma T category (T3b versus T4a versus T4b).[1] ‡DMFS was defined as the time from randomisation to the first diagnosis of distant metastasis. **CI,** confidence interval; **DMFS,** distant metastasis-free survival; **HR,** hazard ratio; **IA1/3;** first/third interim analysis; **ITT,** intent-to-treat; **RFS,** recurrence-free survival; **T,** tumour. **1.** Luke JJ, *et al. Lancet* 2022;399:1718–1729. **2.** Long GV, *et al. Lancet Oncol* 2022;23:1378–1388. **3.** Long GV, *et al. Lancet Oncol* 2022;23:1378–1388. Supplementary appendix.

KEYTRUDA® (pembrolizumab)

KEYNOTE-716:

Efficacy data from interim analyses of RFS and DMFS (IA4)

View the initial analysis ›

View the latest data ›

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

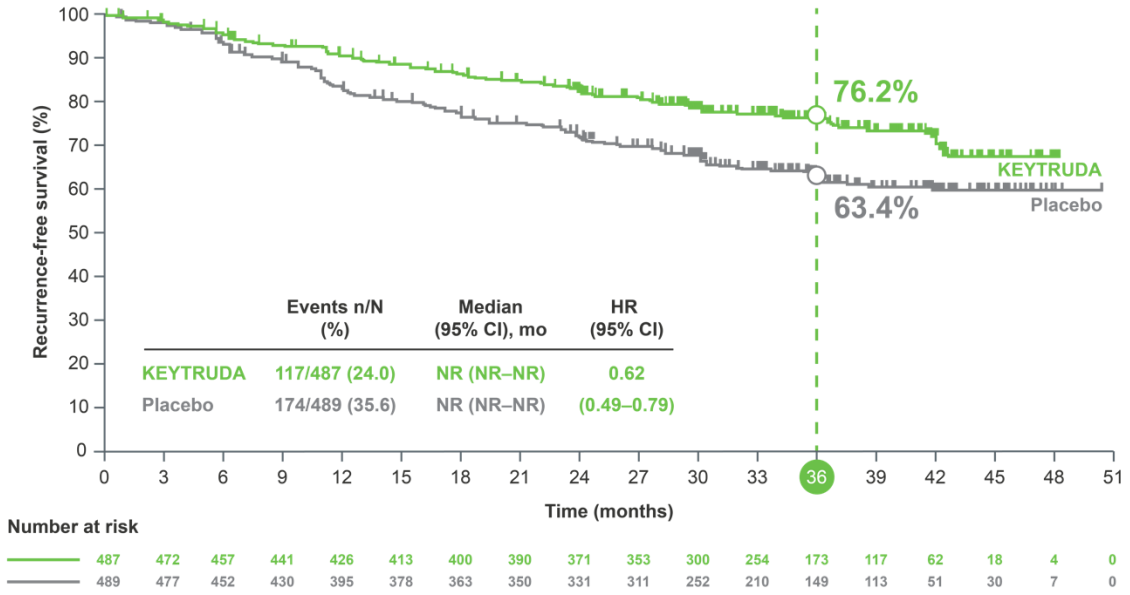
KEYTRUDA® (pembrolizumab)

RFS following treatment with KEYTRUDA versus placebo after 39.4 months median follow-up[1]

Exploratory long-term analysis: significance was not tested, therefore no statistical conclusions can be drawn from this analysis

IA4

Kaplan-Meier estimates of RFS in the ITT population*



Adapted from Luke JJ, *et al. J Clin Oncol* 2024.[1]

38%
relative risk reduction

- KEYTRUDA demonstrated a **38% relative risk reduction** in disease recurrence versus placebo
  - Patients with events: 24.0% (n=117/487) vs 35.6% (n=174/489)
  - HR: 0.62; 95% CI: 0.49–0.79
  - Statistical superiority of KEYTRUDA versus placebo for RFS was not tested at IA4

View RFS subgroup analysis
View RFS in Stage IIB
View RFS in Stage IIC

IA4 analysis cut-off date: 4 January 2023.[1]
The n number displayed represents the number of events in the treatment arm. RFS was defined as time from randomisation to the date of first recurrence of melanoma at any site (local, in-transit or regional lymph nodes or distant recurrence) or death due to any cause, whichever occurred first. *Based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by melanoma T category (T3b versus T4a versus T4b).[2] **CI,** confidence interval; **HR,** hazard ratio; **IA4,** fourth interim analysis; **ITT,** intent-to-treat; **RFS,** recurrence-free survival.

1. Luke JJ, *et al. J Clin Oncol* 2024;42:1619–1624. **2**. Luke JJ, *et al. Lancet* 2022;399:1718–1729.

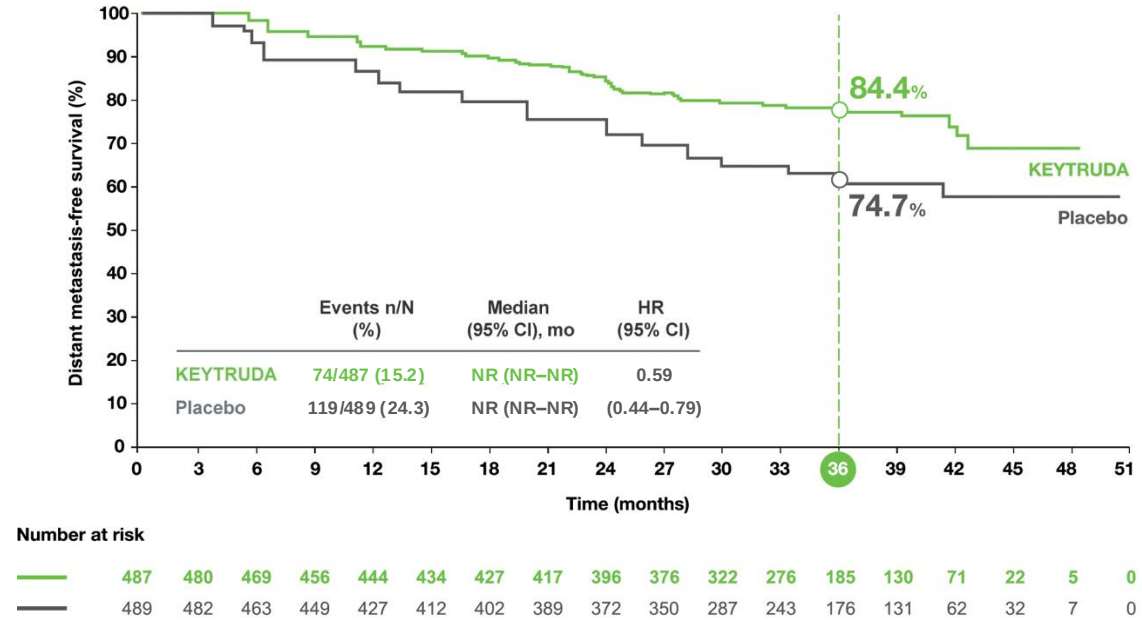
KEYTRUDA® (pembrolizumab)

DMFS following treatment with KEYTRUDA versus placebo after 39.4 months median follow-up[1]

Exploratory long-term analysis: significance was not tested, therefore no statistical conclusions can be drawn from this analysis

IA4

Kaplan-Meier estimates of DMFS in the ITT population*



Adapted from Luke JJ, *et al. J Clin Oncol* 2024.[1]

41%
relative risk reduction

- KEYTRUDA demonstrated a **41% relative risk reduction** in distant metastasis versus placebo
  - Patients with events: 15.2% (n=74/487) vs 24.3% (n=119/489)
  - HR: 0.59; 95% CI: 0.44–0.79
  - Statistical superiority of KEYTRUDA versus placebo for DMFS was not tested at IA4

View DMFS subgroup analysis

IA4 analysis cut-off date: 4 January 2023.[1]
The n number displayed represents the number of events in the treatment arm. *Based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by melanoma T category (T3b versus T4a versus T4b).[2] **CI,** confidence interval; **DMFS,** distant metastasis-free survival; **HR,** hazard ratio; **IA4,** fourth interim analysis; **ITT,** intent-to-treat; **T,** tumour.

