

KEYNOTE-522: Neoadjuvant KEYTRUDA[®] (pembrolizumab) + chemotherapy followed by adjuvant KEYTRUDA monotherapy in patients with triple-negative breast cancer (TNBC)

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Please refer to the full Summary of Product Characteristics for KEYTRUDA and patient-targeted Risk Minimisation Materials before prescribing, to minimise the risk of treatment. Patients should also receive the Risk Minimisation Materials.

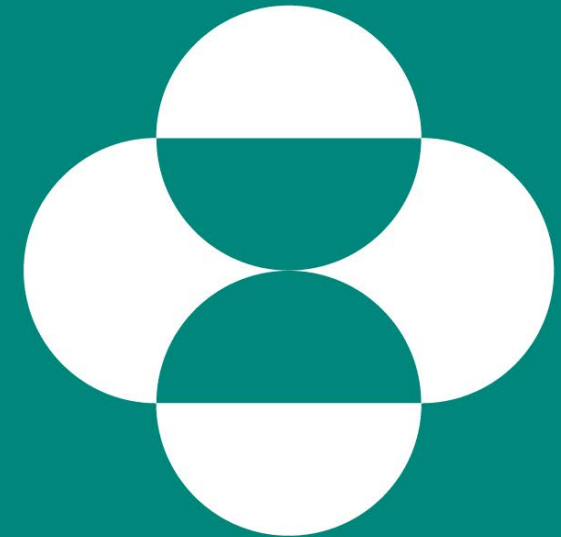
Adverse events should be reported. Reporting forms and information can be found at <https://yellowcard.mhra.gov.uk/> (please note that the MHRA Yellow Card link will redirect you to an external website, for which MSD does not review or control the content) or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Merck Sharp & Dohme (UK) Limited (Tel: 020 8154 8000).

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Job code: GB-OBR-00218 Date of preparation: July 2026

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Heritage of KEYTRUDA and MoA with chemotherapy



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**KEYTRUDA and
chemotherapy:
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mechanisms of action**

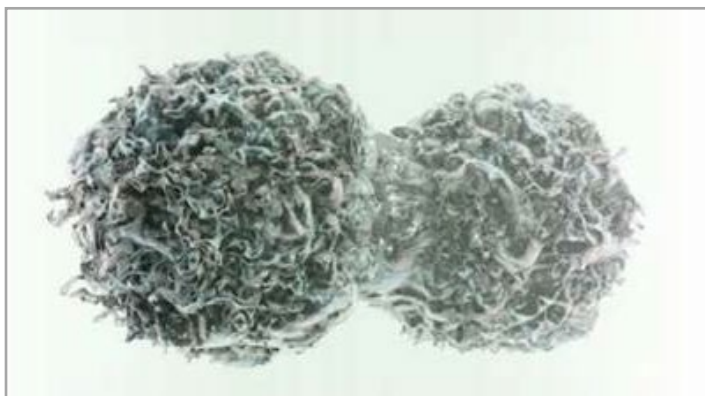
**KEYTRUDA +
chemotherapy licence
in early-stage TNBC**

**KEYTRUDA in the
early-stage
TNBC pathway**



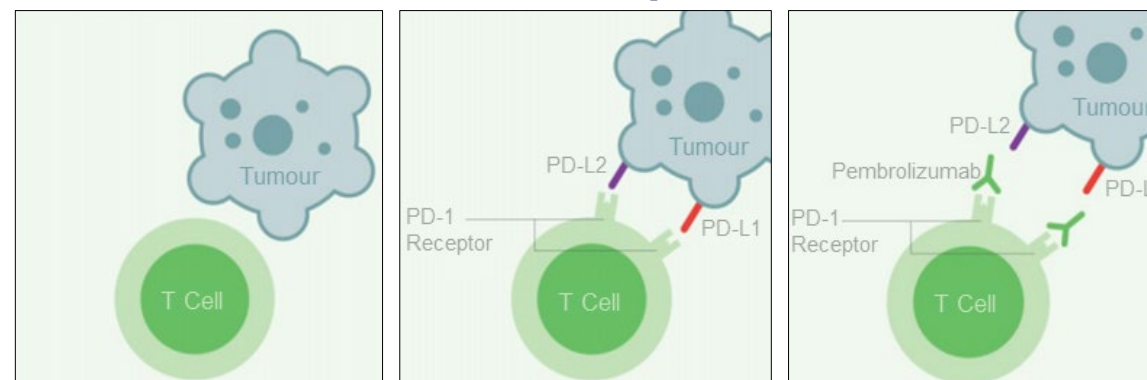
KEYTRUDA and chemotherapy: Two different mechanisms of action

Chemotherapy induces immunogenic cell death



- Chemotherapy results in the immunogenic death of tumour cells, leading to the release of tumour antigens that can be recognised by the immune system¹
- Chemotherapy has been shown to increase tumour expression of PD-L1²

KEYTRUDA activates the anti-tumour immune response



- PD-L1 (and PD-L2) on tumour cells bind to PD-1 on T cells to prevent their activation, leading to immune evasion^{1,3}
- KEYTRUDA is a humanised monoclonal antibody that binds to PD-1, blocking its interaction with PD-L1/-L2 and leading to activation of the anti-tumour response^{4,5}

When combined with immunotherapies such as KEYTRUDA, chemotherapy may increase tumour immunogenicity and activate an immune response by increasing antigen shedding and presentation, and by stimulating T-cell infiltration²

PD-1, programmed death receptor-1; PD-L1, programmed death ligand-1; PD-L2, programmed death ligand-2.

1. Emens LA and Middleton G. *Cancer Immunol Res* 2015;3:436–443; 2. Bailly C et al. *NAR Cancer* 2020;2(1):zcaa002; 3. Yi M et al. *J Hematol Oncol* 2021;14:10; 4. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: <https://www.medicines.org.uk/emc/product/2498/smpc>. Accessed August 2025; 5. Pardoll DM. *Nat Rev Cancer* 2012;12:252–264.

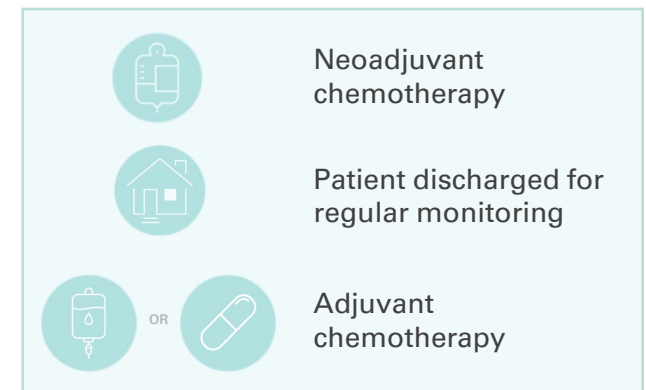
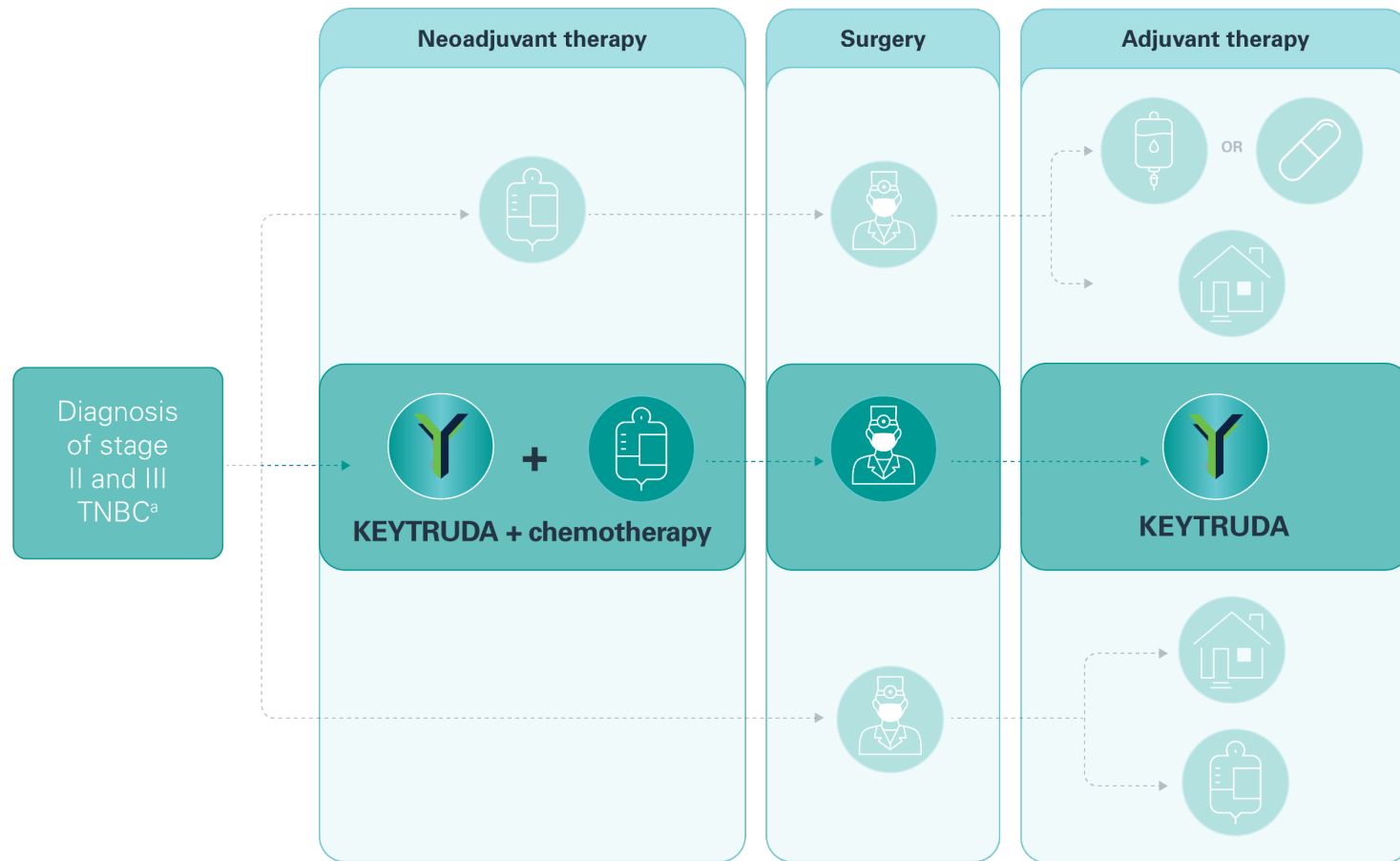


KEYTRUDA + chemotherapy licence in early-stage TNBC

KEYTRUDA, in combination with chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment after surgery, is indicated in the treatment of adults with locally advanced or early-stage TNBC at high risk of recurrence



KEYTRUDA in the early-stage TNBC pathway¹⁻⁴



^aStage IIA, IIB, IIIA and IIIB early TNBC, and IIIC TNBC, as defined by the primary tumour-regional lymph node staging criteria of the AJCC (7th Edition).³

AJCC, American Joint Committee on Cancer; NICE, National Institute for Health and Care Excellence; TNBC, triple-negative breast cancer.

1. NICE. Early and locally advanced breast cancer: diagnosis and management. <https://www.nice.org.uk/guidance/ng101/chapter/Recommendations>. Accessed August 2025;

2. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: <https://www.medicines.org.uk/emc/product/2498/smpc>. Accessed August 2025;

3. AJCC. *AJCC Cancer Staging Manual*. 7th ed. USA: Springer; 2010; 4. NICE. Technology appraisal guidance [TA851] December 2022. Available at:

<https://www.nice.org.uk/guidance/ta851>. Accessed August 2025.



KEYNOTE-522: Study overview



Click the links below to navigate to the section of interest

Study design

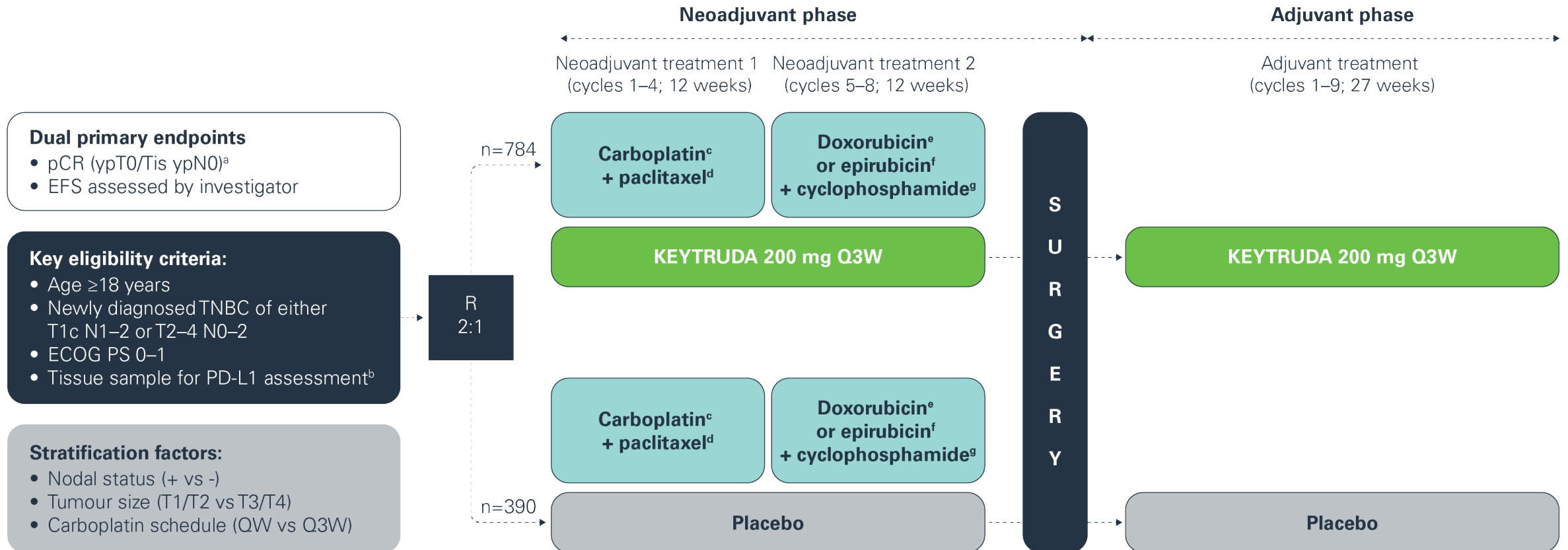
Primary endpoints

**Key patient
characteristics**

**Patient baseline
characteristics**



KEYNOTE-522: Study design^{1,2}



Adapted from Schmid P et al. 2020 and Schmid P et al. 2022.

AEs were assessed during each phase of the study, as well as the study as a whole.

^aBlinded assessment performed by local pathologist; ^bMust consist of at least two separate tumour cores from the primary tumour; ^cCarboplatin dose was AUC 5 Q3W or AUC 1.5 QW;

^dPaclitaxel dose was 80 mg/m² QW; ^eDoxorubicin dose was 60 mg/m² Q3W; ^fEpirubicin dose was 90 mg/m² Q3W; ^gCyclophosphamide dose was 600 mg/m² Q3W.

AE, adverse event; AUC, area under the curve; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; pCR, pathologic complete response; PD-L1, programmed death ligand-1; Q3W, every 3 weeks; QW, once a week; R, randomisation; TNBC, triple-negative breast cancer.

1. Schmid P et al. *N Engl J Med* 2020;382:810–821 (plus supplementary appendix); 2. Schmid P et al. *N Engl J Med* 2022;386:556–567 (plus supplementary appendix).



KEYNOTE-522: Primary endpoints^{1,2}

The primary endpoints of the KEYNOTE-522 trial were pCR and EFS, and were defined as follows:

pCR: The absence of invasive cancer in the breast and lymph nodes (ypT0/Tis ypN0). Blinded assessment performed by local pathologist at the time of definitive surgery

EFS: The time from randomisation to the first occurrence of any of the following events:

- Progression of disease that precludes definitive surgery
- Local or distant recurrence
- Second primary malignancy, OR
- Death due to any cause



KEYNOTE-522: Key patient characteristics

Key characteristics of the KEYTRUDA + chemotherapy arm of the KEYNOTE-522 trial:



Median patient age of 49 years (range: 22–80 years)



Primary tumour classification of 74% for T1/2 and 26% for T3/4



Nodal involvement was positive for 52% and negative for 48%



75% of patients with Stage II disease and 25% with Stage III disease

Total population: 1174 patients (KEYTRUDA + chemotherapy [n=784] and placebo + chemotherapy [n=390])



KEYNOTE-522: Patient baseline characteristics^{1,2}

Characteristic, n (%)	KEYTRUDA + chemotherapy (n=784)	Placebo + chemotherapy (n=390)
Median age (range), years	49 (22–80)	48 (24–79)
≤65 years	701 (89.4)	342 (87.7)
Menopausal status		
Premenopausal	438 (55.9)	221 (56.7)
Postmenopausal	345 (44.0)	169 (43.3)
PD-L1 status ^a		
Positive	656 (83.7)	317 (81.3) ^b
Negative	127 (16.2)	69 (17.7)
ECOG PS		
0	678 (86.5)	341 (87.4)
1	106 (13.5)	49 (12.6)
Lactase dehydrogenase level		
≤ULN	631 (80.5)	309 (79.2)
>ULN	149 (19.0)	80 (20.5)
Administration of carboplatin		
QW	449 (57.3)	223 (57.2)
Q3W	335 (42.7)	167 (42.8)
Primary tumour classification		
T1/T2	580 (74.0)	290 (74.4)
T3/T4	204 (26.0)	100 (25.6)
Nodal involvement		
Positive	405 (51.7)	200 (51.3)
Negative	379 (48.3)	190 (48.7)

Characteristic, n (%)	KEYTRUDA + chemotherapy (n=784)	Placebo + chemotherapy (n=390)
Overall disease stage		
Stage II	590 (75.3)	291 (74.6)
Stage III	194 (24.7)	98 (25.1)
HER2 status score		
0–1	595 (75.9)	286 (73.3)
≥2	188 (24.0)	104 (26.7)

Adapted from Schmid P et al. 2020.

^aPD-L1 assessed at a central laboratory using the PD-L1 IHC 22C3 pharmDx assay and measured using the CPS (number of PD-L1-positive tumour cells, lymphocytes and macrophages divided by the total number of viable tumour cells ×100);¹ ^bFinal analysis reports 316 patients (81.0%) as PD-L1 positive (CPS ≥1) in the placebo + chemotherapy arm.²

CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; PD-L1, programmed death ligand-1; Q3W, every 3 weeks; QW, once a week; ULN, upper limit of normal range.

1. Schmid P et al. *N Engl J Med* 2020;382:810–821 (plus supplementary appendix); 2. Schmid P et al. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2026, 29 May–2 June, Chicago, IL USA.