1. Luke JJ, *et al. J Clin Oncol* 2024;42:1619–1624. **2**. Luke JJ, *et al. Lancet* 2022;399:1718–1729.

KEYTRUDA® (pembrolizumab)

KEYNOTE-716:

Safety data from interim analyses (IA1, IA4)

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

The safety profile of KEYTRUDA among the patients with resected melanoma enrolled in KEYNOTE-716 was consistent with previous analyses.

- View the summary at IA1 and IA3 ›
- View the summary at IA4 ›
- View treatment-related adverse events at IA4 ›
- View immune-related adverse events at IA4 ›

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

KEYTRUDA® (pembrolizumab)

Summary of adverse events during the initial analyses of KEYNOTE-716[1,2]

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

Adverse events reported by 14.4-month median follow-up[1]

Adverse event, n (%)	KEYTRUDA (n=483)	Placebo (n=486)
Any	449 (93)	433 (89)
Grade 3–4	125 (26)	83 (17)
Led to discontinuation	75 (16)	20 (4)
Led to death	0 (0)	4 (1)*
Treatment-related	386 (80)	296 (61)
Grade 3–4	78 (16)	21 (4)
Led to death	0 (0)	0 (0)

Adverse events reported by 27.4-month median follow-up[2]

Adverse event, n (%)	KEYTRUDA (n=483)	Placebo (n=486)
Any	462 (96)	445 (92)
Led to discontinuation	85 (17)	23 (5)
Led to death	1 (<1)†	5 (1)†
Treatment-related	400 (83)	309 (64)
Grade 3–4	83 (17)	24 (5)
Led to discontinuation	77 (16)	12 (3)
Led to death	0 (0)	0 (0)

Proportion of patients experiencing adverse events at the third interim analysis was similar to the initial analysis[2]

For further details on adverse events and risk management, please refer to the SmPC and Risk Management Materials.

IA1 data cut-off: 4 December 2020.[1] IA3 data cut-off: 4 January 2022.[2]
***Four deaths occurred: one due to COVID-19-related pneumonia, one due to pneumonia, one due to recurrent cancer and one due to suicide.[1] †One death occurred in the KEYTRUDA group due to COVID-19-related pneumonia, five deaths occurred in the placebo group: one due to COVID-19-related pneumonia, one due to pneumonia, one due to malignant neoplasm, one due to recurrent cancer and one due to suicide.[2] **COVID-19,** coronavirus disease 2019; **IA,** interim analysis; **SmPC,** Summary of Product Characteristics.

1. Luke JJ, *et al. Lancet* 2022;399:1718–1729. **2.** Long GV, *et al. Lancet Oncol* 2022;23:1378–1388.

KEYTRUDA® (pembrolizumab)

Summary of adverse events during KEYNOTE-716 after 3 years[1,2]

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

Adverse events reported by 39.4-month median follow-up

Adverse event, n (%)	KEYTRUDA (n=483)	Placebo (n=486)
Any	461 (95.4)	446 (91.8)
Treatment-related	399 (82.6)	309 (63.6)
Grade 3–4	83 (17.2)	25 (5.1)
Led to discontinuation	77 (15.9)	12 (2.5)
Immune-mediated and infusion reactions	183 (37.9)	46 (9.5)
Grade 3–4	53 (11.0)	6 (1.2)

- The safety profile of KEYTRUDA among the patients with resected melanoma enrolled in KEYNOTE-716 was consistent with previous analyses
- No patients died due to treatment-related adverse events in either treatment arm

For further details on adverse events and risk management, please refer to the SmPC and Risk Management Materials.

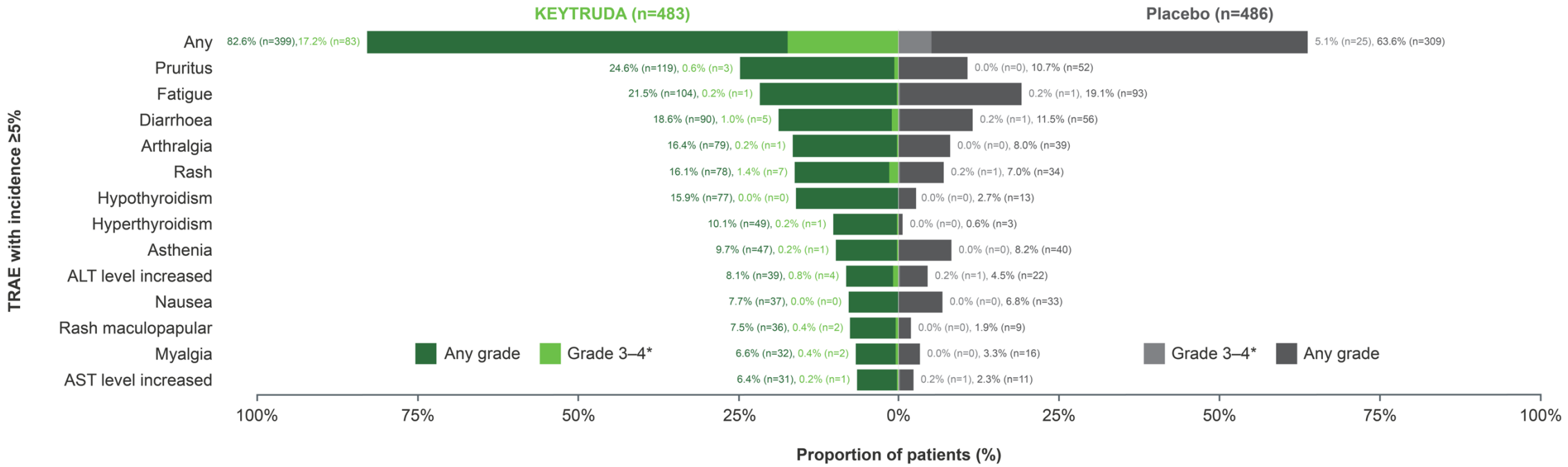
IA4 analysis cut-off date: 4 January 2023.[1]
IA4, fourth interim analysis.
1. Luke JJ, *et al. J Clin Oncol* 2024;42:1619–1624. **2.** Luke JJ, *et al.* Pembrolizumab versus placebo as adjuvant therapy in stage IIB or IIC melanoma: Final analysis of distant metastasisfree survival in the Phase 3 KEYNOTE-716 study. ASCO. 2–6 June 2023. Chicago, IL, USA. Oral presentation.

KEYTRUDA® (pembrolizumab)

Summary of treatment-related adverse events (TRAEs) after 3 years[1]

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

TRAEs reported by 39.4-month median follow-up



For further details on adverse events and risk management, please refer to the SmPC and Risk Management Materials.