KEYNOTE-522: Results – Efficacy

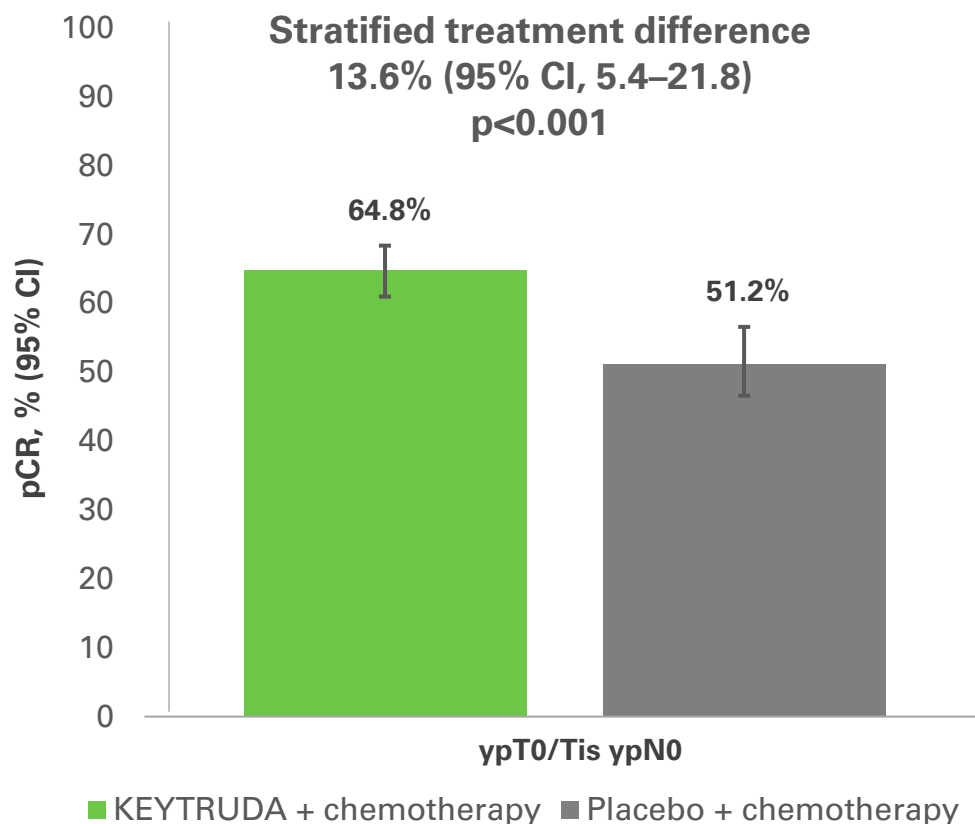


Click the links below to navigate to the section of interest

pCR	EFS <i>(continued)</i>		OS	
pCR in the ITT population (primary analysis)	EFS by pCR (60 months)	Distant recurrence as first EFS event (60 months)	OS in the ITT population (75-month follow-up)	OS in the ITT population (final analysis)
pCR in the ITT population (final analysis)	EFS by disease stage (60 months)	Distant recurrence as first EFS event by pCR (60 months)	OS in key subgroups (75-month follow-up)	OS in key subgroups (final analysis)
EFS	EFS by nodal status (60 months)	EFS in the ITT population (75-month follow-up)	OS by pCR (75-month follow-up)	OS by pCR (final analysis)
EFS in the ITT population (primary analysis)	EFS by disease stage with and without pCR (60 months)	EFS in the ITT population (final analysis)	OS in patients with baseline T2N0 disease (75-month follow-up)	
EFS in key subgroups (primary analysis)	EFS by nodal status with and without pCR (60 months)	EFS in key subgroups (final analysis)		
EFS by pCR (36 months)	EFS in patients with baseline T2N0 disease (60 months)	EFS by pCR (final analysis)		
EFS in key subgroups (60 months)				
			DPFS and DRFS	
			DPFS or DRFS (36 and 60 months)	DPFS or DRFS (final analysis)



KEYNOTE-522: pCR in the ITT population at primary analysis



- Statistically significant improvement was observed in pCR rates with KEYTRUDA + chemotherapy (neoadjuvant treatment) vs placebo + chemotherapy (neoadjuvant treatment) in the primary analysis of KEYNOTE-522 ($p < 0.001$)
- 64.8% of patients (95% CI, 59.9–69.5) achieved pCR in the KEYTRUDA + chemotherapy (neoadjuvant treatment) group vs 51.2% of patients (95% CI, 44.1–58.3) in the placebo + chemotherapy (neoadjuvant treatment) group

Adapted from Schmid P et al. 2020.

Data cutoff: 24 September 2018. KEYTRUDA + chemotherapy (n=401); placebo + chemotherapy (n=201).

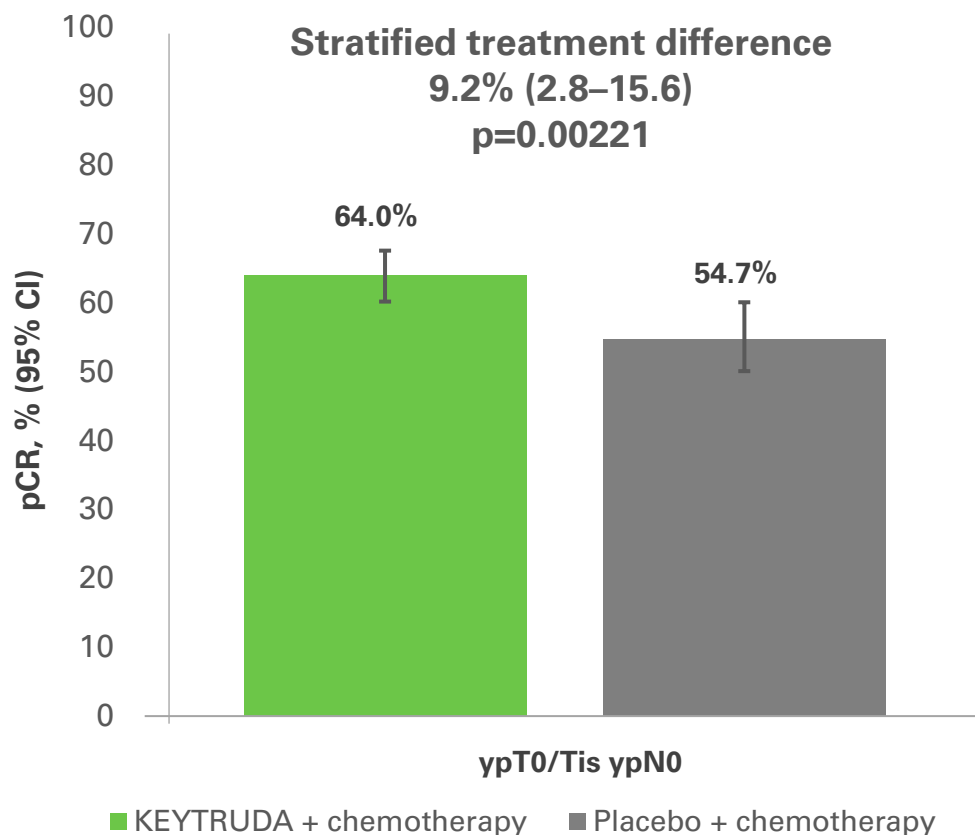
The analysis is based on the Miettinen and Nurminen method stratified according to nodal status (+ vs –), tumour size (T1 [diameter >1–2 cm] to T2 [diameter >2–5 cm] or T3 [diameter >5 cm] to T4 [locally advanced disease]), and frequency of carboplatin administration (QW or Q3W). For the other subgroups, the analysis is based on the unstratified Miettinen and Nurminen method.

CI, confidence interval; ITT, intention-to-treat; pCR, pathologic complete response; Q3W, every 3 weeks; QW, once a week.

Schmid P et al. *N Engl J Med* 2020;382:810–821.



KEYNOTE-522: pCR in the ITT population at final analysis



- Statistically significant improvement in pCR was observed with KEYTRUDA + chemotherapy (neoadjuvant treatment) vs placebo + chemotherapy (neoadjuvant treatment) in the final analysis of KEYNOTE-522 (p=0.00221)
- 64.0% of patients (95% CI, 60.2–67.6) achieved pCR in the KEYTRUDA + chemotherapy (neoadjuvant treatment) group vs 54.7% of patients (95% CI, 49.1–60.1) in the placebo + chemotherapy (neoadjuvant treatment) group

Adapted from KEYTRUDA SmPC.

Data cutoff: 23 March 2021. KEYTRUDA + chemotherapy (n=669); placebo + chemotherapy (n=333).

The analysis is based on the Miettinen and Nurminen method stratified according to nodal status (+ vs –), tumour size (T1 [diameter >1–2 cm] to T2 [diameter >2–5 cm] or T3 [diameter >5 cm] to T4 [locally advanced disease]), and frequency of carboplatin administration (QW or Q3W). For the other subgroups, the analysis is based on the unstratified Miettinen and Nurminen method.

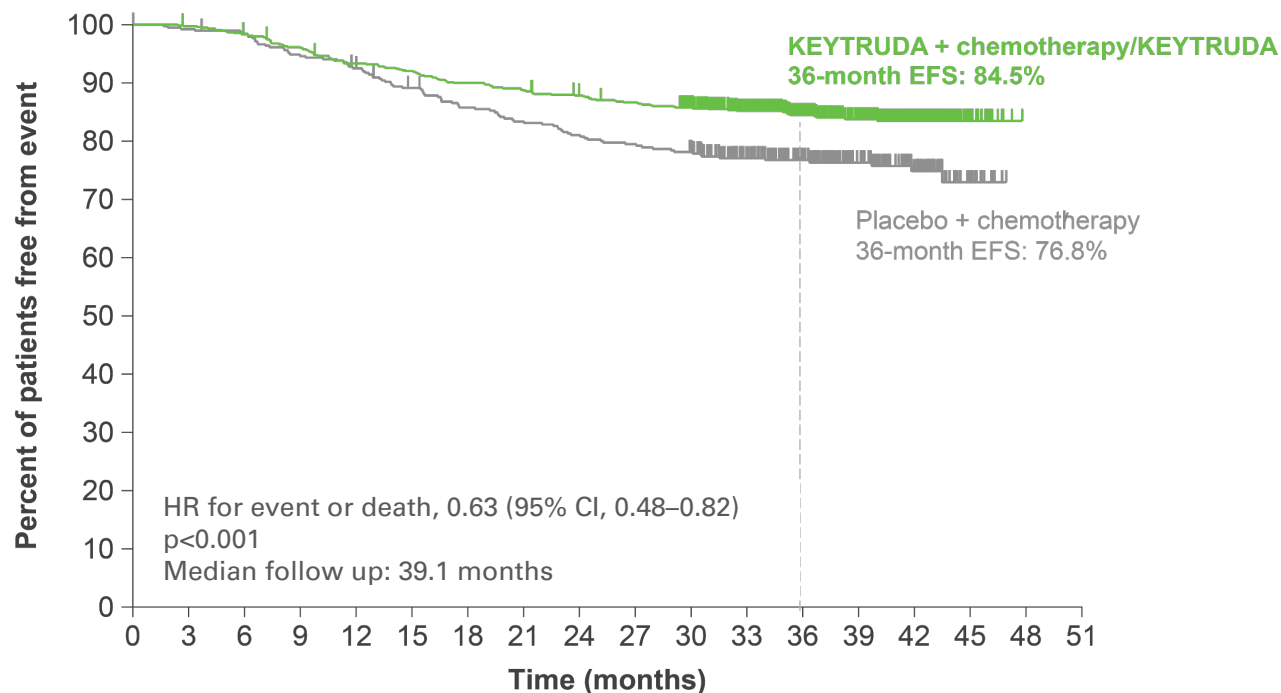
CI, confidence interval; ITT, intention-to-treat; pCR, pathologic complete response; Q3W, every 3 weeks; QW, once a week; SmPC, Summary of Product Characteristics.

KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: <https://www.medicines.org.uk/emc/product/2498/smpc>. Accessed August 2025.

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KEYNOTE-522: EFS in the ITT population at primary analysis



KEYTRUDA + chemotherapy/KEYTRUDA	784	781	769	751	728	718	702	692	681	671	652	551	433	303	165	28	0	0
Placebo + chemotherapy/placebo	390	386	382	368	358	342	328	319	310	304	297	250	195	140	83	17	0	0

Adapted from Schmid P et al. 2022.

- KEYTRUDA + chemotherapy in the neoadjuvant setting, followed by KEYTRUDA monotherapy as adjuvant treatment, resulted in a statistically significant improvement in EFS vs neoadjuvant placebo + chemotherapy followed by adjuvant placebo
- The 36-month estimated EFS was:
 - 84.5% in the neoadjuvant KEYTRUDA + chemotherapy followed by adjuvant KEYTRUDA group (95% CI, 81.7–86.9)
 - 76.8% in the neoadjuvant placebo + chemotherapy followed by adjuvant placebo group (95% CI, 72.2–80.7)
- Median EFS was not reached for either group

[Click here](#) to view the forest plot for EFS in key subgroups

Data cutoff: 23 March 2021.

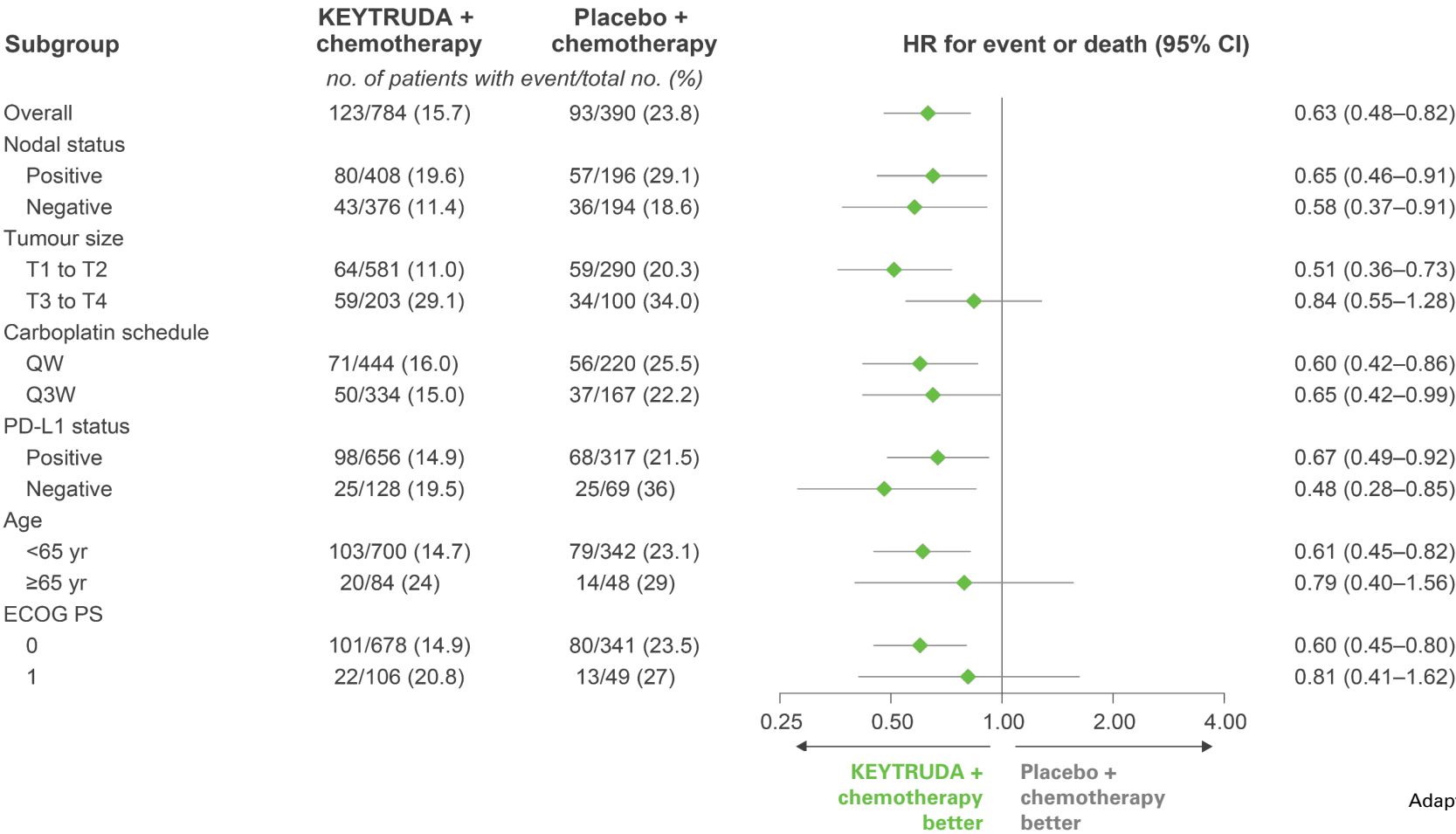
Tick marks indicate data censored at the last time the patient was known to be alive and without an event (disease progression that precludes definitive surgery; local or distant recurrence or a second primary tumour; or death from any cause). The HR and CI were analysed with the use of a Cox regression model with treatment as a covariate stratified according to the randomisation stratification factors of nodal status (+ or –), tumour size (T1/T2 or T3/T4) and frequency of carboplatin administration (QW or Q3W).

CI, confidence interval; EFS, event-free survival; HR, hazard ratio; ITT, intention-to-treat; Q3W, every 3 weeks; QW, once a week.

Schmid P et al. *N Engl J Med* 2022;386:556–567.



KEYNOTE-522: EFS in key subgroups at primary analysis



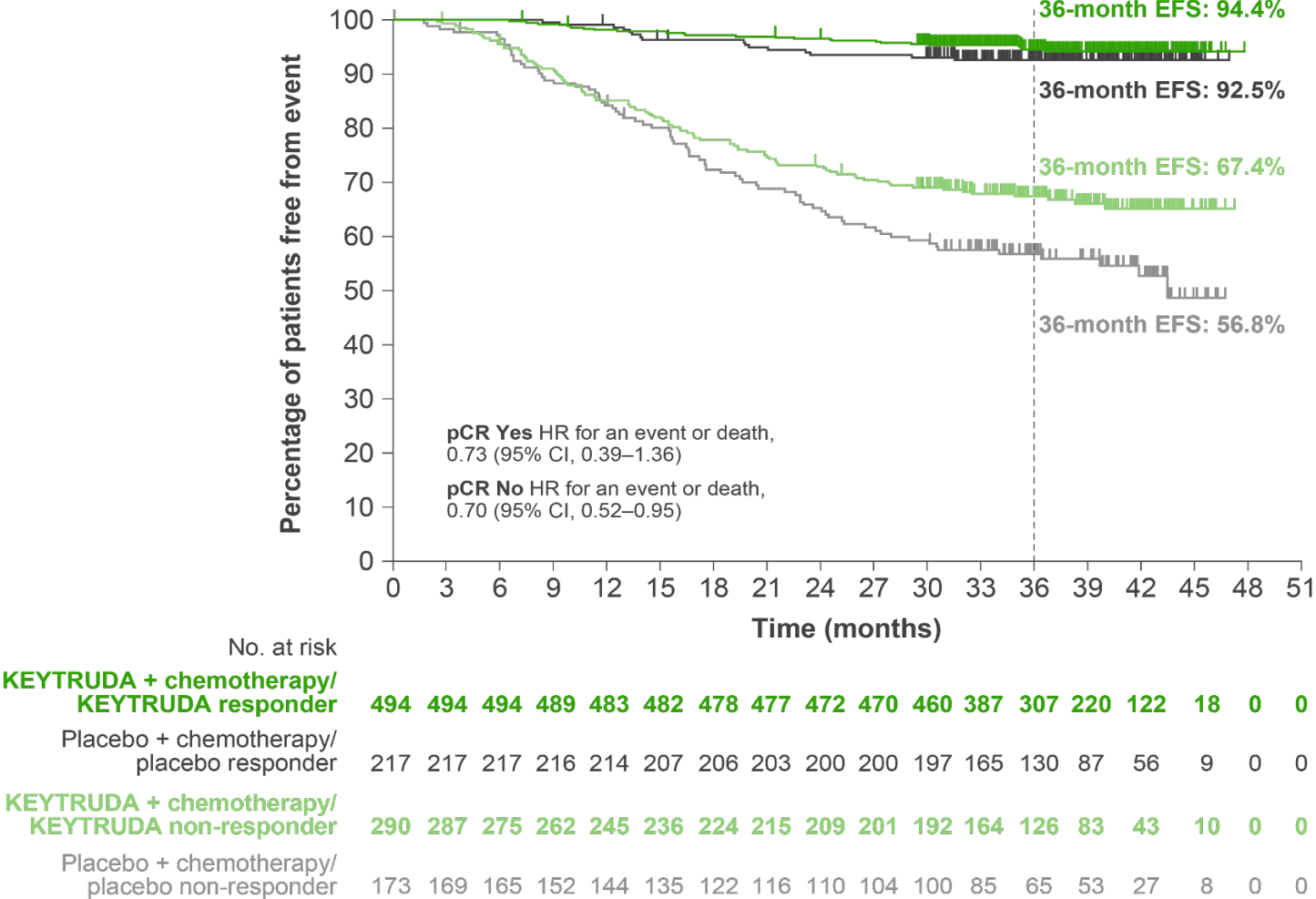
KEYNOTE-522 was not powered to detect differences in treatment effect between these subgroups. Results from exploratory analyses should be interpreted with caution due to modest patient numbers and potential imbalances in baseline characteristics

Adapted from Schmid P et al. 2022.