Adapted from Luke JJ, *et al. J Clin Oncol* 2024.[1]

IA4 analysis cut-off date: 4 January 2023.[1] *There were no grade 5 TRAEs.
ALT, alanine transaminase; **AST,** aspartate aminotransferase; **IA4,** fourth interim analysis; **TRAE,** treatment-related adverse event.

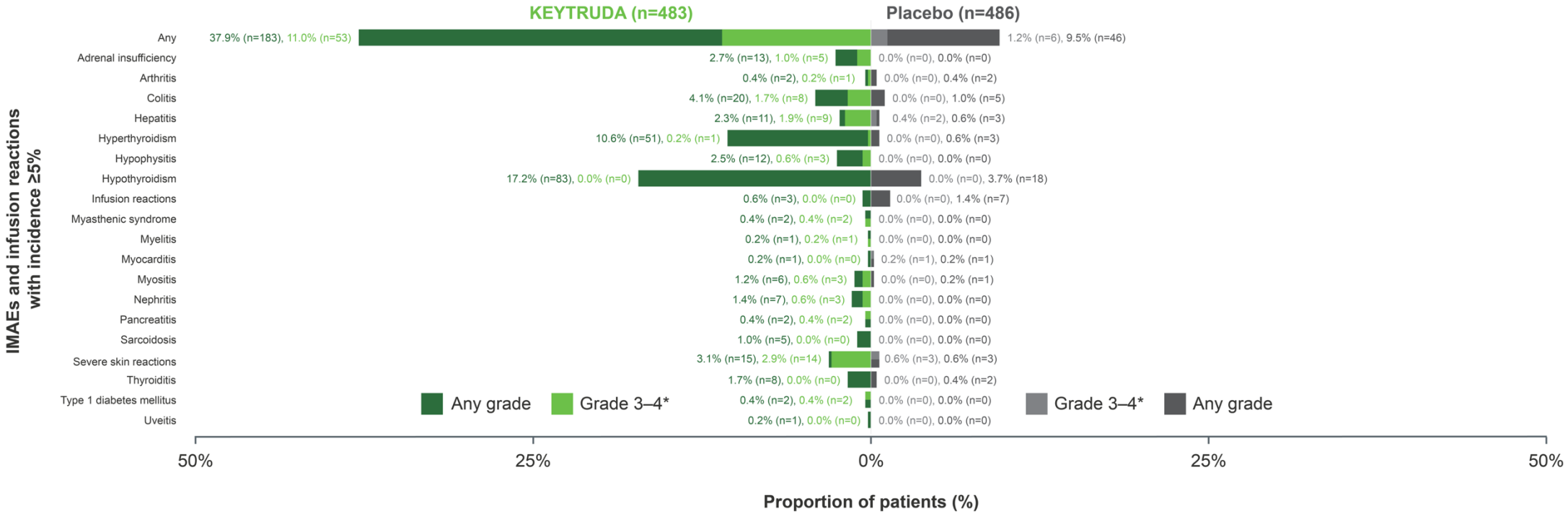
1. Luke JJ, *et al. J Clin Oncol.* 2024;42:1619–1624.

KEYTRUDA® (pembrolizumab)

Summary of immune-mediated adverse events (IMAEs) and infusion reactions after 3 years[1]

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

IMAEs and infusion reactions reported by 39.4-month median follow-up



For further details on adverse events and risk management, please refer to the SmPC and Risk Management Materials.

Adapted from Luke JJ, et al. J Clin Oncol 2024.[1]

IA4 analysis cut-off date: 4 January 2023.[1] *There were no grade 5 IMAEs.
IA4, fourth interim analysis; **IMAE,** immune-mediated adverse event.

1. Luke JJ, *et al. J Clin Oncol.* 2024;42:1619–1624.

KEYTRUDA® (pembrolizumab)

KEYNOTE-716:

Efficacy data from latest analysis of RFS and DMFS

View the initial analysis ›

View the IA4 data ›

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

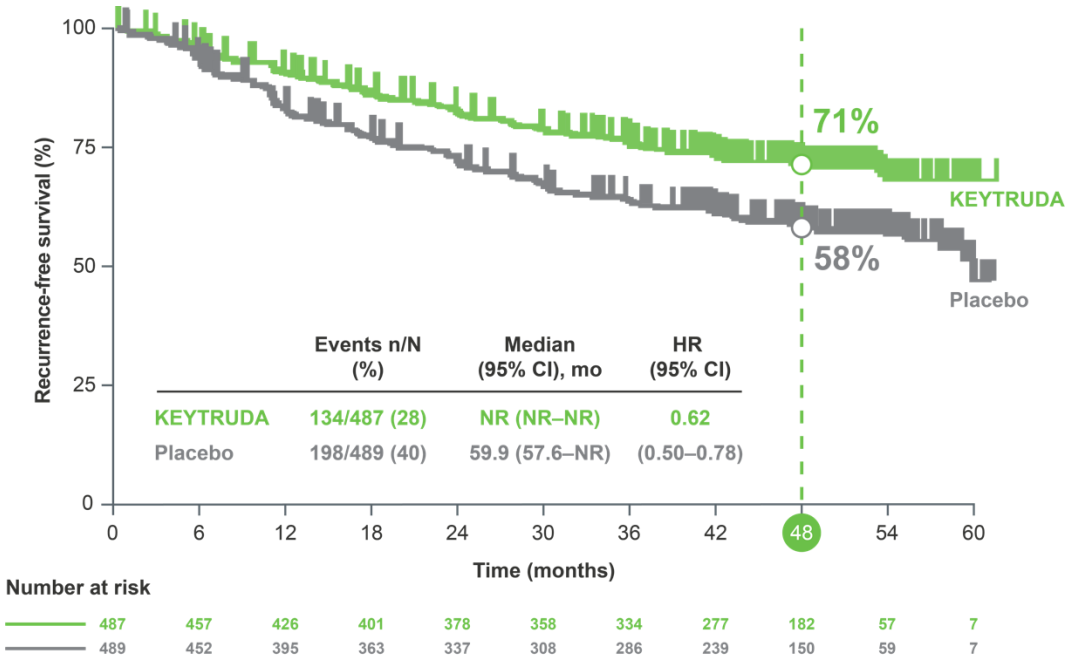
KEYTRUDA® (pembrolizumab)

RFS following treatment with KEYTRUDA versus placebo after 52.8 months median follow-up[1]

Exploratory long-term analysis: significance was not tested, therefore no statistical conclusions can be drawn from this analysis

Pre-IA5

Kaplan-Meier estimates of RFS in the ITT population



Adapted from Luke JJ, *et al. ESMO* 2024.[1]

38%
relative risk reduction

- KEYTRUDA demonstrated a **38% relative risk reduction** in disease recurrence versus placebo
  - Patients with events: 28% (n=134/487) vs 40% (n=198/489)
  - HR: 0.62; 95% CI: 0.50–0.78
  - Statistical superiority of KEYTRUDA versus placebo for RFS was not tested at this timepoint

Analysis cut-off date: 16 February 2024.[1]
CI, confidence interval; **HR,** hazard ratio; **IA5,** fifth interim analysis; **ITT,** intent-to-treat; **mo,** months; **n,** number; **NR,** not reached; **RFS,** recurrence-free survival.
1. Luke JJ, *et al.* Pembrolizumab vs Placebo as Adjuvant Therapy for High-Risk Stage II Melanoma: Long-Term Follow-Up, Rechallenge, and Crossover in KEYNOTE-716. ESMO. 13–17 September 2024. Barcelona, Spain. Oral presentation.