Data cutoff: 23 March 2021.
The HR and CI were analysed with the use of a Cox regression model, with treatment as a covariate and stratified according to the randomisation stratification factors of nodal status (+ or –), tumour size (T1/T2 or T3/T4) and frequency of carboplatin administration (QW or Q3W).
CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; HR, hazard ratio; PD-L1, programmed death ligand-1; Q3W, every 3 weeks; QW, once a week; yr, years.
Schmid P et al. *N Engl J Med* 2022;386:556–567 (plus supplementary appendix).



KEYNOTE-522: Exploratory analysis – EFS by pCR (ypT0/Tis ypN0) at 36 months



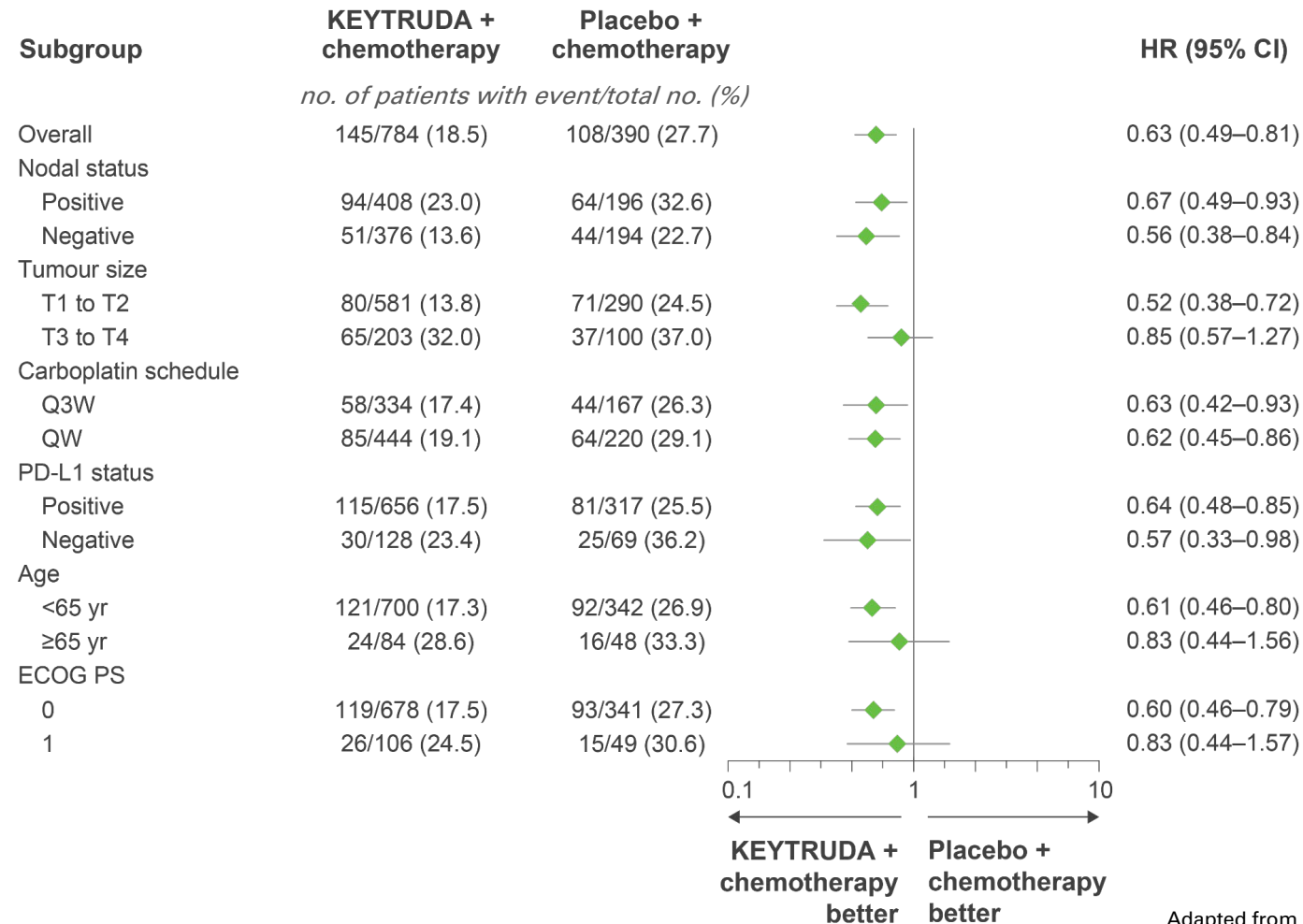
Adapted from Schmid P et al. Presented at ESMO 2023.

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Data cut-off: 23 March 2021.
CI, confidence interval; EFS, event-free survival; HR, hazard ratio; pCR, pathologic complete response.
Schmid P et al. Presented at the European Society of Medical Oncology Congress 2023, 20–24 September, Madrid, Spain.



KEYNOTE-522: Exploratory analysis – EFS in key subgroups at 60 months



KEYNOTE-522 was not powered to detect differences in treatment effect between these subgroups. Results from exploratory analyses should be interpreted with caution due to modest patient numbers and potential imbalances in baseline characteristics

Data cut-off: 23 March 2023.

For the overall population and PD-L1 subgroups, analyses were based on a Cox regression model with Efron's method of tie handling, with treatment as a covariate and stratification by nodal status (positive vs negative), tumour size (T1/T2 vs T3/T4) and frequency of carboplatin administration (QW vs Q3W); for other subgroups, analysis was based on an unstratified Cox model.

CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; HR, hazard ratio; pCR, pathologic complete response;

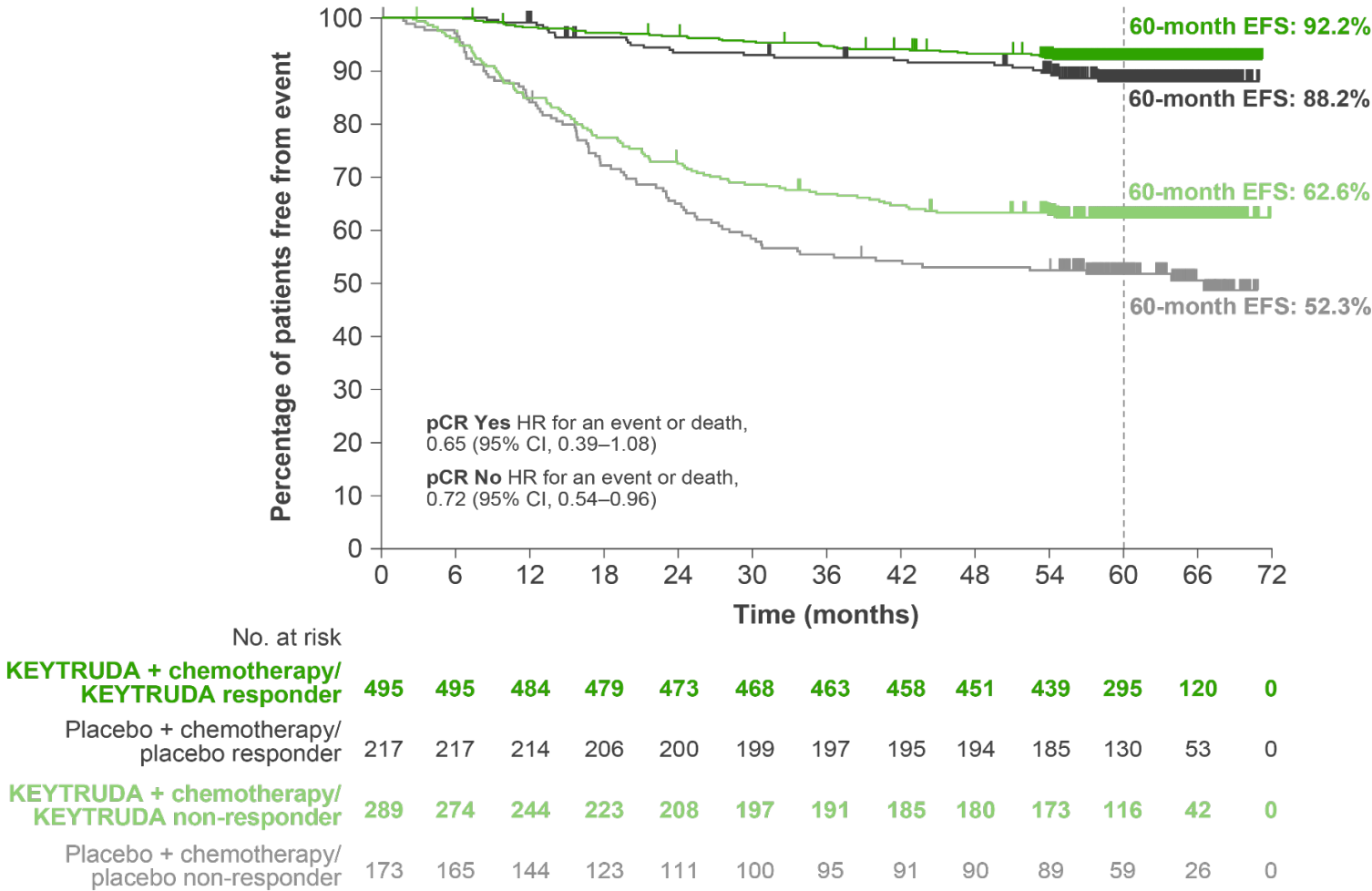
PD-L1, programmed death ligand-1; QW, every week; Q3W, every 3 weeks; yr, years.

Schmid P et al. Presented at the European Society of Medical Oncology (ESMO) Congress 2023, 20–24 September, Madrid, Spain.

Adapted from Schmid P et al. Presented at ESMO 2023.



KEYNOTE-522: Exploratory analysis – EFS by pCR (ypT0/Tis ypN0) at 60 months



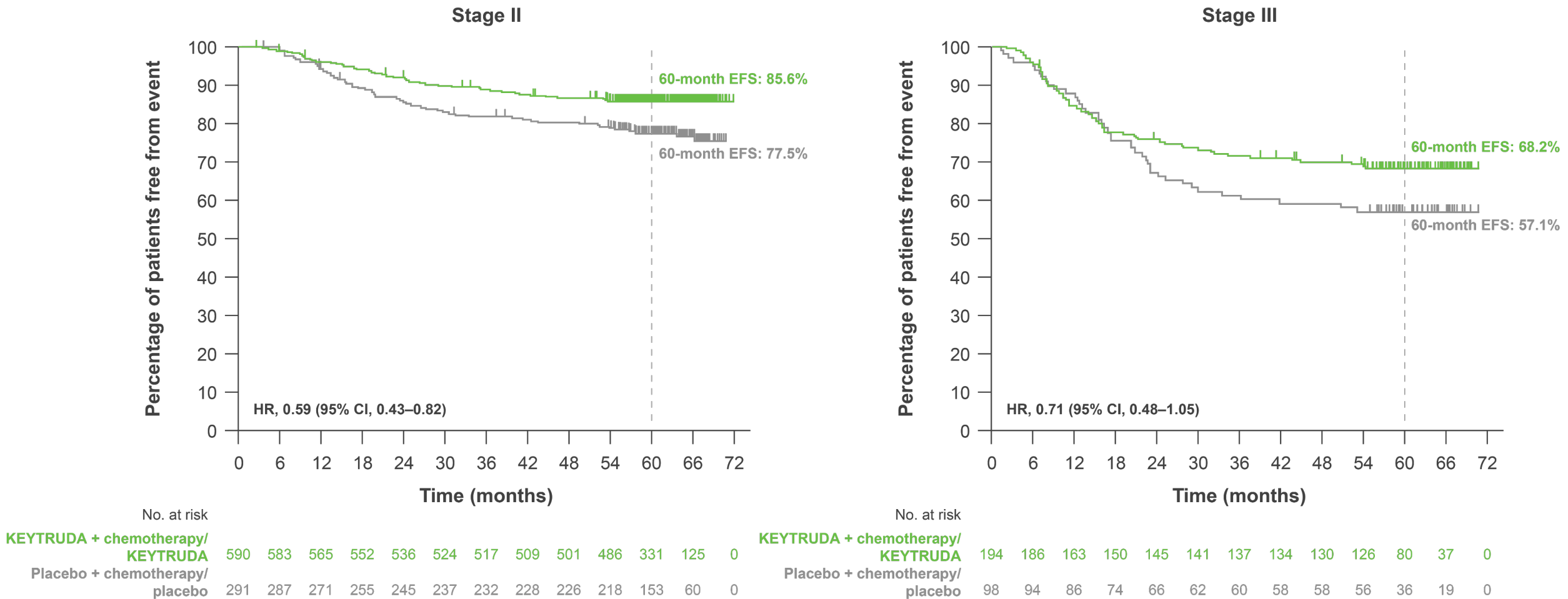
Adapted from Schmid P et al. Presented at ESMO 2023.

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Data cut-off: 23 March 2023.
CI, confidence interval; EFS, event-free survival; HR, hazard ratio; pCR, pathologic complete response.
Schmid P et al. Presented at the European Society of Medical Oncology Congress 2023, 20–24 September, Madrid, Spain.



KEYNOTE-522: Exploratory analysis – EFS by disease stage at 60 months

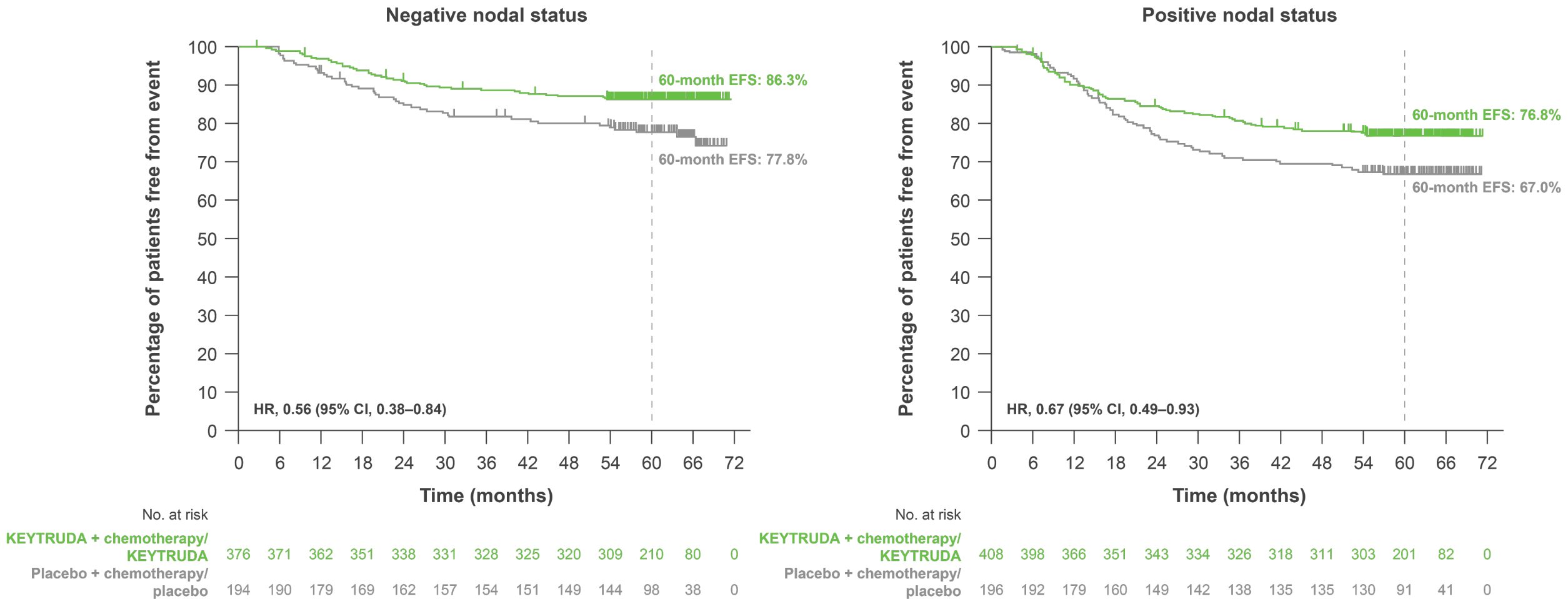


This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

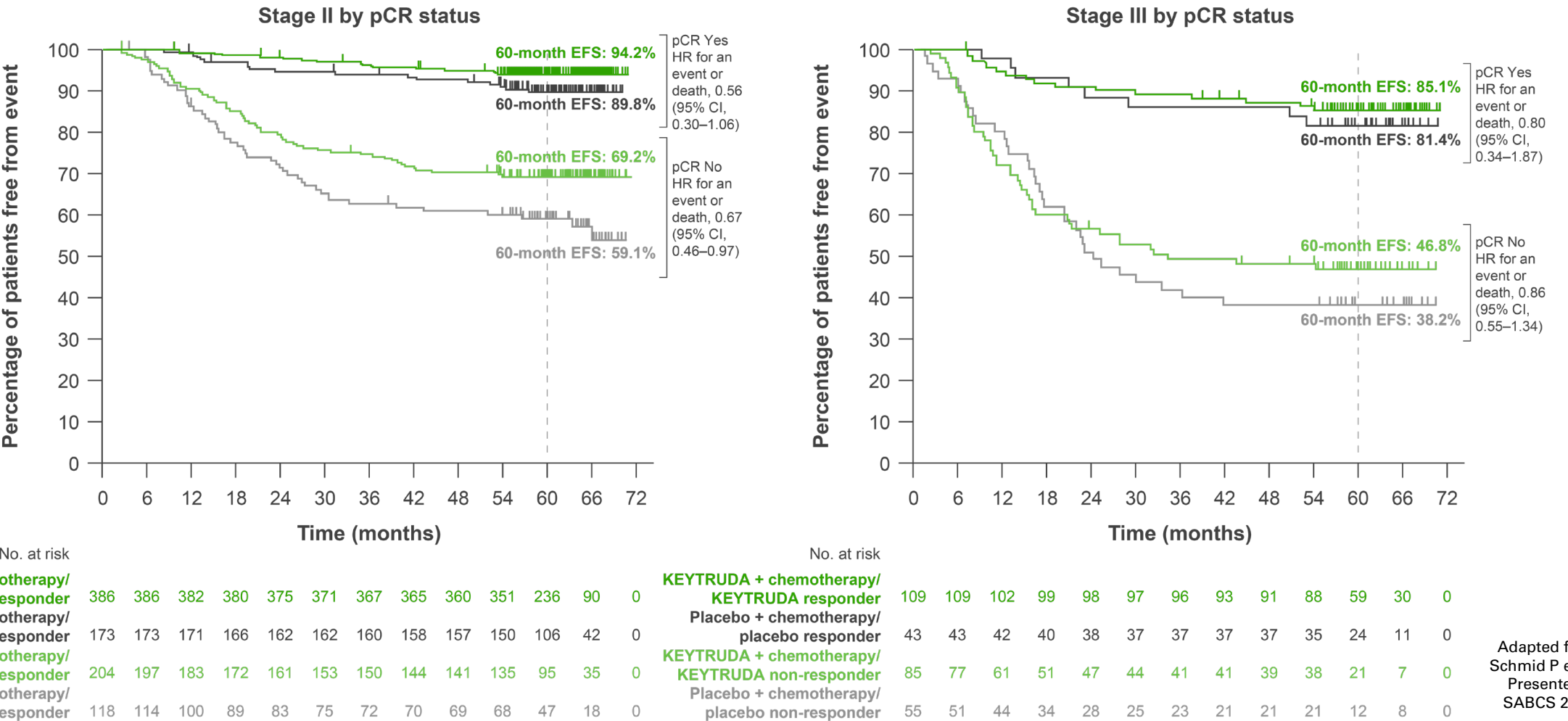
Data cutoff: 23 March 2023.
CI, confidence interval; EFS, event-free survival; HR, hazard ratio.
Schmid P et al. Presented at the San Antonio Breast Cancer Symposium (SABCS) Congress 2023, 5–9 December, San Antonio, USA.