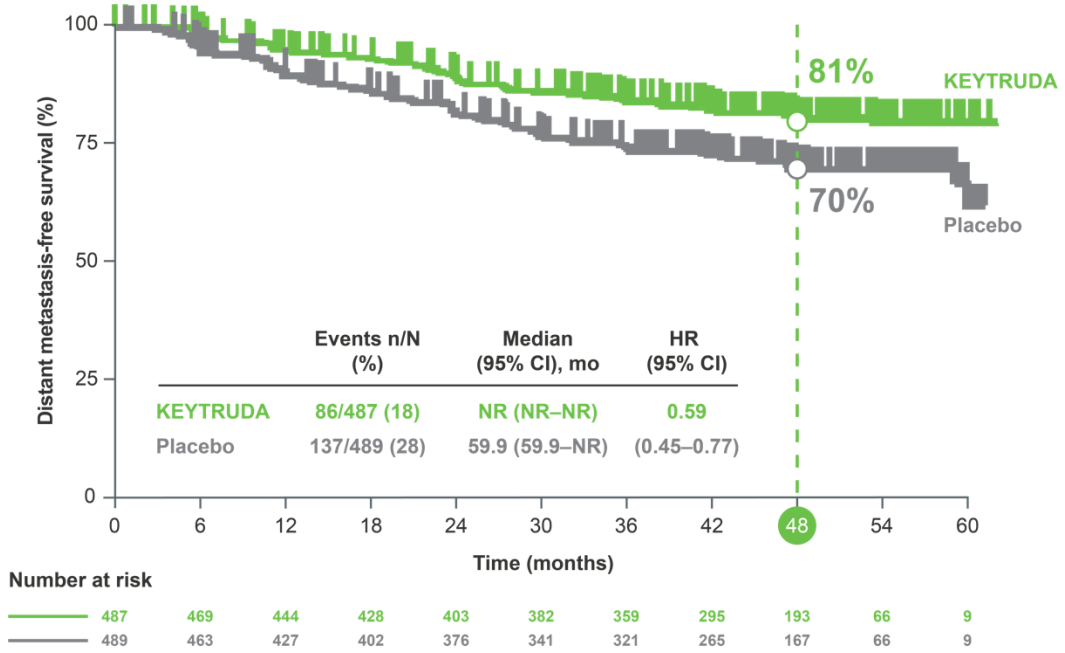
KEYTRUDA® (pembrolizumab)

DMFS following treatment with KEYTRUDA versus placebo after 52.8 months median follow-up[1]

Exploratory long-term analysis: significance was not tested, therefore no statistical conclusions can be drawn from this analysis

Pre-IA5

Kaplan-Meier estimates of DMFS in the ITT population



41%
relative risk reduction

- KEYTRUDA demonstrated a **41% relative risk reduction** in distant metastasis versus placebo
  - Patients with events: 18% (n=86/487) vs 28% (n=137/489)
  - HR: 0.59; 95% CI: 0.45–0.77
  - Statistical superiority of KEYTRUDA versus placebo for DMFS was not tested at this timepoint

Adapted from Luke JJ, *et al. ESMO* 2024.[1]

Analysis cut-off date: 16 February 2024.[1]
CI, confidence interval; **DMFS,** distant metastasis-free survival; **HR,** hazard ratio; **IA5,** fifth interim analysis; **ITT,** intent-to-treat; **mo,** months; **n,** number; **NR,** not reached.

1. Luke JJ, *et al.* Pembrolizumab vs Placebo as Adjuvant Therapy for High-Risk Stage II Melanoma: Long-Term Follow-Up, Rechallenge, and Crossover in KEYNOTE-716. ESMO. 13–17 September 2024. Barcelona, Spain. Oral presentation.

KEYTRUDA® (pembrolizumab)

KEYNOTE-716:

Summary

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

KEYTRUDA®
(pembrolizumab)

Your patients with Stage IIB/C could benefit from adjuvant therapy with KEYTRUDA[1]

During KEYNOTE-716, in patients with Stage IIB and IIC melanoma, KEYTRUDA demonstrated vs placebo:

35% relative reduction in risk of recurrence[2]

- 14.4-month median follow-up (IA1, primary analysis)
- HR: 0.65; 95% CI: 0.46–0.92; p=0.0066*

Sustained improvement in both RFS and DMFS after over 4 years of follow-up[3]

- After four years (52.8-month median follow-up), KEYTRUDA demonstrated:
  - 38% RRR in disease recurrence vs placebo (HR: 0.62; 95% CI: 0.50–0.78)†
  - 41% RRR in distant metastasis vs placebo (HR: 0.59; 95% CI: 0.45–0.77)†

A manageable safety profile, consistent with previous reports[2–4]

- After three years (IA4):
  - Any TRAEs occurred in 82.6% (n=399/483) vs 63.6% (n=309/486) of patients
  - Any IMAEs occurred in 37.9% (n=183/483) vs 9.5% (n=46/486) of patients
  - No patients died due to TRAEs in either treatment arm

No clinically meaningful decrease in HRQOL[5] (as per EORTC QLQ-C30 score)

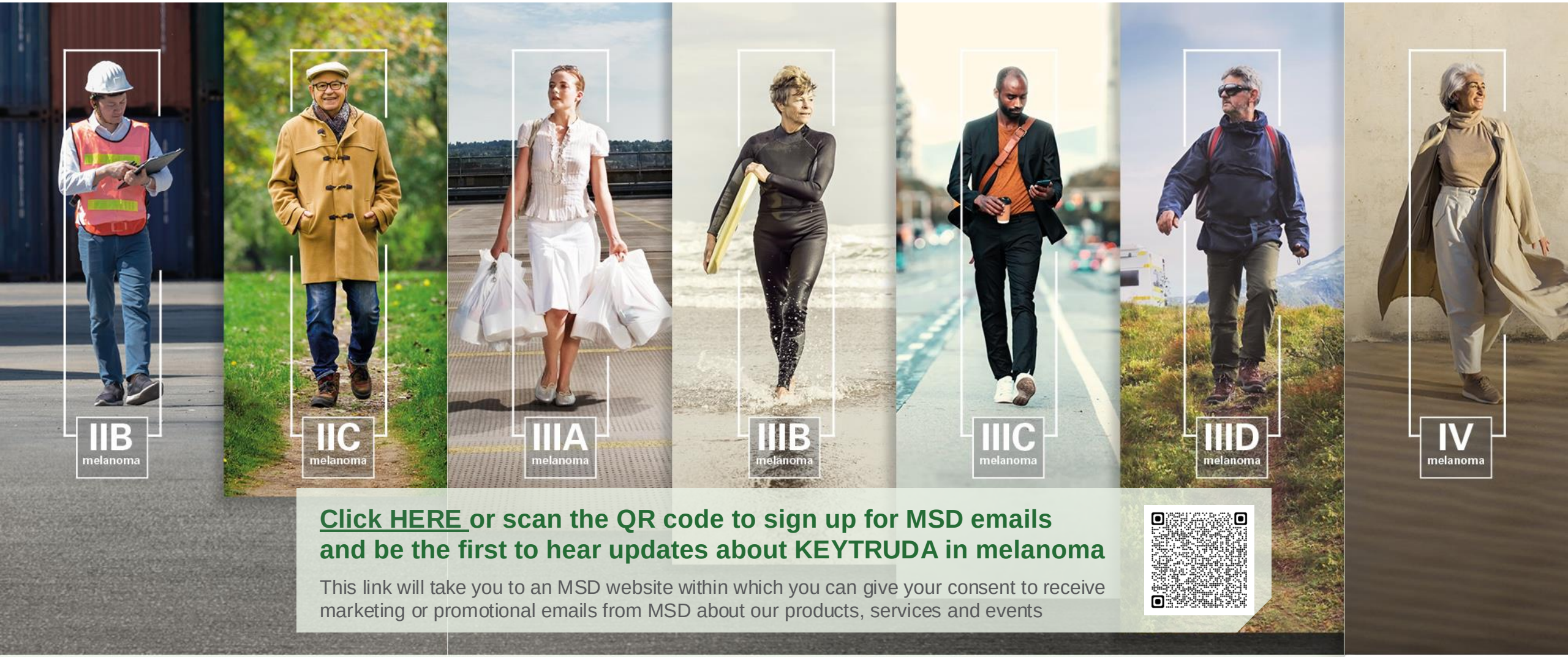
- 20.5-month median follow-up (exploratory analysis)
- ≥10-point change in score was considered clinically meaningful
- LSM change from baseline to Week 48 was -3.27 (95% CI: -4.61 to -1.92)

For further details on adverse events and risk management, please refer to the SmPC and Risk Management Materials.

*Based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by melanoma T category (T3b versus T4a versus T4b).[1] †Statistical superiority of KEYTRUDA versus placebo was not tested at this timepoint. **CI,** confidence interval; **DMFS,** distant metastasis-free survival; **EORTC QLQ-C30,** European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire; **HR,** hazard ratio; **HRQOL,** health-related quality of life; **LSM,** least squares mean; **RFS,** recurrence-free survival; **RRR,** relative risk reduction; **T,** tumour.

1. KEYTRUDA Summary of Product Characteristics. United Kingdom. Available at: https://www.medicines.org.uk/emc/product/2498 Accessed: March 2025. **2.** Luke JJ, *et al. Lancet* 2022;399:1718–1729. **3.** Luke JJ, *et al.* Pembrolizumab vs Placebo as Adjuvant Therapy for High-Risk Stage II Melanoma: Long-Term Follow-Up, Rechallenge, and Crossover in KEYNOTE-716. ESMO. 13–17 September 2024. Barcelona, Spain. Oral presentation. **4.** Luke JJ, *et al. J Clin Oncol.* 2024;42:1619–1624. **5.** Khattak MA, *et al. J Clin Oncol.* 2022;40:9581.

KEYTRUDA® (pembrolizumab)



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)

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

KEYNOTE-716:

Appendix

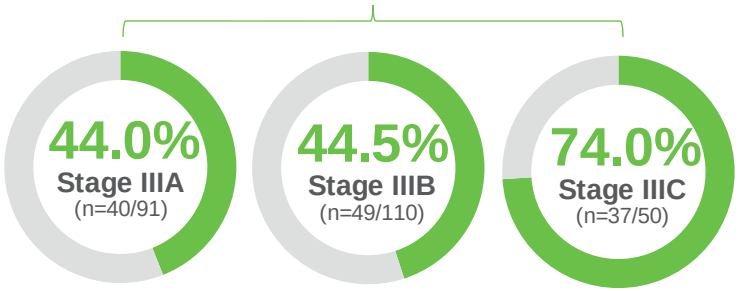
Images are illustrative of the range of patients diagnosed with melanoma.

KEYTRUDA®
(pembrolizumab)

Relapse rates in patients with Stage III melanoma are 44.0%, 44.5% and 74.0% for Stages IIIA, IIIB and IIIC, respectively[1]

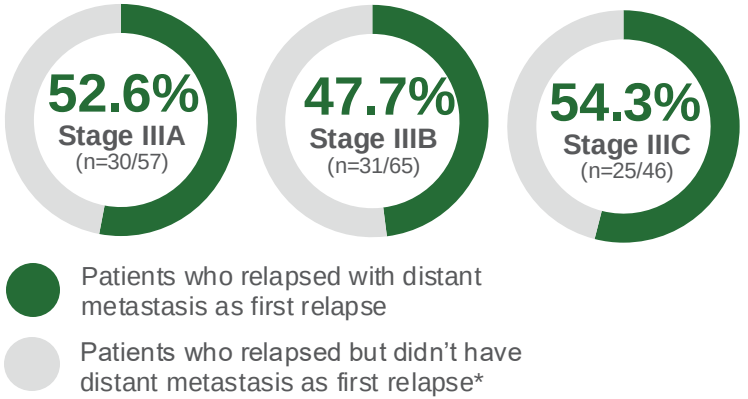
Stage III relapse rates in patients who received watch-and-wait post-surgery[1]

Node positive (M0)



Stage III patients who relapsed with distant metastasis*[1]

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



Data based on 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[2]

- 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[2]
- Median follow-up was 3.1 years[2]

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

Return to Stage IIB/IIC

*The remainder of patients experienced a loco-regional recurrence or a secondary primary melanoma recurrence.
AJCC, American Joint Committee on Cancer; **RFS,** recurrence-free survival.
1. Mohr P, *et al. Melanoma Manag* 2019;6:MMT33. Supplementary appendix. **2.** Mohr P, *et al*. *Melanoma Manag* 2019;6:MMT33.

KEYTRUDA® (pembrolizumab)

The median time to relapse from resection is 5.2 months at Stage IIIC and less than 1.5 years at Stage IIIA[1]

Median time to relapse among patients who relapsed[1]

Stage IIIA
(n=40/91)

Stage IIIB
(n=49/110)

Stage IIIC
(n=37/50)

Data based on 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[2]

- 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[2]
- Median follow-up was 3.1 years[2]

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

Return to Stage IIB/IIC

AJCC, American Joint Committee on Cancer; **RFS,** recurrence-free survival.

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

KEYTRUDA® (pembrolizumab)

Baseline patient characteristics were similar between the KEYTRUDA and placebo arms[1]

	KEYTRUDA (n=487)	Placebo (n=489)
Age, years (IQR)	60 (51–68)	61 (53–69)
<65 years, n (%)	303 (62)	295 (60)
≥65 years, n (%)	184 (38)	194 (40)
Sex, n (%)		
Female	187 (38)	200 (41)
Male	300 (62)	289 (59)
White, n (%)	435 (89)	439 (90)
Geographic region, n (%)		
Not USA	392 (80)	409 (84)
USA	95 (20)	80 (16)

	KEYTRUDA (n=487)	Placebo (n=489)
ECOG PS, n (%)		
0	454 (93)	452 (92)
1	32 (7)	35 (7)
2	0	1 (<1)
Missing	1 (<1)	1 (<1)
T category, n (%)		
T3a	2 (<1)	0
T3b	200 (41)	201 (41)
T4a	113 (23)	116 (24)
T4b	172 (35)	172 (35)
Disease stage, n (%)		
IIB	309 (63)	316 (65)
IIC	171 (35)	169 (35)

Return to study design

Adapted from Luke JJ, *et al. Lancet* 2022.[1]