KEYNOTE-522: Exploratory analysis – EFS by nodal status at 60 months



KEYNOTE-522: Exploratory analysis – EFS by disease stage in patients with and without pCR at 60 months

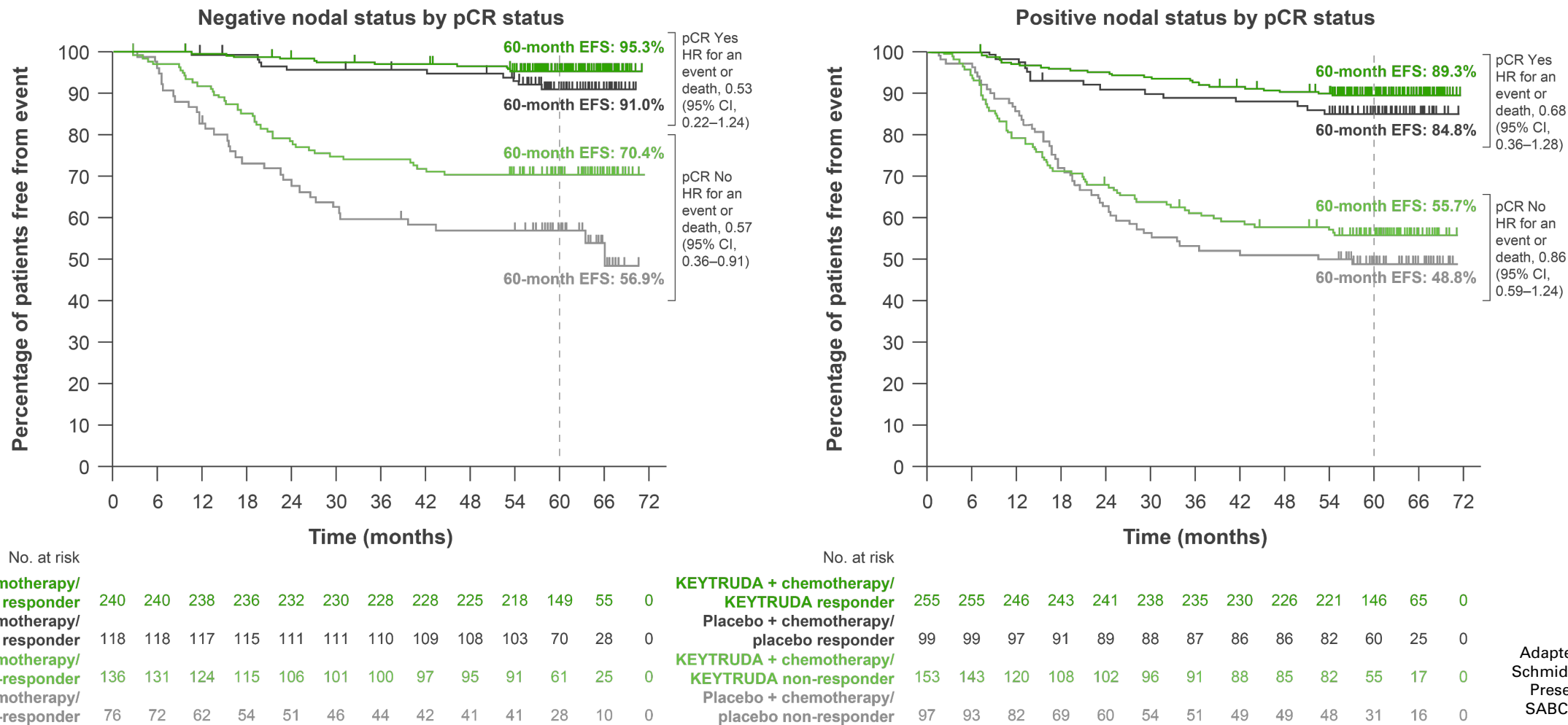


This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Data cutoff: 23 March 2023.
CI, confidence interval; EFS, event-free survival; HR, hazard ratio; pCR, pathologic complete response.
Schmid P et al. Presented at the San Antonio Breast Cancer Symposium (SABCS) Congress 2023, 5–9 December, San Antonio, USA.



KEYNOTE-522: Exploratory analysis – EFS by nodal status in patients with and without pCR at 60 months

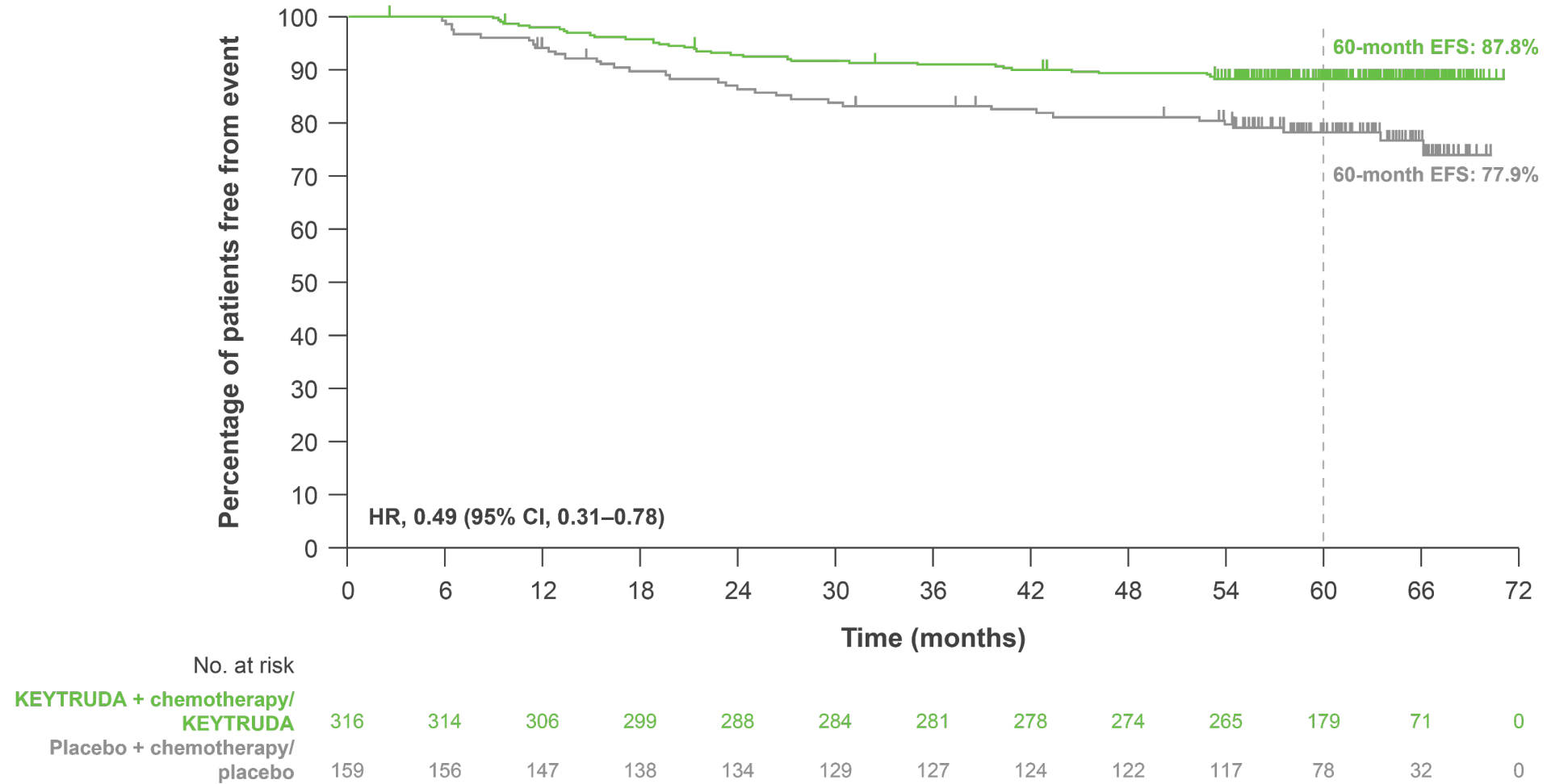


This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Data cutoff: 23 March 2023.
CI, confidence interval; EFS, event-free survival; HR, hazard ratio; pCR, pathologic complete response.
Schmid P et al. Presented at the San Antonio Breast Cancer Symposium (SABCS) Congress 2023, 5–9 December, San Antonio, USA.



KEYNOTE-522: Exploratory analysis – EFS in patients with baseline T2N0 disease at 60 months



Adapted from
Schmid P et al.
Presented at
SABCS 2023.

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Data cutoff: 23 March 2023.

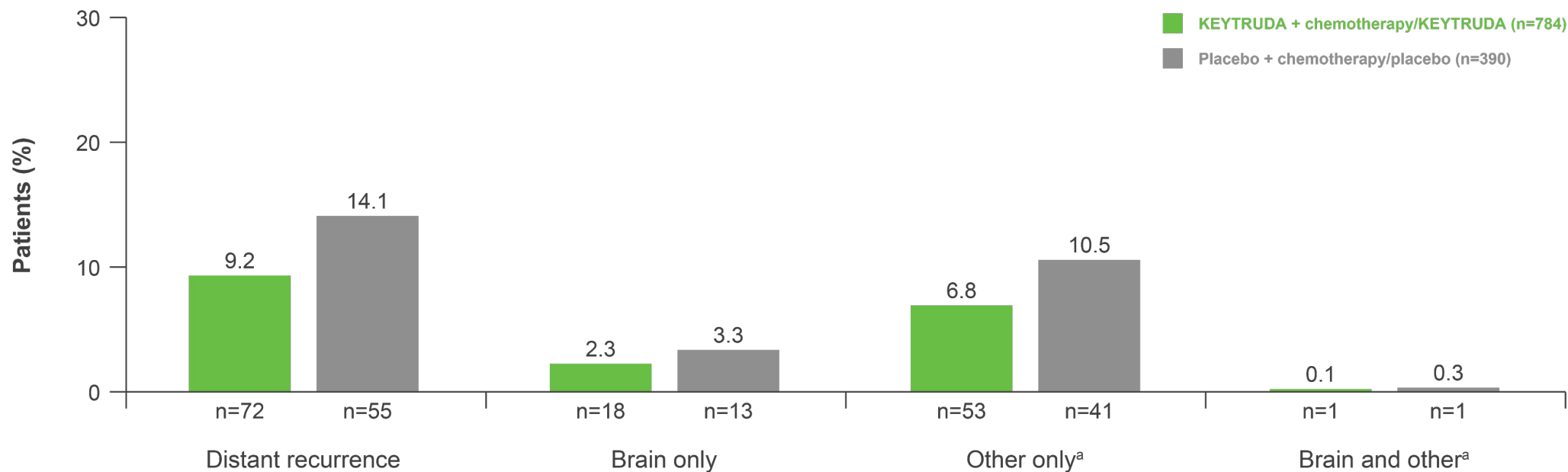
CI, confidence interval; EFS, event-free survival; HR, hazard ratio.

Schmid P et al. Presented at the San Antonio Breast Cancer Symposium (SABCS) Congress 2023, 5–9 December, San Antonio, USA.

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KEYNOTE-522: Exploratory analysis – Distant recurrence as first EFS event at 60 months



Adapted from Schmid P et al. Presented at SABCS 2023.

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Data cutoff: 23 March 2023.

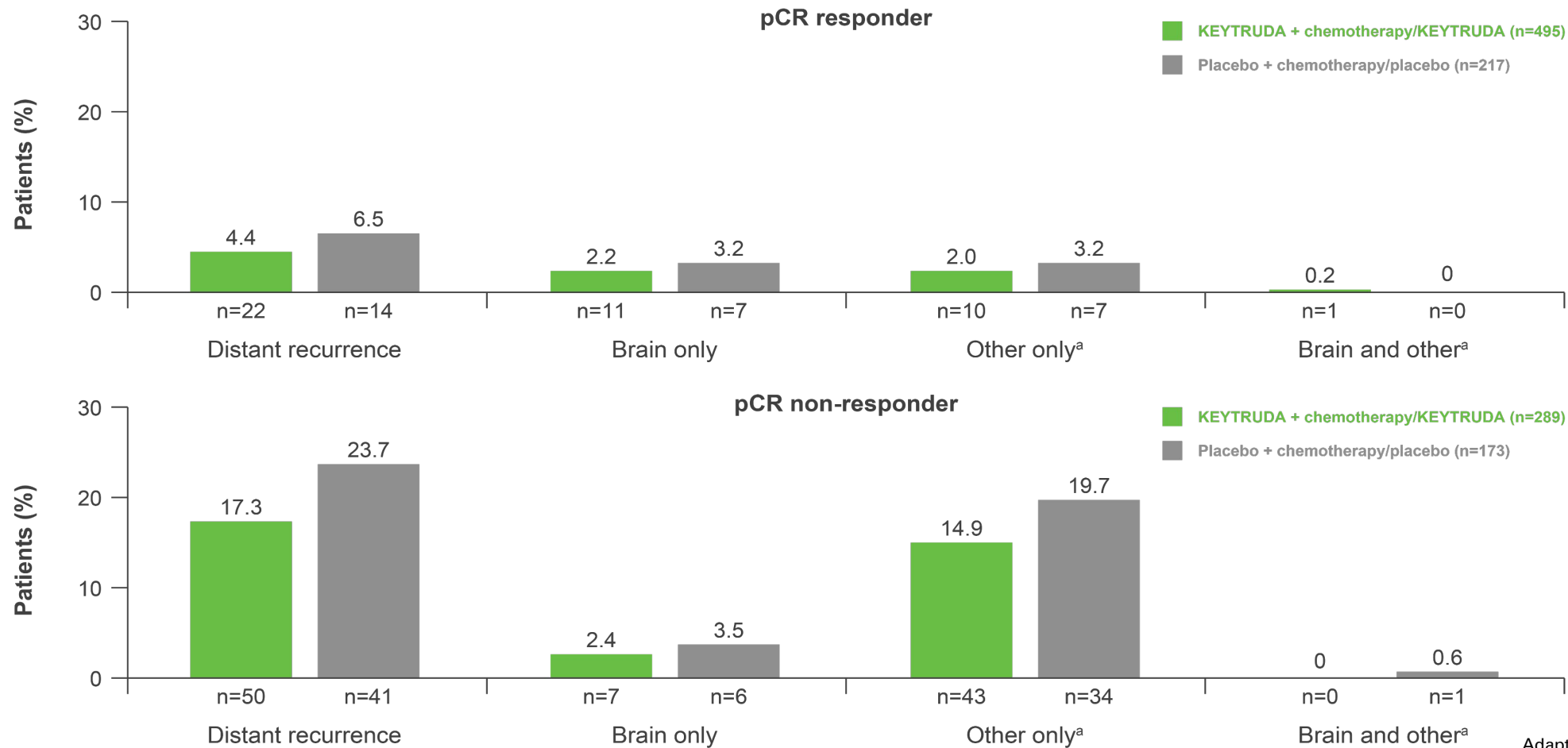
^aOther refers to non-brain distant recurrence sites, which were classified per clinical identification.

EFS, event-free survival.

Schmid P et al. Presented at the San Antonio Breast Cancer Symposium (SABCS) Congress 2023, 5–9 December, San Antonio, USA.



KEYNOTE-522: Exploratory analysis – Distant recurrence as first EFS event by pCR (ypT0/Tis ypN0) at 60 months



Adapted from Schmid P et al.
Presented at SABCS 2023.

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Data cutoff: 23 March 2023.

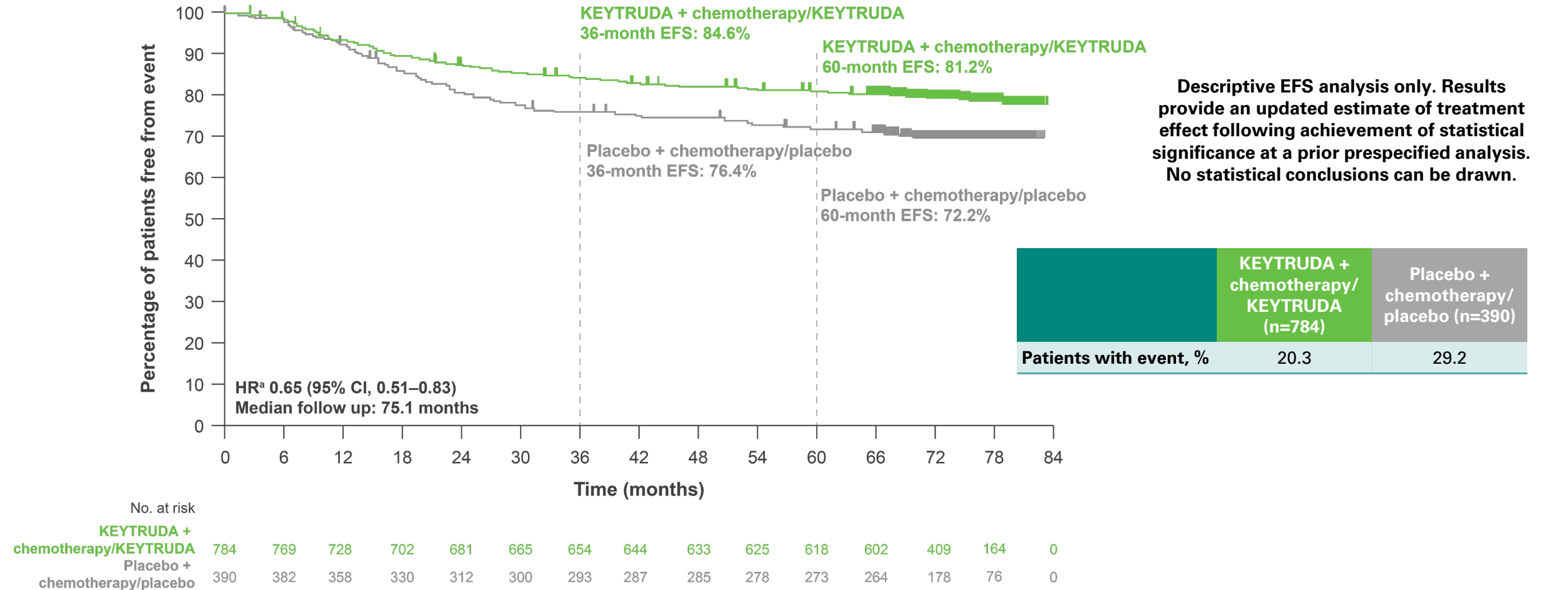
^aOther refers to non-brain distant recurrence sites, which were classified per clinical identification.