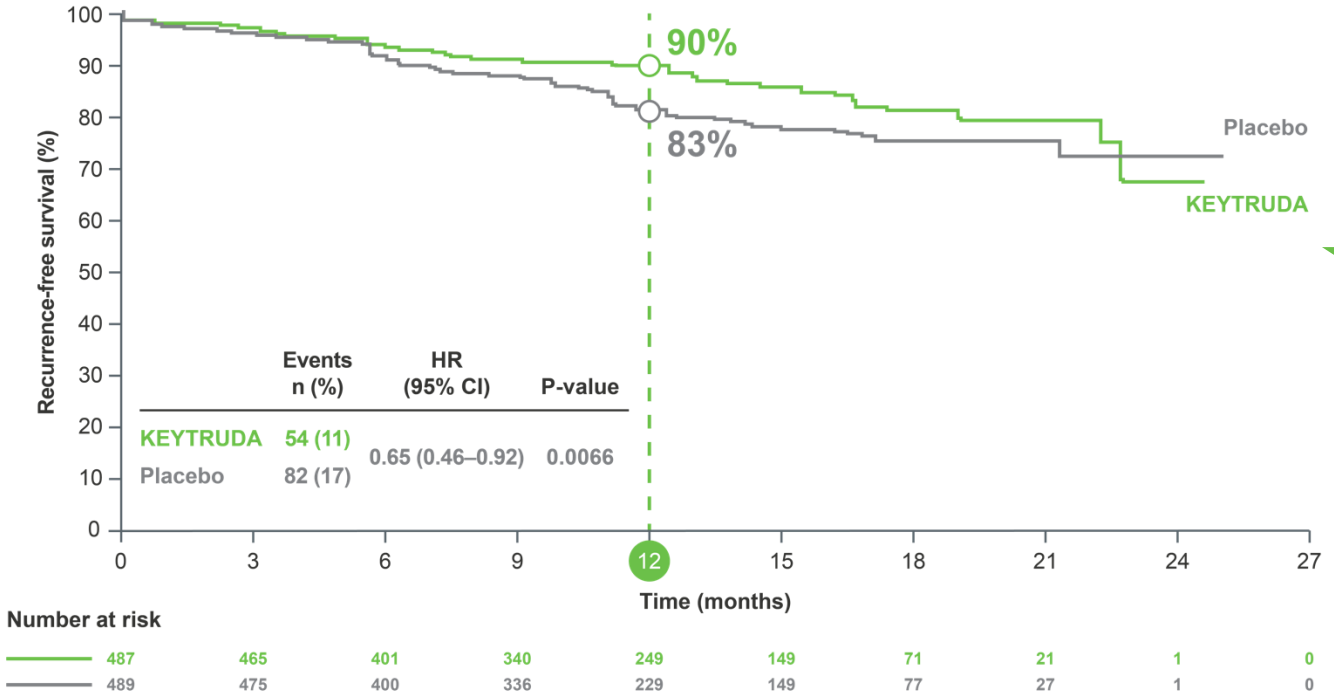
T-category is based on TNM staging.[1]
Disease stage is defined by the 8th AJCC 2017 classification.[1]
AJCC, American Joint Committee on Cancer; **ECOG PS,** Eastern Cooperative Oncology Group performance status; **IQR,** interquartile range; **T,** tumour; **TNM,** tumour, node, metastasis.
1. Luke JJ, *et al. Lancet* 2022;399:1718–1729.

KEYTRUDA® (pembrolizumab)

Recurrence-free survival following treatment with KEYTRUDA versus placebo[1]

IA1

Kaplan-Meier estimates of RFS* in the ITT population at the first interim analysis†



Adapted from Luke JJ, *et al. J Clin Oncol* 2022.[1]

35% relative risk reduction

- KEYTRUDA demonstrated a **35% relative risk reduction** in disease recurrence versus placebo
  - Patients with events: 11% (n=54/487) vs 17% (n=82/489)
  - HR: 0.65; 95% CI: 0.46–0.92
  - P=0.0066

Return to the summary

IA1 data cut-off: 4 December 2020.[1] The n number displayed represents the number of events in the treatment arm. *RFS was defined as time from randomisation to the date of first recurrence of melanoma at any site (local, in-transit or regional lymph nodes or distant recurrence) or death due to any cause, whichever occurred first.[1] †Based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by melanoma T category (T3b versus T4a versus T4b).[1]

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

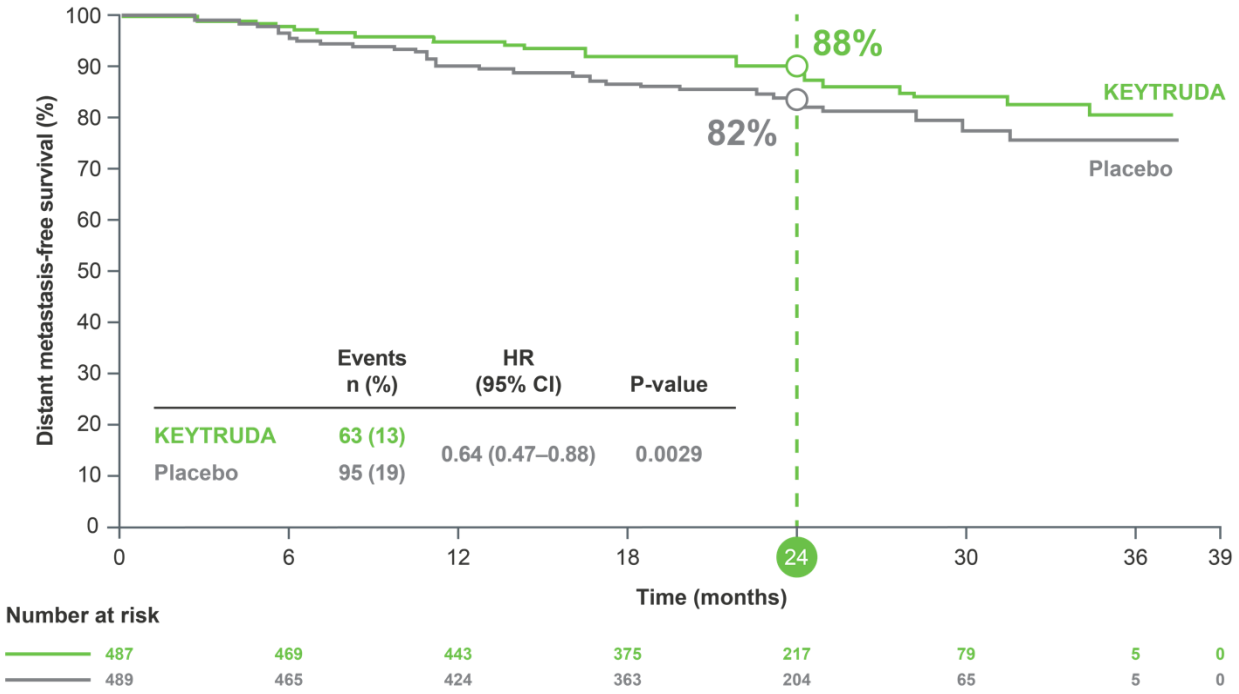
1. Luke JJ, *et al. Lancet* 2022;399:1718–1729.

KEYTRUDA® (pembrolizumab)

Distant metastasis-free survival* following treatment with KEYTRUDA versus placebo[1]

IA3

Kaplan-Meier estimates of DMFS in the ITT population at the third interim analysis†



Adapted from Long GV, *et al. Lancet Oncol* 2022.[1]

36%
relative risk reduction

- KEYTRUDA demonstrated a **36% relative risk reduction** in disease recurrence versus placebo
  - Patients with events: 13% (n=63/487) vs 19% (n=95/489)
  - HR: 0.64; 95% CI: 0.47–0.88
  - P=0.0029

Return to the summary

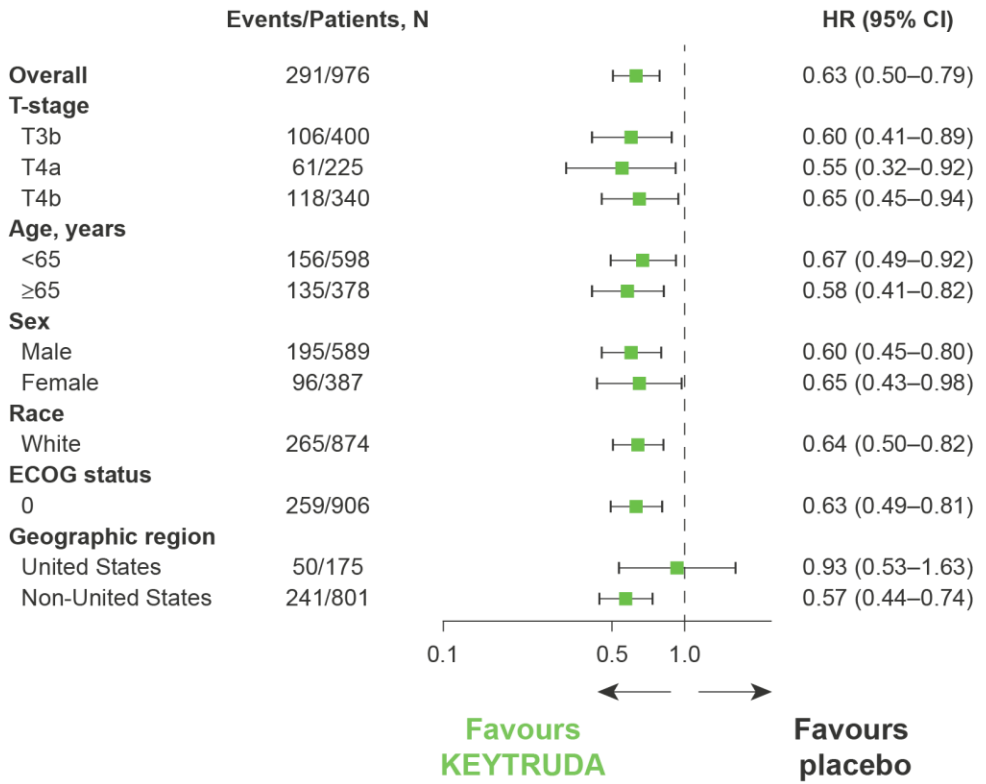
IA3 data cut-off: 4 January 2022.[1] The n number displayed represents the number of events in the treatment arm. *DMFS was defined as the time from randomisation to the first diagnosis of distant metastasis.[1] †Based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by melanoma T category (T3b versus T4a versus T4b).[1]
CI, confidence interval; **DMFS,** distant metastasis-free survival; **HR,** hazard ratio; **IA,** interim analysis; **ITT,** intention-to-treat; **T,** tumour.

1. Long GV, *et al. Lancet Oncol* 2022;23:1378–1388.

KEYTRUDA® (pembrolizumab)

RFS in key patient subgroups following treatment with KEYTRUDA versus placebo after 39.4 months median follow-up (IA4)[1]

KEYNOTE-716 was not powered to detect differences in the treatment effect in these subgroups; therefore, results from exploratory analyses should be interpreted with caution because of the modest patient numbers and potential imbalances in baseline characteristics within subgroups.



Return to RFS analysis

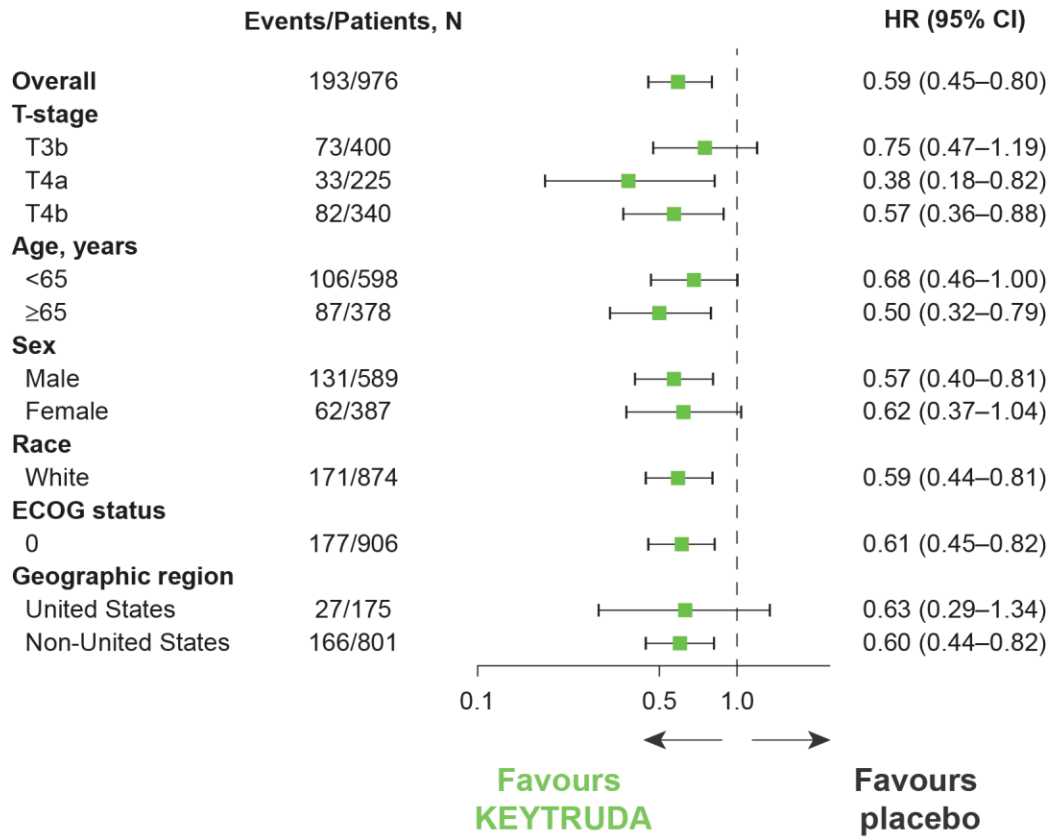
Adapted from Luke JJ, *et al. J Clin Oncol* 2024.[1]

IA4 analysis data cut-off: 4 January 2023.[1]
CI, confidence interval; **ECOG,** Eastern Cooperative Oncology Group; **HR,** hazard ratio; **IA4,** fourth interim analysis; **RFS,** recurrence-free survival; **T,** tumour.
1. Luke JJ, *et al. J Clin Oncol*. 2024;42:1619–1624.

KEYTRUDA® (pembrolizumab)

DMFS in key patient subgroups following treatment with KEYTRUDA versus placebo after 39.4 months median follow-up (IA4)[1]

KEYNOTE-716 was not powered to detect differences in the treatment effect in these subgroups; therefore, results from exploratory analyses should be interpreted with caution because of the modest patient numbers and potential imbalances in baseline characteristics within subgroups.