EFS, event-free survival; pCR, pathologic complete response.

Schmid P et al. Presented at the San Antonio Breast Cancer Symposium (SABCS) Congress 2023, 5–9 December, San Antonio, USA.



KEYNOTE-522: Exploratory analysis – EFS in the ITT population at 75-month follow-up



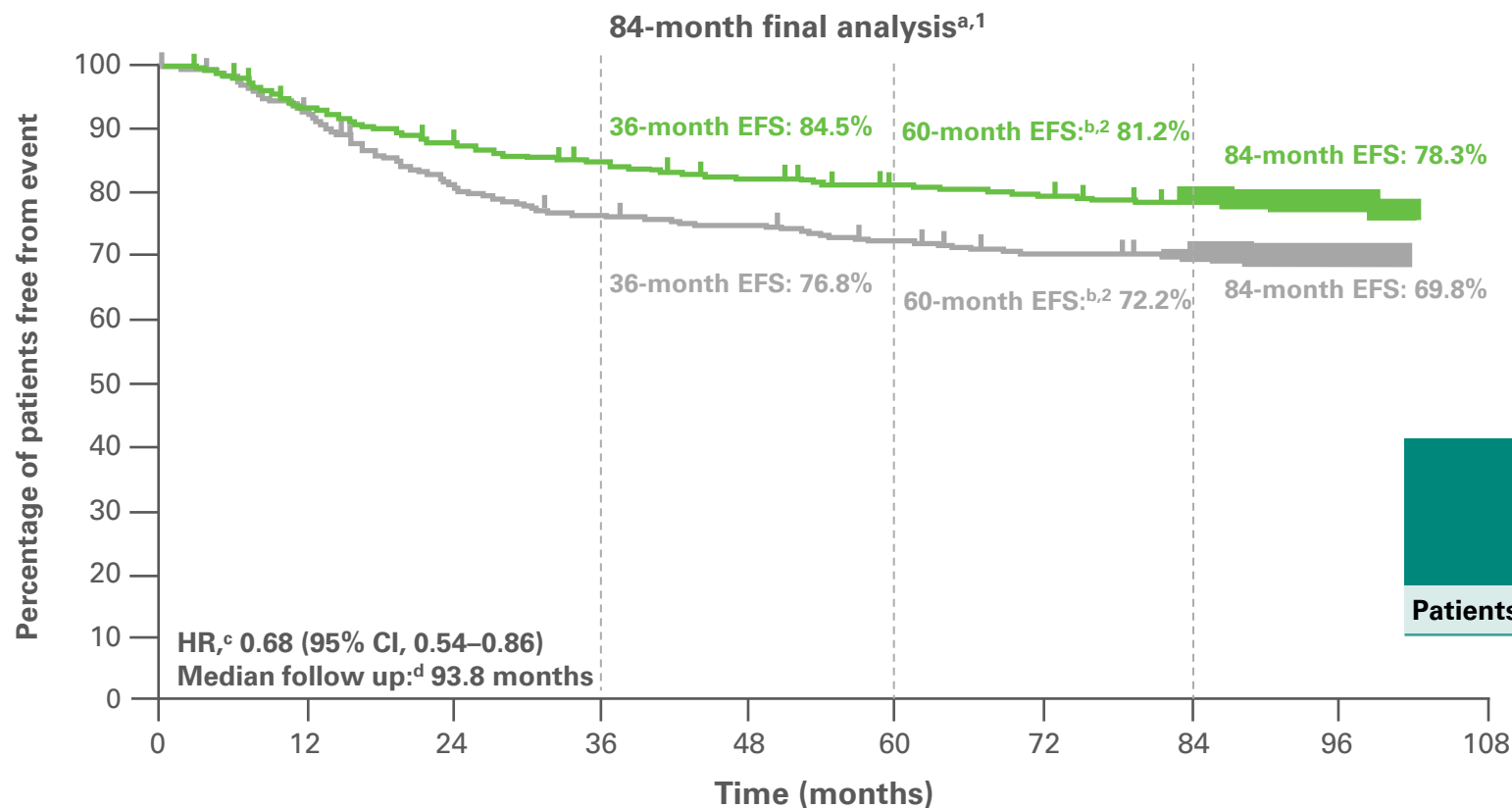
Descriptive EFS analysis only. Results provide an updated estimate of treatment effect following achievement of statistical significance at a prior prespecified analysis. No statistical conclusions can be drawn.

Data cut-off: 22 March 2024.
^aHR (CI) analysed based on a Cox regression model with treatment as a covariate stratified by the randomisation stratification factors.
CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat.
Schmid P et al. Presented at the European Society of Medical Oncology (ESMO) Congress 2024, 13–17 September, Barcelona, Spain.

Adapted from Schmid P et al. Presented at ESMO 2024.



KEYNOTE-522: Exploratory analysis – EFS in the ITT population at final analysis¹



Descriptive EFS analysis only. Results provide an updated estimate of treatment effect following achievement of statistical significance at a prior prespecified analysis. No statistical conclusions can be drawn.

	KEYTRUDA + chemotherapy/ KEYTRUDA (n=784)	Placebo + chemotherapy/ placebo (n=390)
Patients with event, %	21.9	30.3

No. at risk

KEYTRUDA + chemotherapy/KEYTRUDA	784	728	681	654	635	620	608	590	188	0
Placebo + chemotherapy/placebo	390	358	312	293	286	274	264	259	85	0

^aData cutoff: 14 October 2025;¹ ^bData cutoff: 22 March 2024.²

^cHR (CI) analysed based on a Cox regression model with treatment as a covariate stratified by the randomisation stratification factors;¹ ^dDefined as the time from randomisation to data cutoff.¹

CI, confidence interval; EFS, event-free survival; HR, hazard ratio; ITT, intention-to-treat.

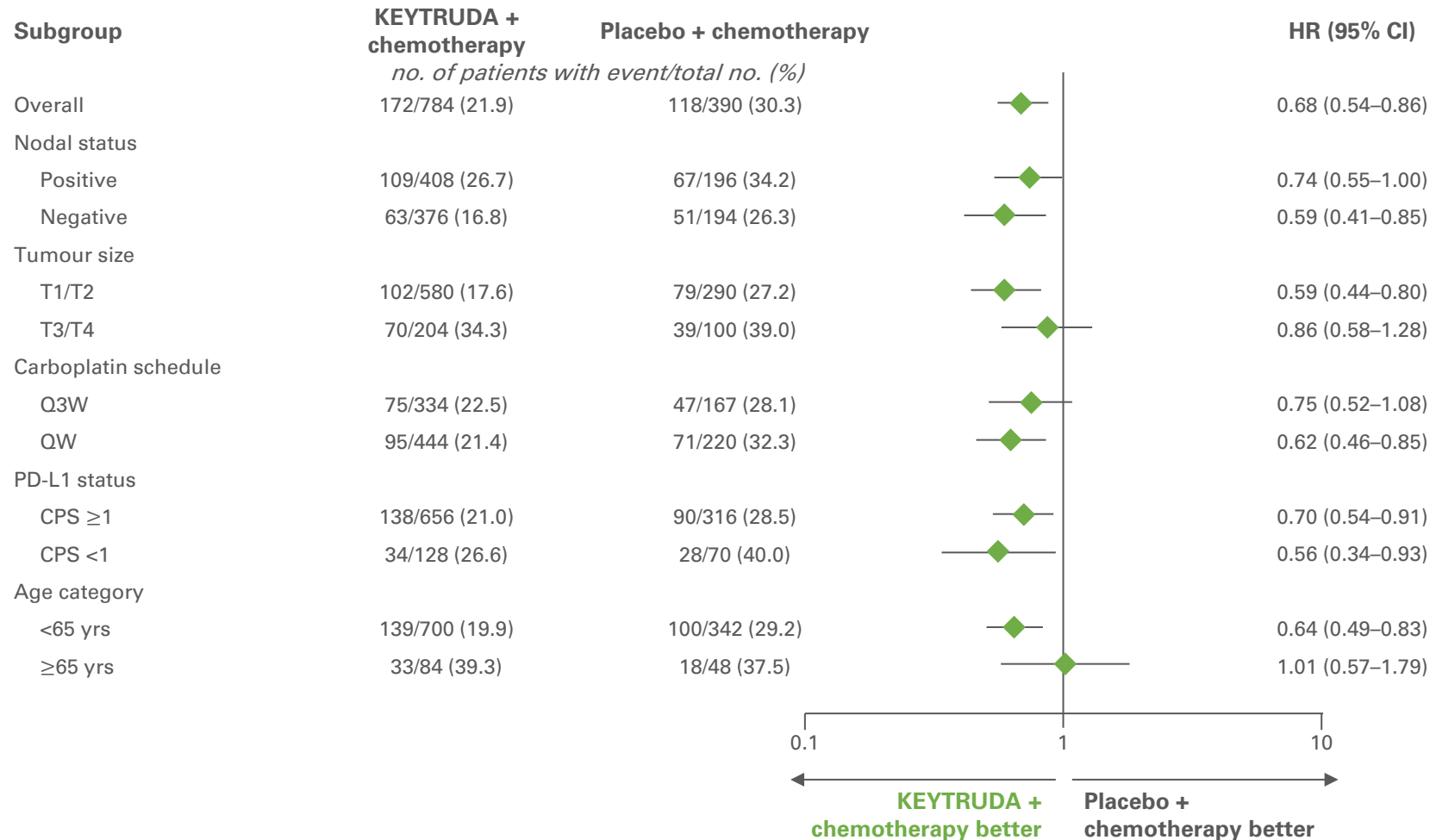
1. Schmid P et al. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2026, 29 May–2 June, Chicago, USA;

2. Schmid P et al. Presented at the European Society of Medical Oncology (ESMO) Congress 2024, 13–17 September, Barcelona, Spain.

Adapted from Schmid P et al. Presented at ASCO 2026.¹



KEYNOTE-522: Exploratory analysis – EFS in key subgroups at final analysis



KEYNOTE-522 was not powered to detect differences in treatment effect between these subgroups. Results from exploratory analyses should be interpreted with caution due to modest patient numbers and potential imbalances in baseline characteristics

Adapted from Schmid P et al. Presented at ASCO 2026.

Data cutoff: 14 October 2025.

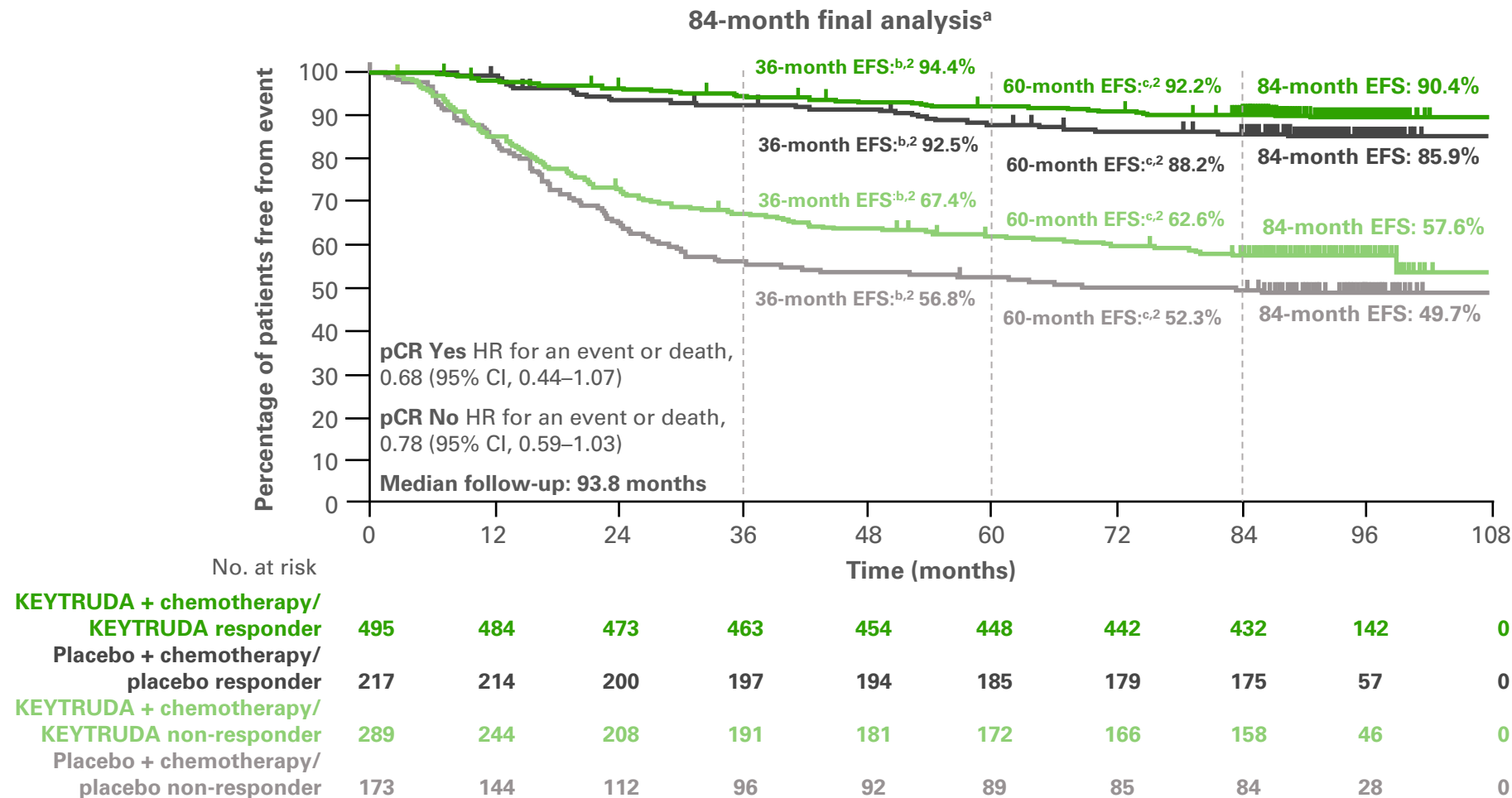
For the overall population and PD-L1 subgroups, analyses were based on a Cox regression model with Efron's method of tie handling, with treatment as a covariate and stratification by nodal status (positive vs negative), tumour size (T1/T2 vs T3/T4) and frequency of carboplatin administration (QW vs Q3W); for other subgroups, analysis was based on an unstratified Cox model.

CI, confidence interval; CPS, combined positive score; EFS, event-free survival; HR, hazard ratio; PD-L1, programmed death ligand-1; Q3W, every 3 weeks; QW, once a week; yr, years.

Schmid P et al. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2026, 29 May–2 June, Chicago, USA.



KEYNOTE-522: Exploratory analysis – EFS by pCR (ypT0/Tis ypN0) at final analysis¹



Adapted from Schmid P et al.
Presented at ASCO 2026.¹

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

^aData cutoff: 14 October 2025. This is a non-randomised subgroup analysis based on the post-treatment outcomes of pCR; HRs should be interpreted with caution;¹ ^bData cutoff: 23 March 2021;² ^cData cutoff: 23 March 2023.²

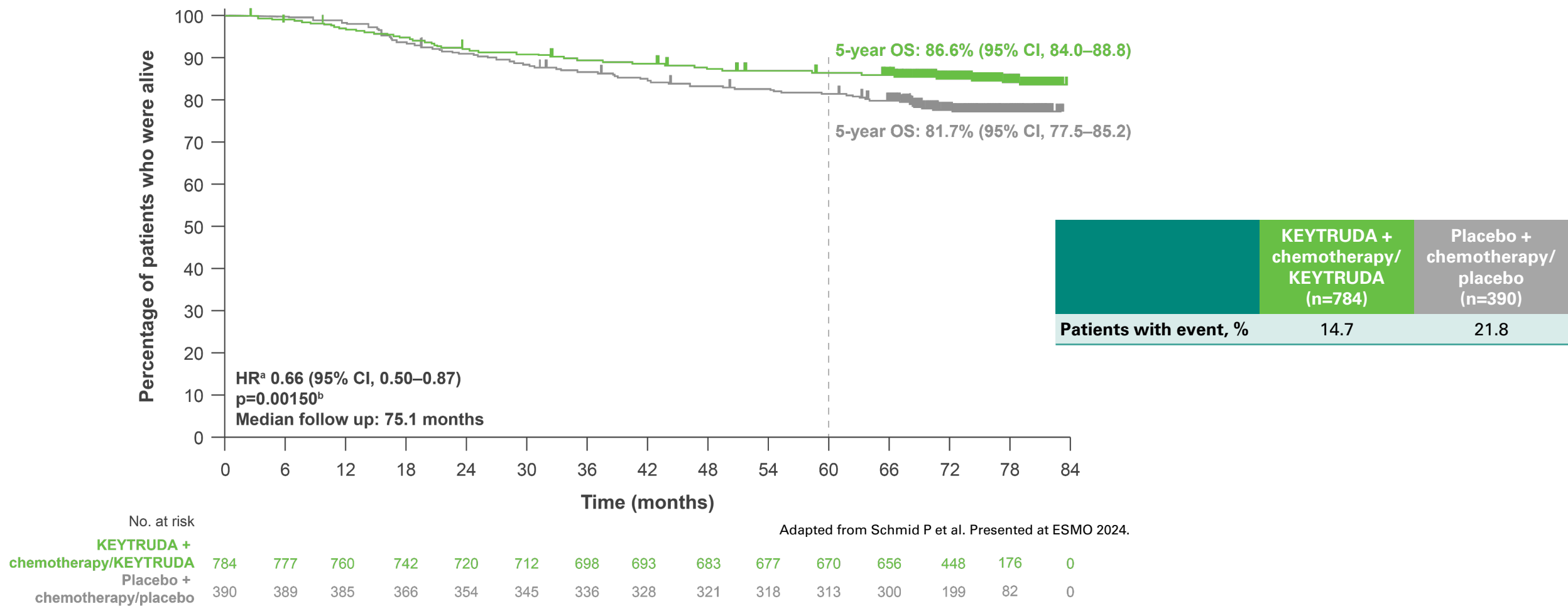
CI, confidence interval; EFS, event-free survival; HR, hazard ratio; pCR, pathologic complete response.

1. Schmid P et al. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2026, 29 May–2 June, Chicago, USA;

2. Schmid P et al. Presented at the European Society of Medical Oncology Congress 2023, 20–24 September, Madrid, Spain.



KEYNOTE-522: Key secondary endpoint – OS in the ITT population at 75-month follow-up



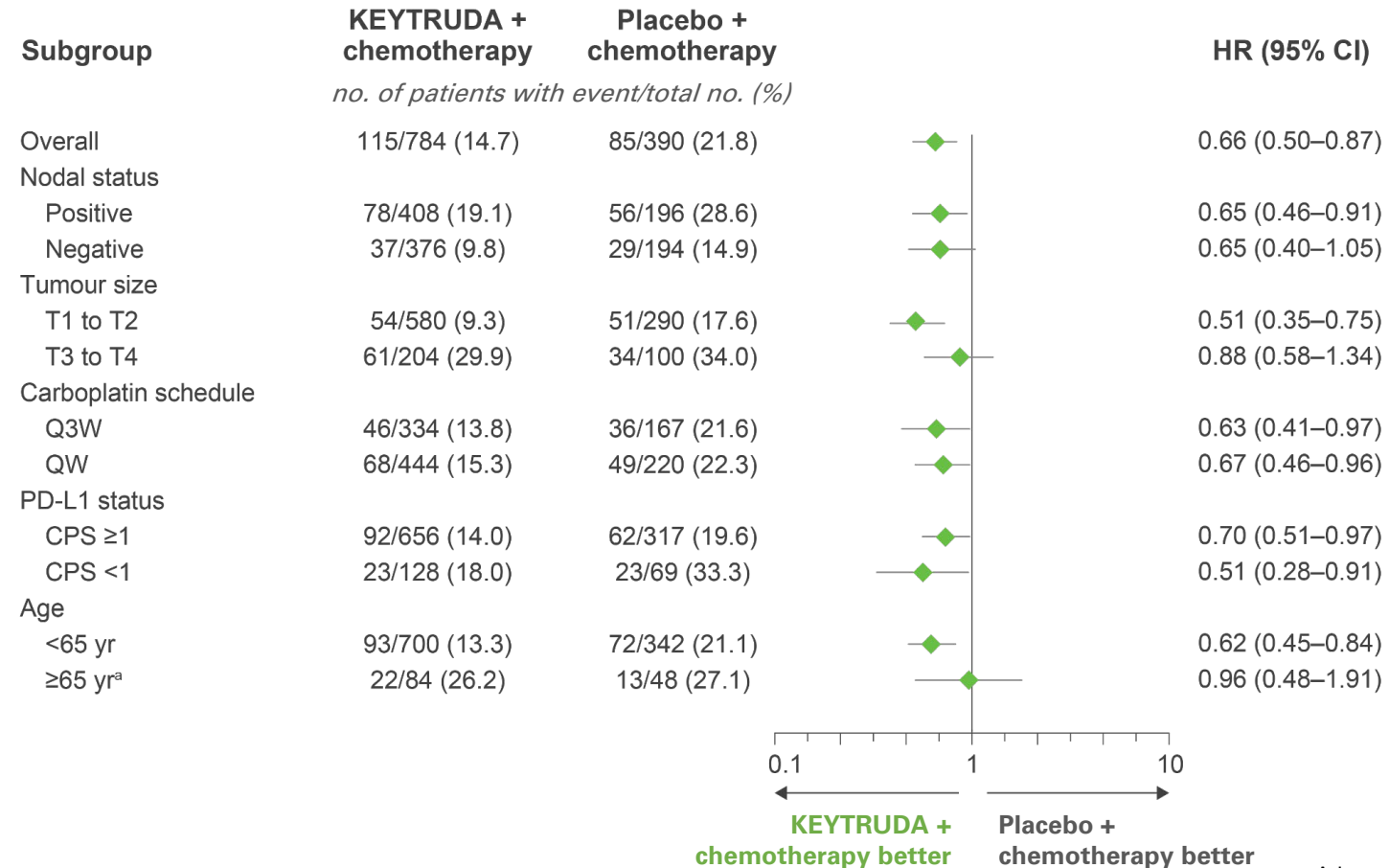
Data cutoff: 22 March 2024.

^aThe unstratified piecewise HR was 0.87 (95% CI, 0.57–1.32) before the 2-year follow up and 0.51 (95% CI, 0.35–0.75) afterwards. The weighted average HR with weights of number of events before and after 2-year follow up was 0.66; ^bWith 200 events (67.3% information fraction), the observed p-value crossed the prespecified nominal boundary of 0.00503 (one-sided) at this interim analysis. CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; OS, overall survival.

Schmid P et al. Presented at the European Society for Medical Oncology (ESMO) Congress 2024, 13–17 September, Barcelona, Spain.



KEYNOTE-522: Exploratory analysis – OS in key patient subgroups at 75-month follow-up



Adapted from Schmid P et al. Presented at ESMO 2024.

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Data cutoff: 22 March 2024.

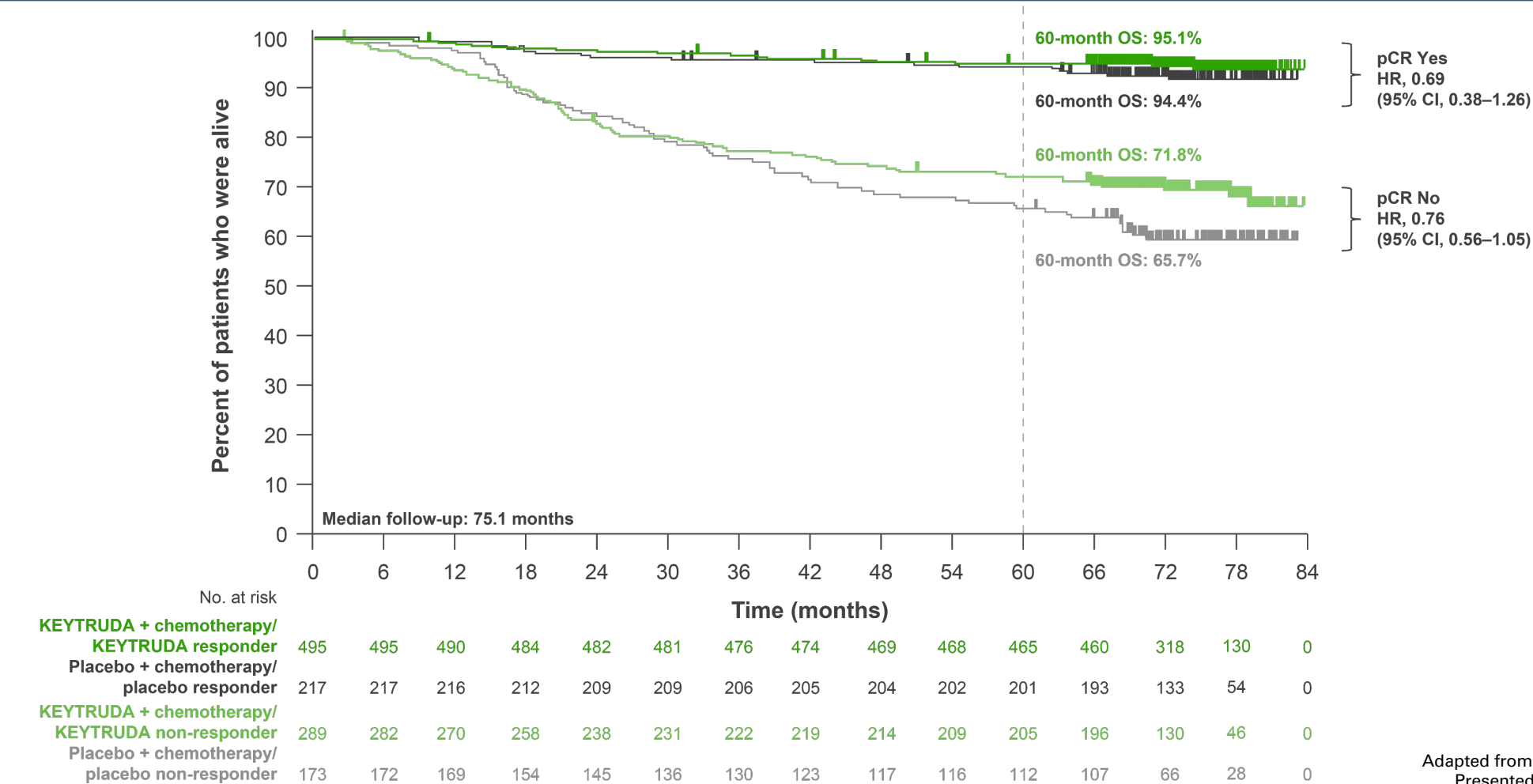
^aBased on the small sample size and few events, results should be interpreted with caution. For overall population and PD-L1 subgroups, analyses were based on Cox regression model with Efron's method of tie handling, with treatment as a covariate and stratified by nodal status (positive vs negative), tumour size (T1/T2 vs T3/T4), and frequency of carboplatin (Q3W vs QW); for other subgroups, analysis was based on an unstratified Cox model.

CI, confidence interval; CPS, combined positive score; HR, hazard ratio; OS, overall survival; PD-L1, programmed death ligand-1; Q3W, every 3 weeks; QW, once a week; yr, years.

Schmid P et al. Presented at the European Society for Medical Oncology (ESMO) Congress 2024, 13–17 September, Barcelona, Spain.



KEYNOTE-522: Exploratory analysis – OS by pCR (pathological stage ypT0/Tis ypN0) at 75-month follow-up



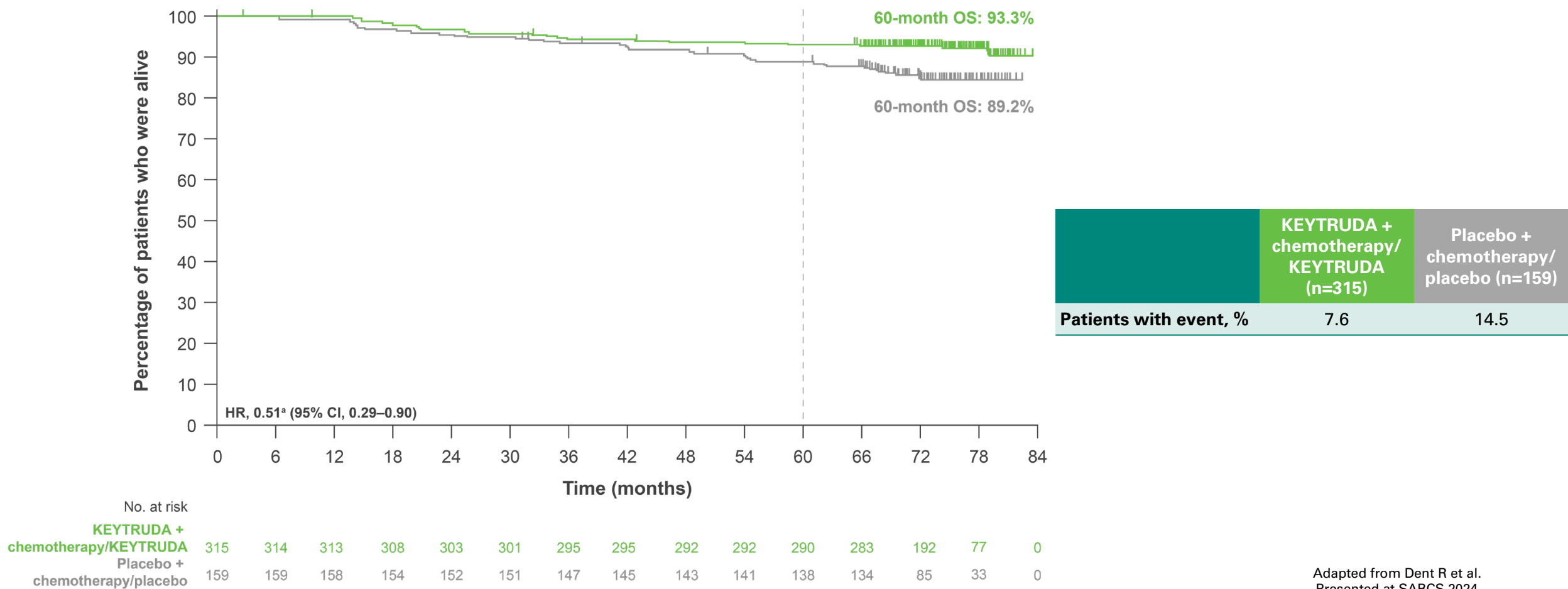
Adapted from Schmid P et al.
Presented at ESMO 2024.

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Data cutoff: 22 March 2024.
 This is a non-randomised subgroup analysis based on the post-treatment outcome of pCR. HRs should therefore be interpreted with caution.
 CI, confidence interval; HR, hazard ratio; OS, overall survival; pCR, pathologic complete response.
 Schmid P et al. Presented at the European Society for Medical Oncology (ESMO) Congress 2024, 13–17 September, Barcelona, Spain.



KEYNOTE-522: Exploratory analysis – OS in patients with baseline T2N0 disease at 75-month follow-up



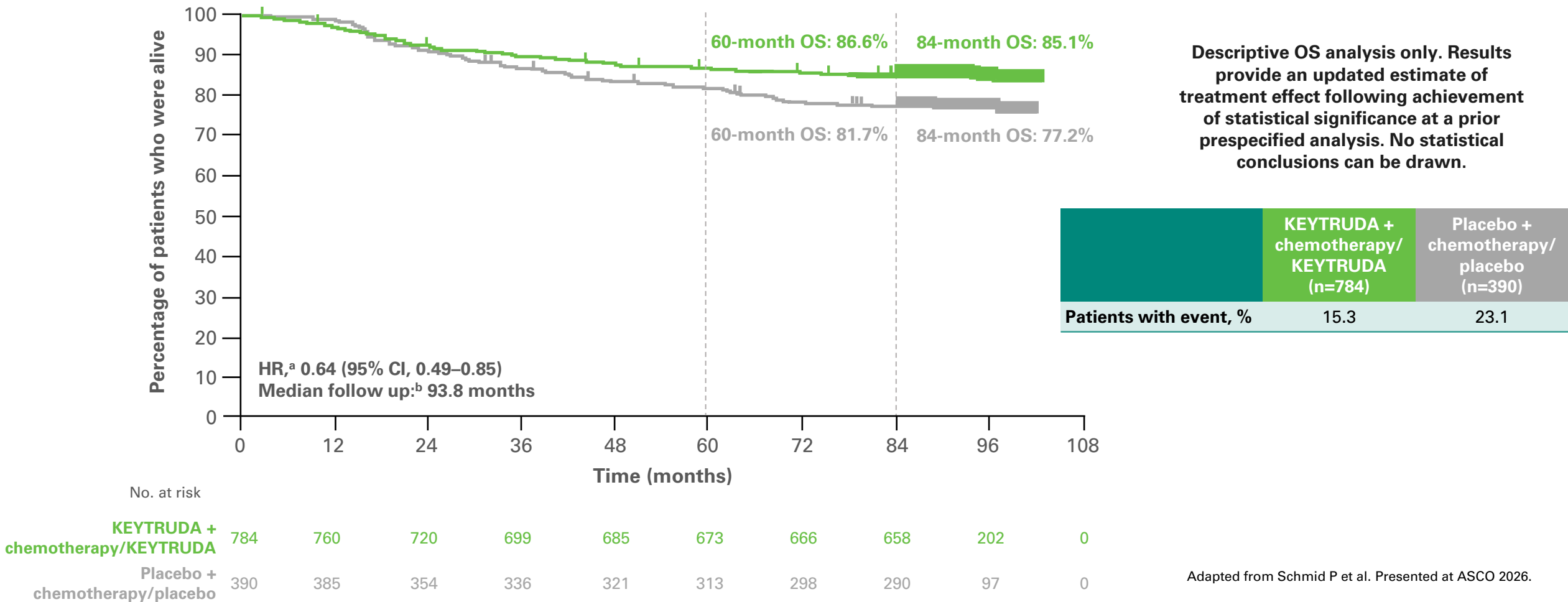
Adapted from Dent R et al.
Presented at SABCS 2024.

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Data cutoff: 22 March 2024.
^aHR (CI) analysed based on an unstratified Cox regression model with treatment as a covariate.
CI, confidence interval; HR, hazard ratio; OS, overall survival.
Dent R et al. Presented at the San Antonio Breast Cancer Symposium 2024, 10–13 December, San Antonio, USA.



KEYNOTE-522: Key secondary endpoint – OS in the ITT population at final analysis

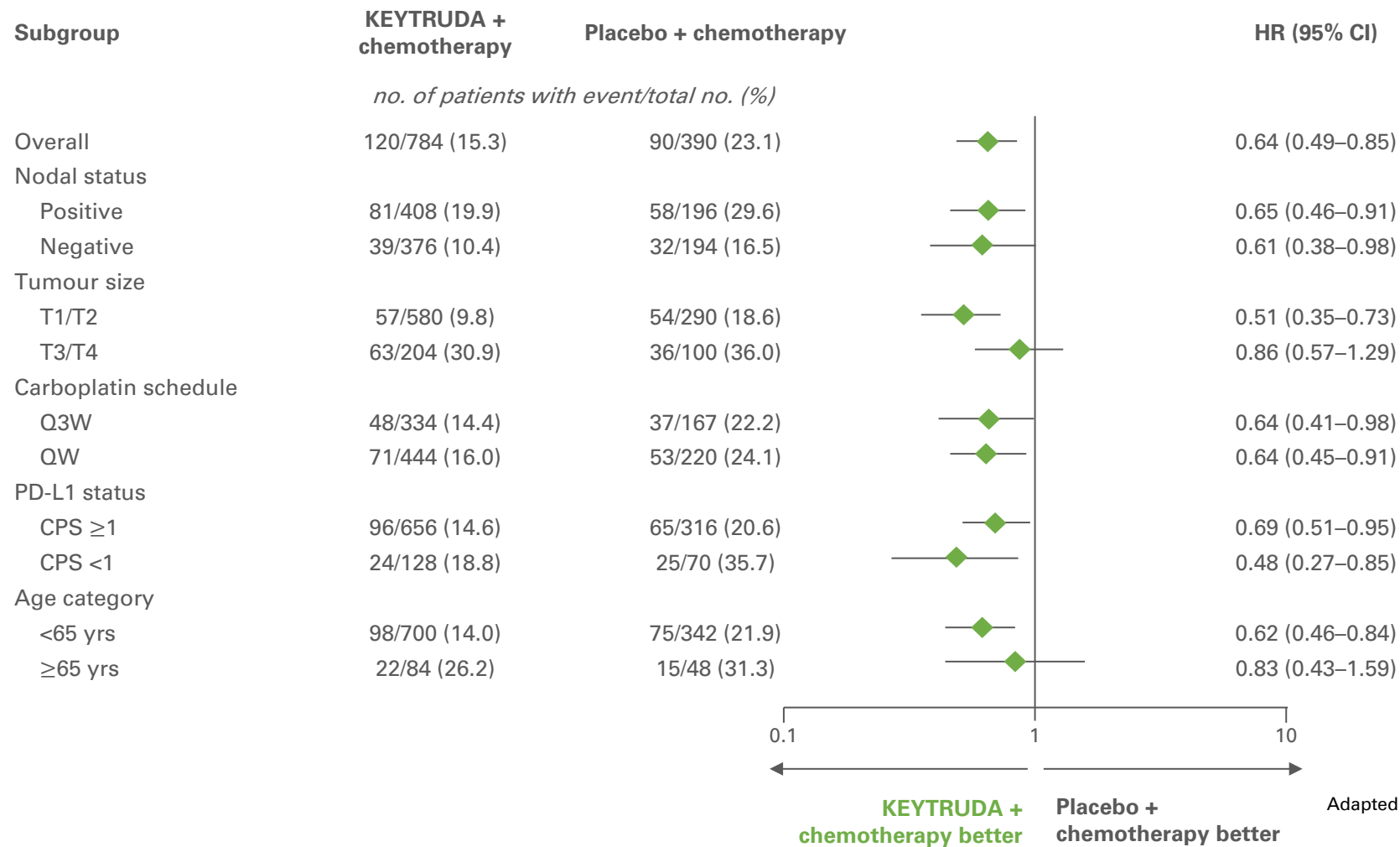


Adapted from Schmid P et al. Presented at ASCO 2026.