Adapted from Luke JJ, *et al. J Clin Oncol* 2024 & Luke JJ, *et al.* 2023.[1,2]

Return to DMFS analysis

IA4 analysis data cut-off: 4 January 2023.[1]
CI, confidence interval; **DMFS,** distant metastasis-free survival; **ECOG,** Eastern Cooperative Oncology Group; **HR,** hazard ratio; **IA4,** fourth interim analysis; **T,** tumour.
1. Luke JJ, *et al. J Clin Oncol*. 2024;42:1619–1624. **2.** Luke JJ, *et al.* Pembrolizumab versus placebo as adjuvant therapy in stage IIB or IIC melanoma: Final analysis of distant metastasis-free survival in the Phase 3 KEYNOTE-716 study. ASCO. 2–6 June 2023. Chicago, IL, USA. Oral presentation.

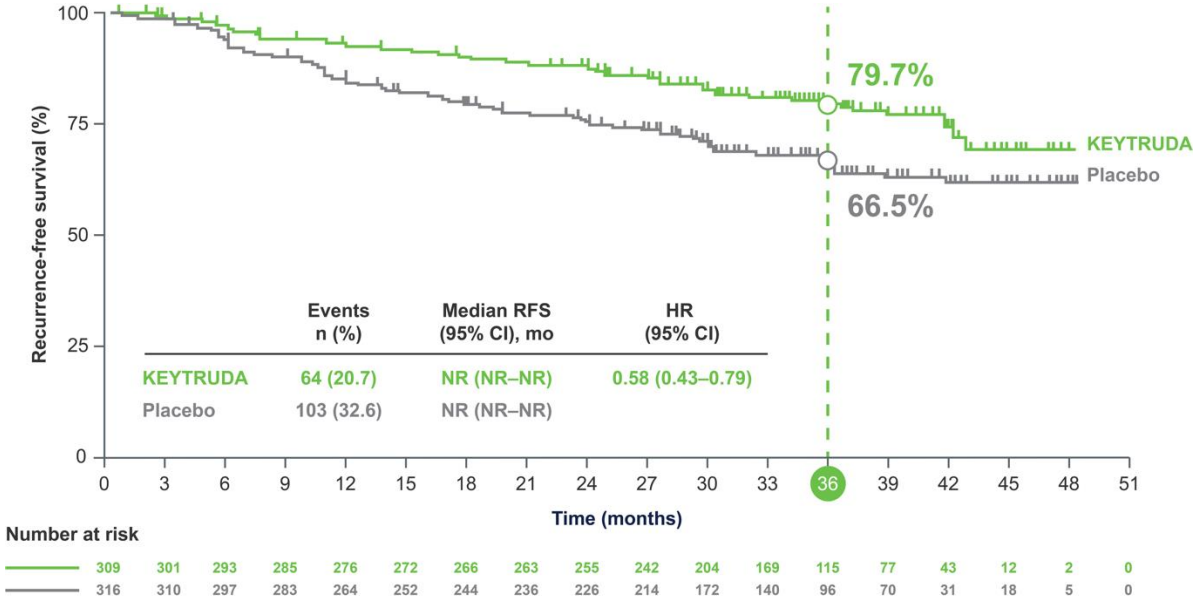
KEYTRUDA® (pembrolizumab)

RFS in Stage IIB following treatment with KEYTRUDA versus placebo after 39.4 months median follow-up[1]

Exploratory long-term analysis: significance was not tested, therefore no statistical conclusions can be drawn from this analysis

IA4

Kaplan-Meier estimates of RFS in Stage IIB patients



Adapted from Luke JJ, *et al. J Clin Oncol.* 2024.[1]

- KEYTRUDA demonstrated a **42% relative risk reduction** in disease recurrence versus placebo
  - Patients with events: 20.7% (n=64/309) vs 32.6% (n=103/316)
  - HR: 0.58; 95% CI: 0.43–0.79
  - Statistical superiority of KEYTRUDA versus placebo for RFS was not tested at this timepoint

Return to RFS analysis

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

Analysis cut-off date: 4 January 2023.[1]
CI, confidence interval; **HR,** hazard ratio; **IA4,** fourth interim analysis; **NR,** not reached; **RFS,** recurrence-free survival.
1. Luke JJ, *et al. J Clin Oncol.* 2024;7:1619–1624.

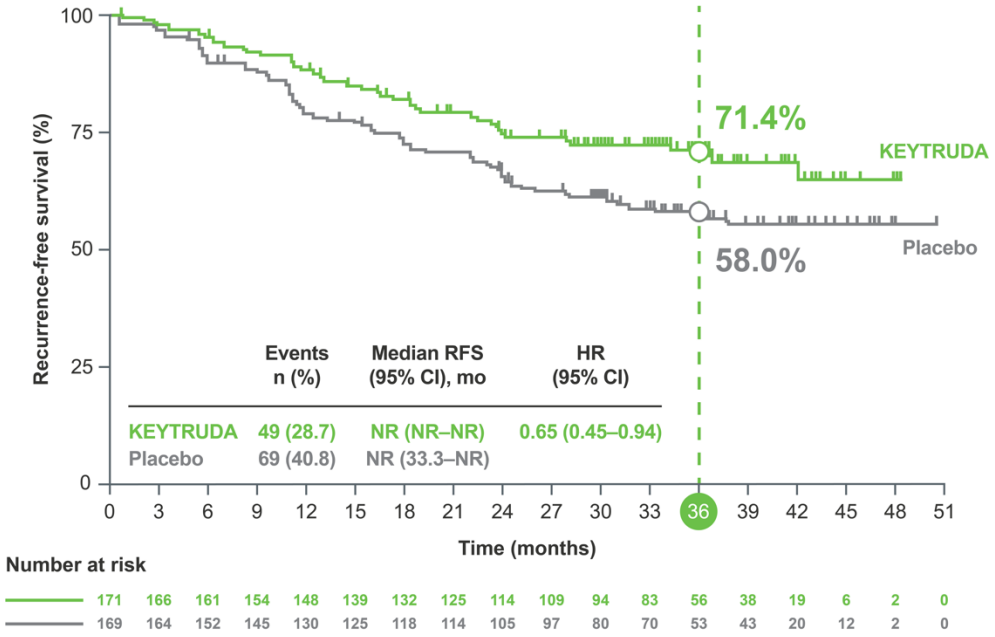
KEYTRUDA® (pembrolizumab)

RFS in Stage IIC following treatment with KEYTRUDA versus placebo after 39.4 months median follow-up[1]

Exploratory long-term analysis: significance was not tested, therefore no statistical conclusions can be drawn from this analysis

IA4

Kaplan-Meier estimates of RFS in Stage IIC patients



Adapted from Luke JJ, *et al. J Clin Oncol.* 2024.[1]

- KEYTRUDA demonstrated a **35% relative risk reduction** in disease recurrence versus placebo
  - Patients with events: 28.7% (n=49/171) vs 40.8% (n=69/169)
  - HR: 0.65; 95% CI: 0.45–0.94
  - Statistical superiority of KEYTRUDA versus placebo for RFS was not tested at IA4

Return to RFS analysis

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

Analysis cut-off date: 4 January 2023.[1]
CI, confidence interval; **HR,** hazard ratio; **IA4,** fourth interim analysis; **NR,** not reached; **RFS,** recurrence-free survival.
1. Luke JJ, *et al. J Clin Oncol.* 2024;7:1619–1624.

KEYTRUDA® (pembrolizumab)