Data cutoff: 14 October 2025.
^aHR (CI) analysed based on a Cox regression model with treatment as a covariate stratified by the randomisation stratification factors; ^bDefined as the time from randomisation to data cutoff.
CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; OS, overall survival.
Schmid P et al. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2026, 29 May–2 June, Chicago, USA.



KEYNOTE-522: Exploratory analysis – OS in key patient subgroups at final analysis



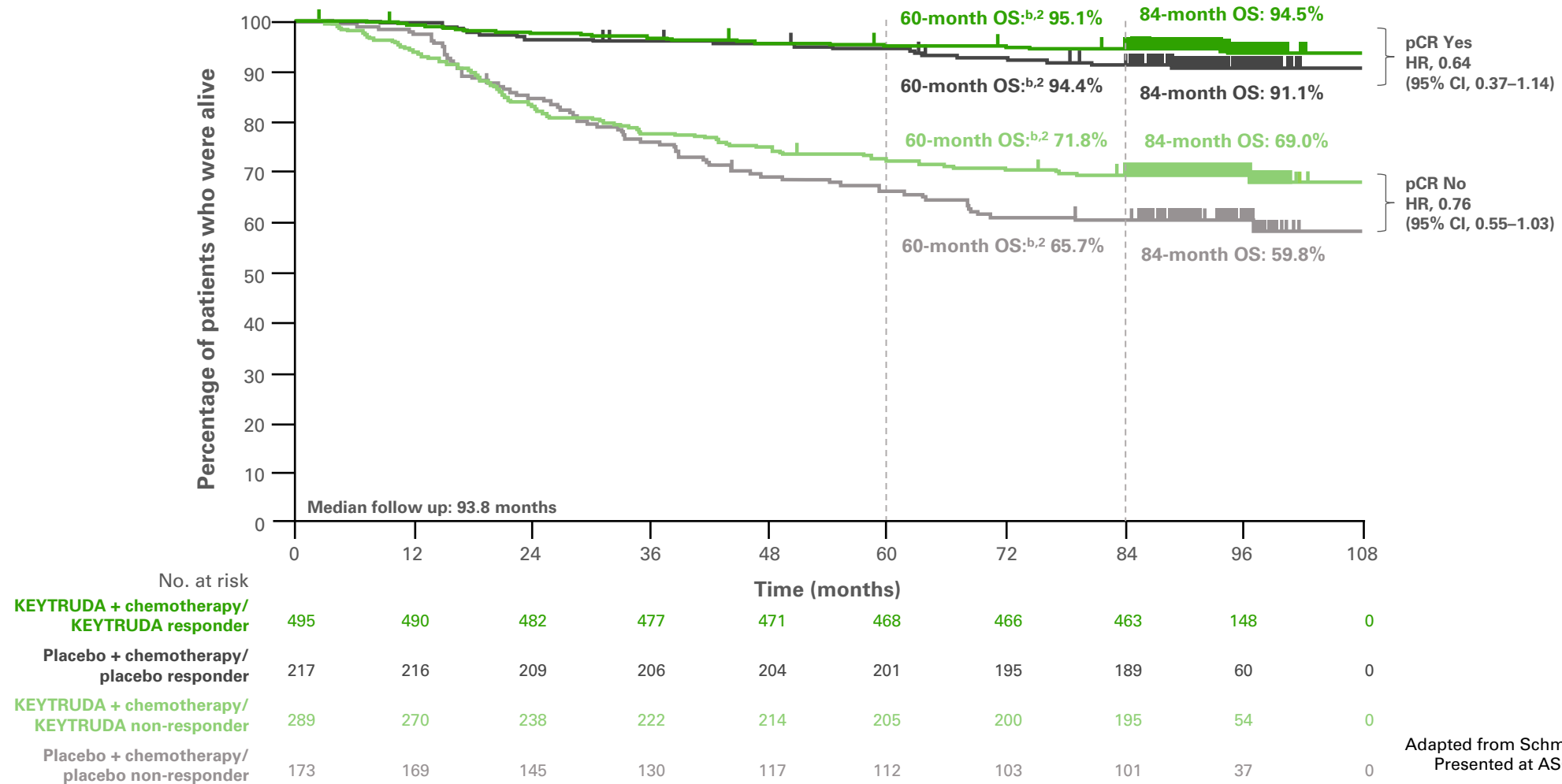
This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Adapted from Schmid P et al. Presented at ASCO 2026.

Data cutoff: 14 October 2025.
For the overall population and PD-L1 subgroups, analyses were based on a Cox regression model with Efron’s method of tie handling, with treatment as a covariate and stratification by nodal status (positive vs negative), tumour size (T1/T2 vs T3/T4) and frequency of carboplatin administration (QW vs Q3W); for other subgroups, analysis was based on an unstratified Cox model.
CI, confidence interval; CPS, combined positive score; HR, hazard ratio; OS, overall survival; PD-L1, programmed death ligand-1; Q3W, every 3 weeks; QW, once a week; yr, years.
Schmid P et al. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2026, 29 May–2 June, Chicago, USA.



KEYNOTE-522: Exploratory analysis – OS by pCR (pathological stage ypT0/Tis ypN0) at final analysis^{a,1}



This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

^aData cutoff: 14 October 2025. This is a non-randomised subgroup analysis based on the post-treatment outcome of pCR. HRs should therefore be interpreted with caution;¹ ^bData cutoff: 22 March 2024.²

CI, confidence interval; HR, hazard ratio; OS, overall survival; pCR, pathologic complete response.

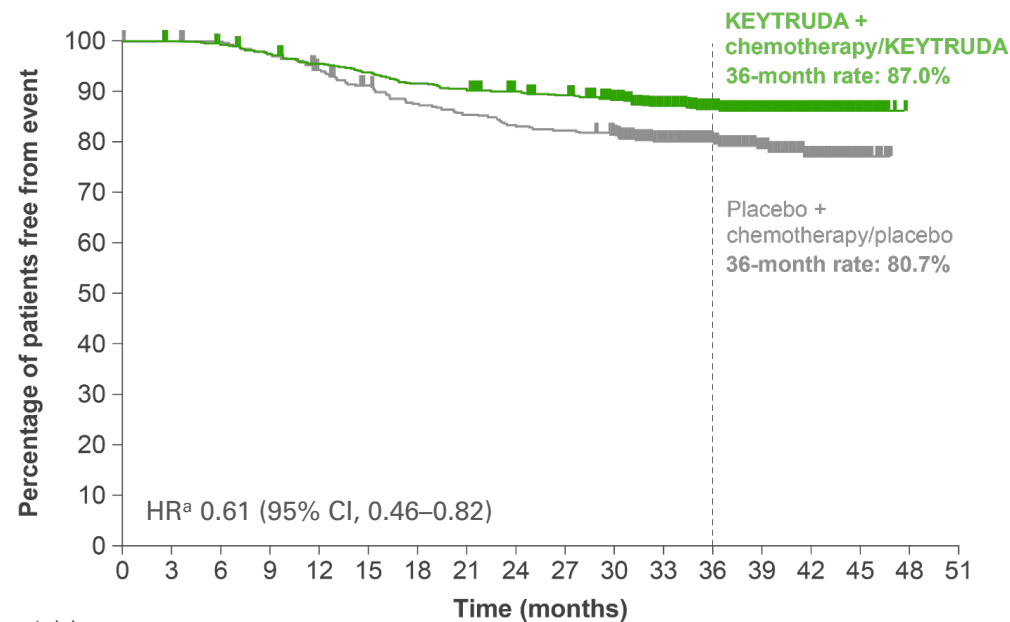
1. Schmid P et al. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2026, 29 May–2 June, Chicago, USA

2. Schmid P et al. Presented at the European Society for Medical Oncology (ESMO) Congress 2024, 13–17 September, Barcelona, Spain.



KEYNOTE-522: Exploratory analysis – DPFS or DRFS at 36 and 60 months

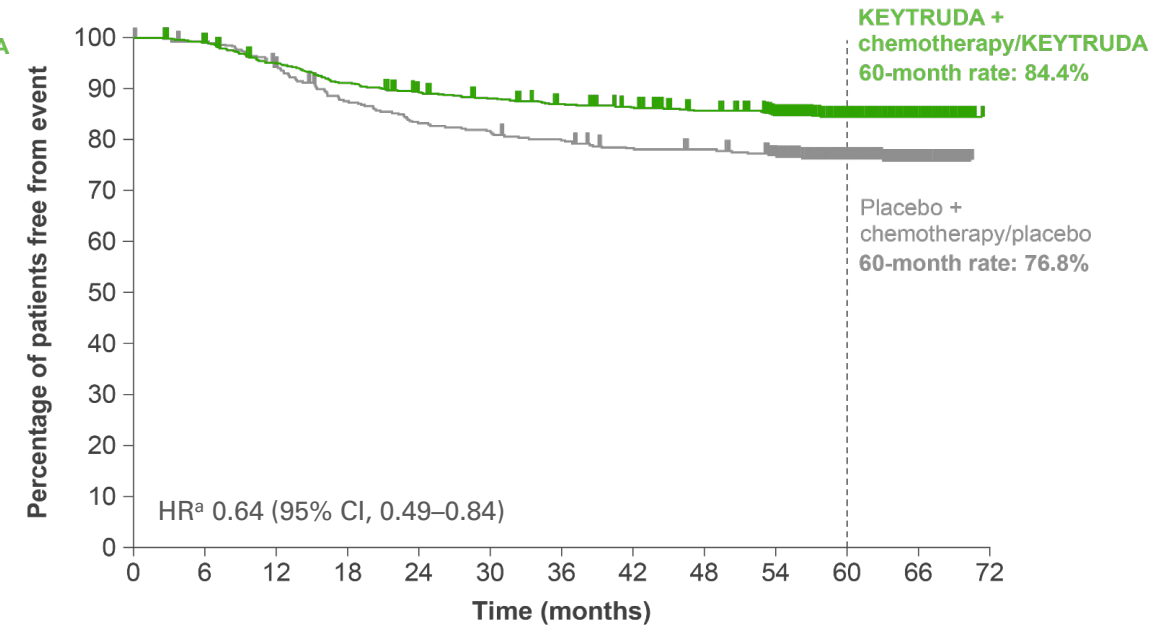
36 months



No. at risk

KEYTRUDA + chemotherapy/KETRUDA	784	782	773	758	741	728	711	702	692	685	663	561	439	308	167	29	0	0
Placebo + chemotherapy/placebo	390	389	387	379	367	352	337	330	321	317	312	259	202	143	84	17	0	0

60 months



784	774	742	711	692	681	667	659	645	626	416	164	0
390	387	367	338	322	316	308	298	295	287	195	82	0

Adapted from Schmid P et al. Presented at ESMO 2023.

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Data cut-off: 23 March 2021 and 23 March 2023.

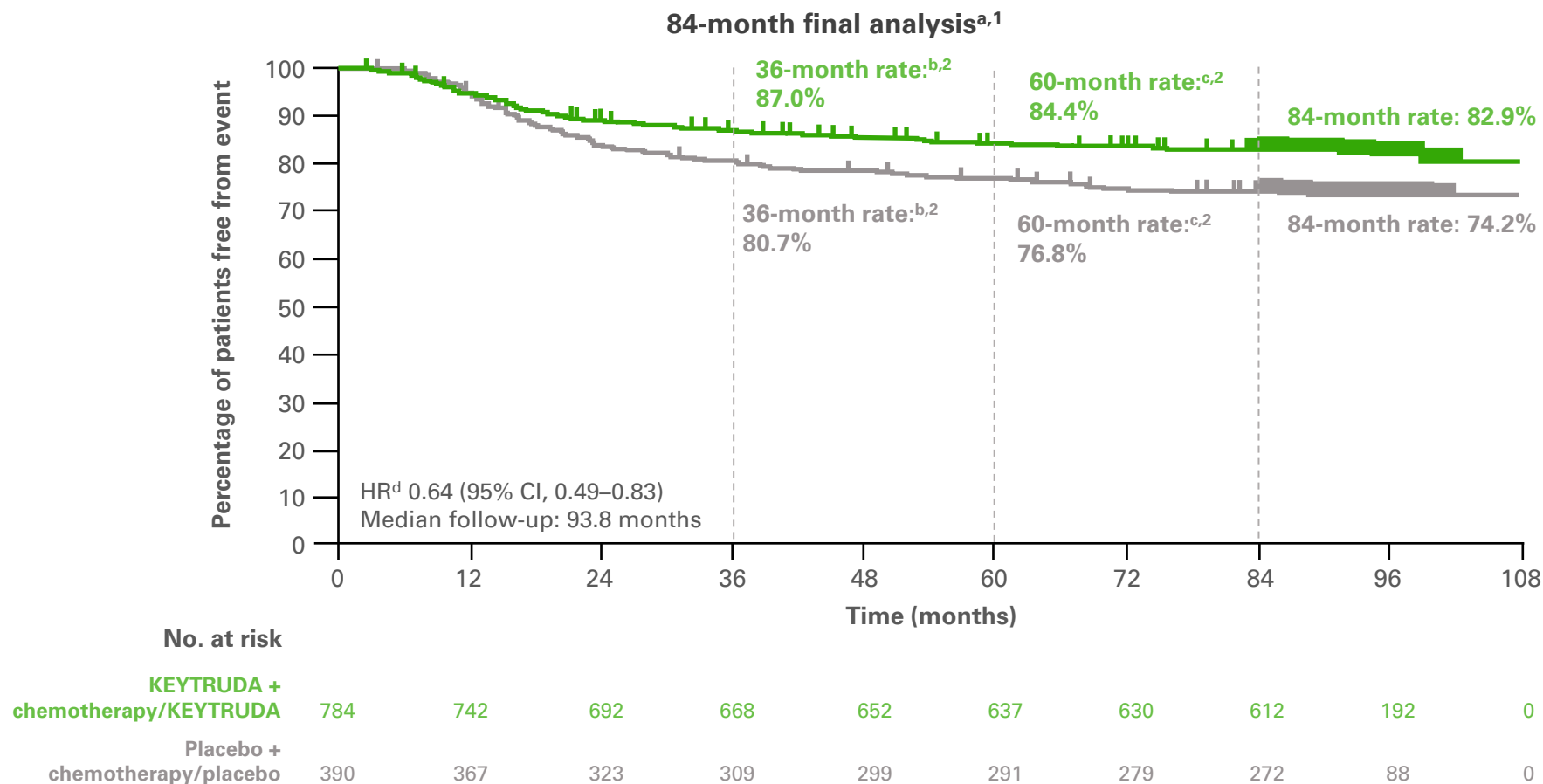
^aHR (CI) analysed based on a Cox regression model with treatment as a covariate stratified by randomisation stratification factors.

CI, confidence interval; DPFS, distant progression-free survival; DRFS, distant recurrence-free survival; HR, hazard ratio.

Schmid P et al. Presented at the European Society of Medical Oncology Congress 2023, 20–24 September, Madrid, Spain.



KEYNOTE-522: Exploratory analysis – DPFS or DRFS at final analysis¹



Adapted from Schmid P et al. Presented at ASCO 2026.¹

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

^aData cutoff: 14 October 2025;¹ ^bData cutoff: 23 March 2021;² ^cData cutoff: 23 March 2023;² ^dHR (CI) analysed based on a Cox regression model with treatment as a covariate stratified by randomisation stratification factors.¹

CI, confidence interval; DPFS, distant progression-free survival; DRFS, distant recurrence-free survival; HR, hazard ratio.

1. Schmid P et al. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2026, 29 May–2 June, Chicago, USA;

2. Schmid P et al. Presented at the European Society of Medical Oncology Congress 2023, 20–24 September, Madrid, Spain.

[UK Prescribing Information](#)



KEYNOTE-522: Results – Safety



Click the links below to navigate to the section of interest

Safety assessments

Neoadjuvant phase

**Summary of
any-grade AEs in the
neoadjuvant phase
(primary analysis)**

**AEs of interest in the
neoadjuvant phase
(primary analysis)**

Adjuvant phase

**TRAEs in the adjuvant
phase (36 months)**

**Immune-mediated AEs
and infusion reactions
in the adjuvant phase
(36 months)**

Combined phase

**Summary of safety
results in the
combined phase
(36 months)**

**Summary of any grade
TRAEs in the
combined phase
(75-month follow-up)**

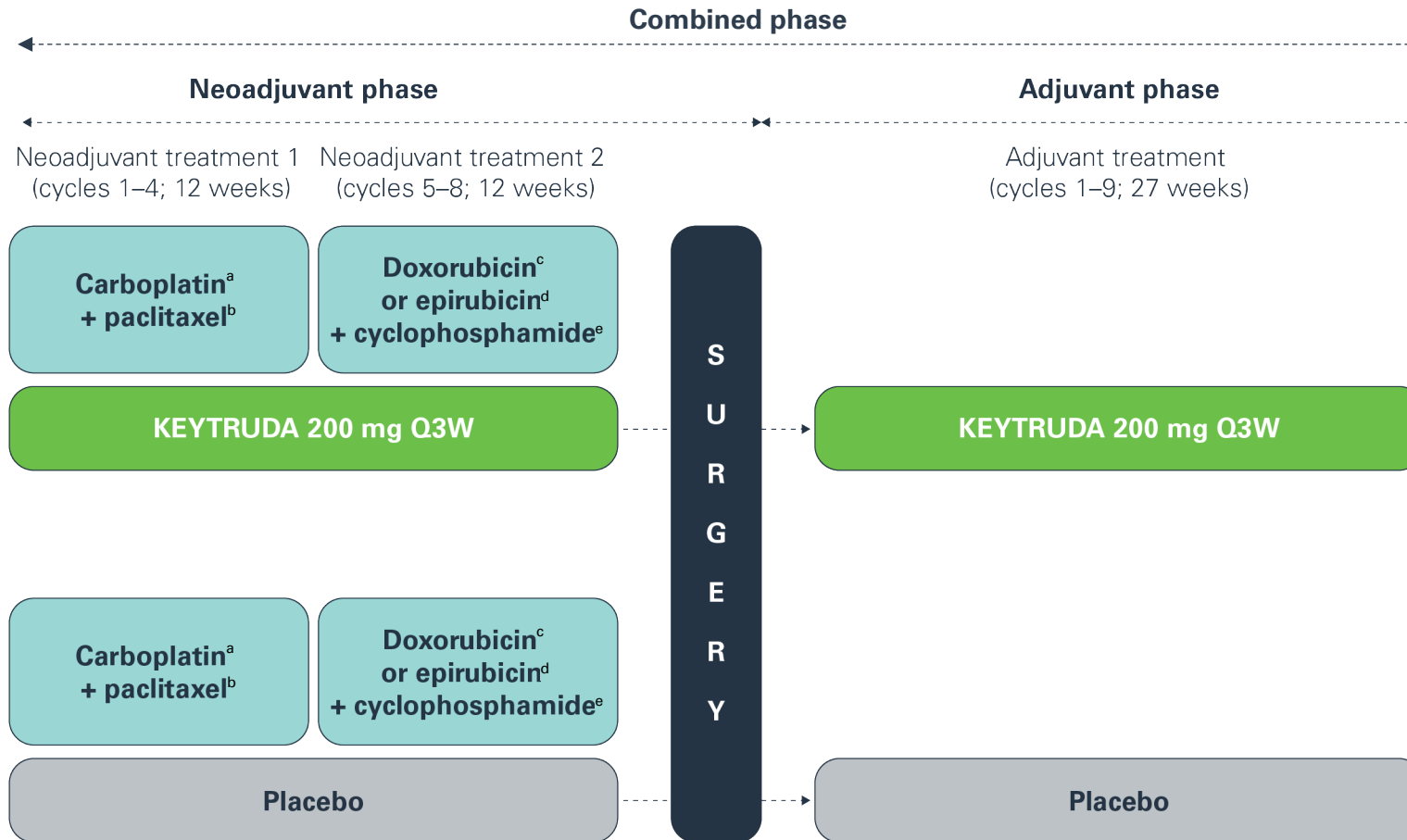
**Summary of
immune-mediated AEs
in the combined phase
(75-month follow-up)**

**Summary of any
grade TRAEs in the
combined phase
(final analysis)**

**Summary of
immune-mediated AEs
in the combined phase
(final analysis)**



KEYNOTE-522: Safety assessments^{1,2}



AEs were assessed during each phase of the study, as well as the study as a whole

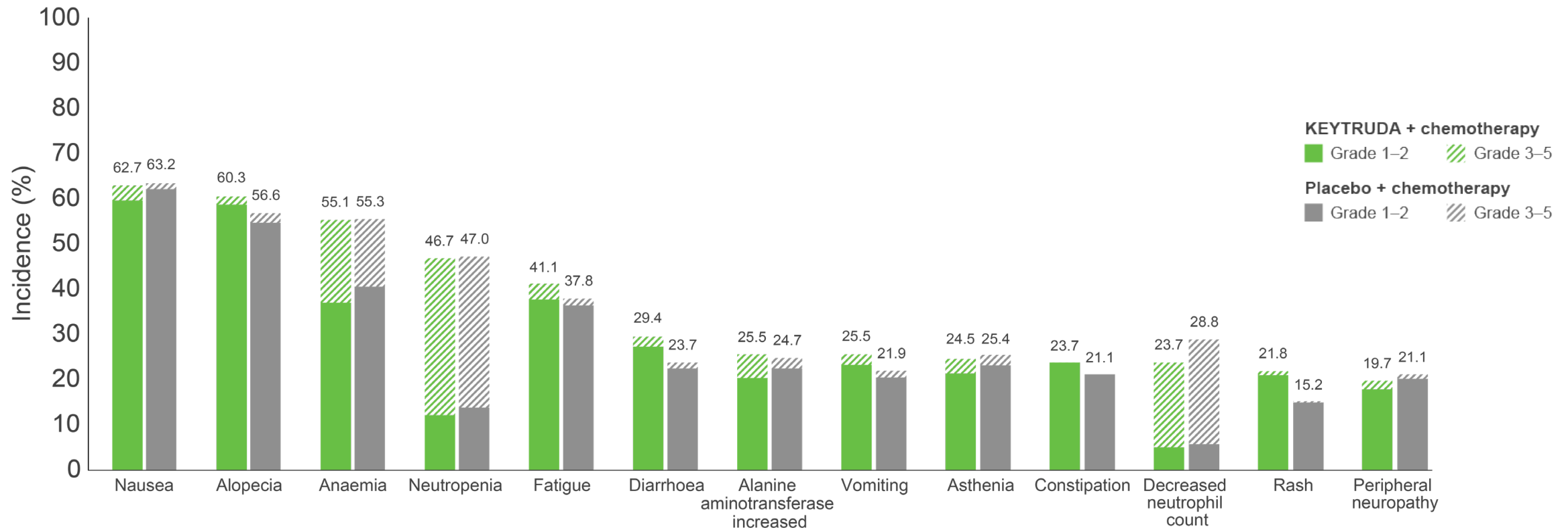
Adapted from Schmid P et al. 2020 and Schmid P et al. 2022.

^aCarboplatin dose was AUC 5 Q3W or AUC 1.5 QW; ^bPaclitaxel dose was 80 mg/m² QW; ^cDoxorubicin dose was 60 mg/m² Q3W; ^dEpirubicin dose was 90 mg/m² Q3W; ^eCyclophosphamide dose was 600 mg/m² Q3W. AE, adverse event; AUC, area under the curve; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; pCR, pathologic complete response; PD-L1, programmed death ligand-1; Q3W, every 3 weeks; QW, once a week; R, randomisation; TNBC, triple-negative breast cancer.

1. Schmid P et al. *N Engl J Med* 2020;382:810–821 (plus supplementary appendix); 2. Schmid P et al. *N Engl J Med* 2022;386:556–567 (plus supplementary appendix).



KEYNOTE-522: Summary of any-grade AEs occurring in $\geq 20\%$ of patients in the neoadjuvant phase at primary analysis



The tabular data for this plot is shown in the appendix. [Click here](#) to view.

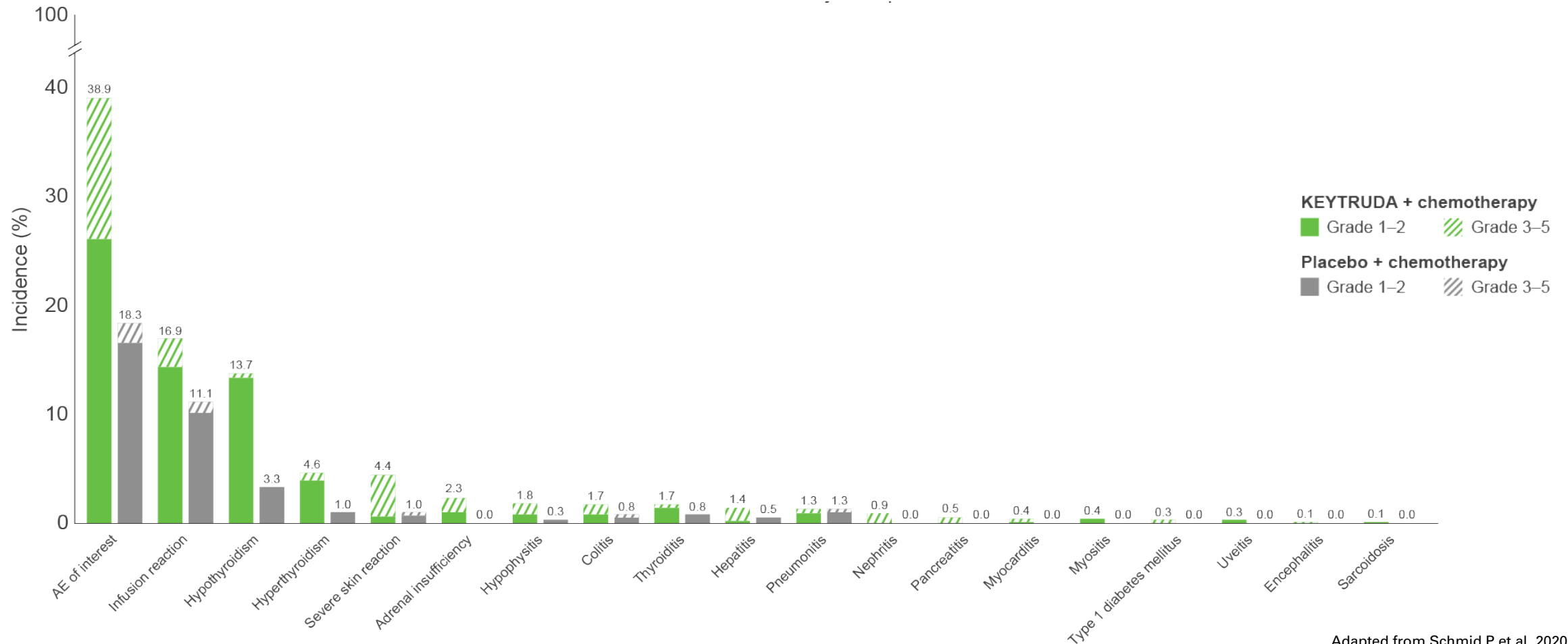
Adapted from Schmid P et al. 2020.

Listed are AEs that occurred during the treatment period or within 30 days after the treatment period (or, for serious AEs, within 90 days) in patients who were randomised and received at least one trial drug or surgery. The severity of the AEs was graded according to the Common Terminology Criteria for Adverse Events, v4.0, of the National Cancer Institute. Patients may have had more than one event.

AE, adverse event.
Schmid P et al. *N Engl J Med* 2020;382:810–821.



KEYNOTE-522: AEs of interest in the neoadjuvant phase at primary analysis^a



Adapted from Schmid P et al. 2020.

The tabular data for this plot is shown in the appendix. [Click here](#) to view.

Listed are AEs that occurred during the treatment period or within 30 days after the treatment period (or, for serious AEs, within 90 days) in patients who were randomised and received at least one trial drug or surgery. The severity of the AEs was graded according to the Common Terminology Criteria for Adverse Events, v4.0, of the National Cancer Institute. Patients may have had more than one event.

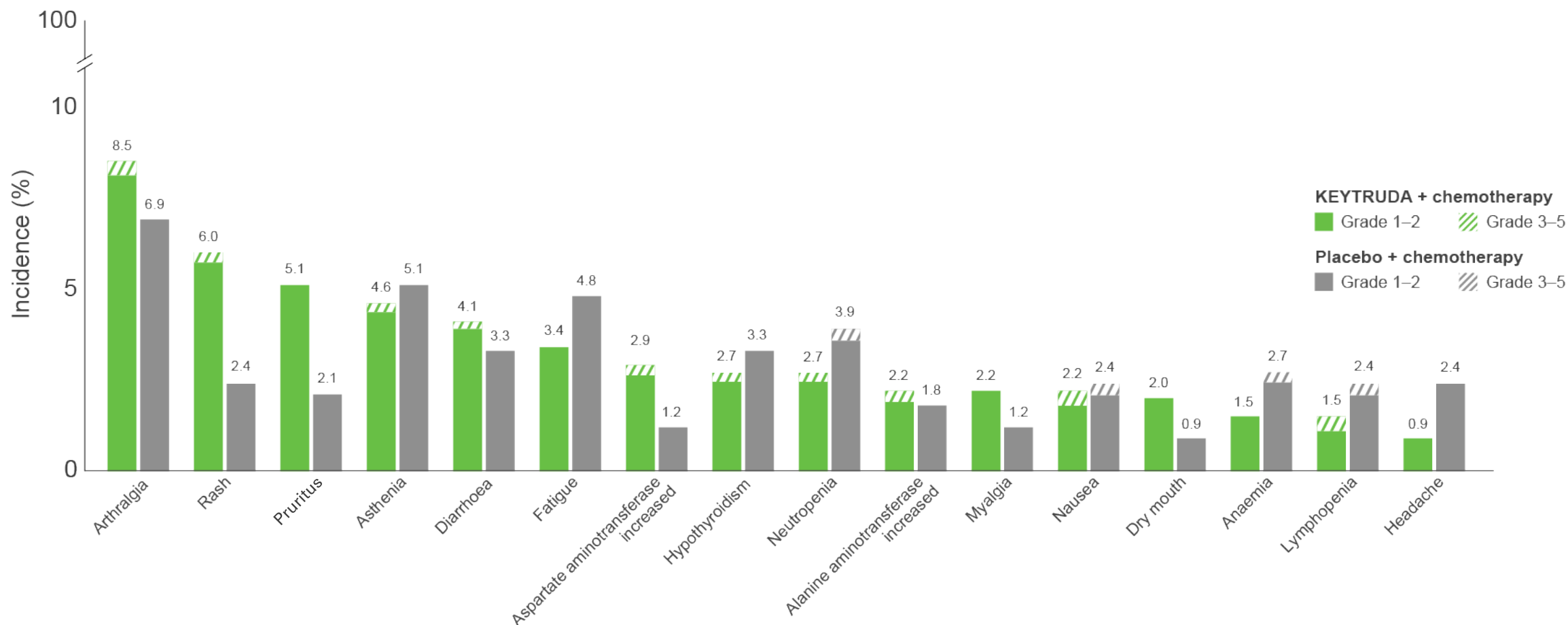
^aAEs of interest were determined according to a list of terms specified by the sponsor, regardless of attribution to any trial treatment by the investigators.

AE, adverse event.

Schmid P et al. *N Engl J Med* 2020;382:810–821 (plus supplementary appendix).



KEYNOTE-522: TRAEs occurring in $\geq 2\%$ of patients in the adjuvant phase at 36 months



The tabular data for this plot is shown in the appendix. [Click here](#) to view.

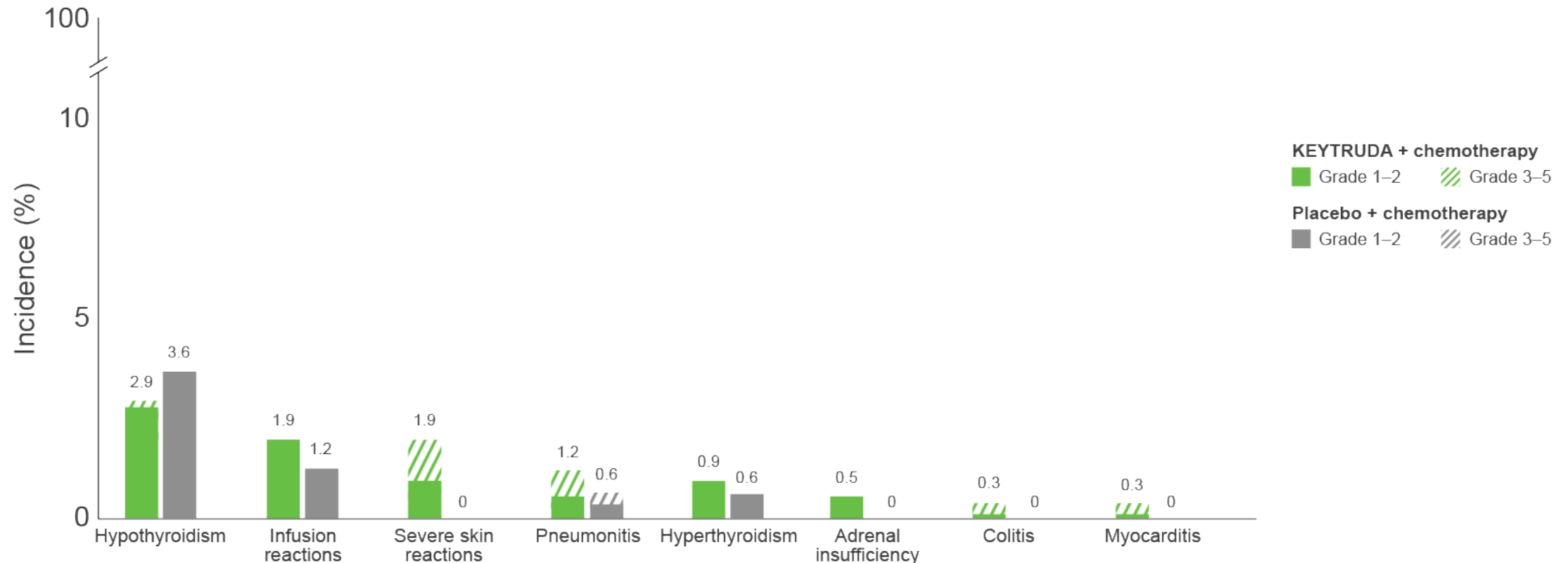
Adapted from Schmid P et al. Presented at ESMO 2021.

Listed are AEs that occurred during the treatment period or within 30 days after the treatment period (or, for serious AEs, within 90 days) in patients who were randomised and received at least one trial drug or surgery. The severity of the AEs was graded according to the Common Terminology Criteria for Adverse Events, v4.0, of the National Cancer Institute. Patients may have had more than one event. AE, adverse event; TRAE, treatment-related adverse event.

Schmid P et al. Presented at the European Society for Medical Oncology (ESMO) Virtual Plenary 2021, 16–21 September.



KEYNOTE-522: Immune-mediated AEs and infusion reactions in the adjuvant phase at 36 months¹



The tabular data for this plot is shown in the appendix. [Click here](#) to view.

Adapted from Schmid P et al. Presented at ESMO 2021.

Listed are AEs that occurred during the treatment period or within 30 days after the treatment period (or, for serious AEs, within 90 days) in patients who were randomised and received at least one trial drug or surgery. The severity of the AEs was graded according to the Common Terminology Criteria for Adverse Events, v4.0, of the National Cancer Institute. Patients may have had more than one event. Immune-mediated AEs were determined according to the sponsor, regardless of attribution to any trial treatment.² Grade 5 immune-mediated AE was autoimmune encephalitis (n=1) in the KEYTRUDA + chemotherapy group.¹ AE, adverse event.

1. Schmid P et al. Presented at the European Society for Medical Oncology (ESMO) Virtual Plenary 2021, 16–21 September; 2. Schmid P et al. *N Engl J Med* 2020;382:810–821.

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KEYNOTE-522: Summary of safety results in the combined (neoadjuvant and adjuvant) phase at 36 months

Immune-mediated AEs and infusion reactions

	KEYTRUDA + chemotherapy/ KEYTRUDA (n=783)	Placebo + chemotherapy/ placebo (n=389)
Any	341 (43.6)	85 (21.9)
Grade 1–2	224 (28.6)	77 (19.8)
Grade 3–4	115 (14.7)	8 (2.1) ^a
Grade 5	2 (0.3) ^b	0
Led to dose reduction^c		
Chemotherapy ^d	1 (0.1) ^e	0
Led to treatment interruption		
KEYTRUDA/placebo	43 (5.5)	9 (2.3)
Chemotherapy ^d	88 (11.2)	25 (6.4)
Led to discontinuation of any drug		
KEYTRUDA/placebo	61 (7.8)	4 (1.0)
Chemotherapy ^d	45 (5.7)	7 (1.8)

Time to onset and management of the most common (≥20 patients) immune-mediated AEs and infusion reactions

	KEYTRUDA + chemotherapy/ KEYTRUDA (n=783)	Placebo + chemotherapy/ placebo (n=389)
Infusion reactions, n (%)	141 (18.0)	45 (11.6)
Median time to onset (range), days	16 (1–458)	22 (1–325)
Treated with corticosteroids, n	85	28
Hypothyroidism, n (%)	118 (15.1)	22 (5.7)
Median time to onset (range), days	105 (7–510)	255 (7–527)
Treated with thyroid replacement, n	106	13
Severe skin reactions, n (%)	45 (5.7)	4 (1.0)
Median time to onset (range), days	64 (4–479)	50.5 (32–186)
Treated with corticosteroids, n	28	0
Hyperthyroidism, n (%)	41 (5.2)	7 (1.8)
Median time to onset (range), days	107 (20–470)	184 (1–284)
Adrenal insufficiency, n (%)	20 (2.6)	0
Median time to onset (range), days	175.5 (100–383)	-
Treated with hormone replacement, n	20	-

Adapted from Cortés J et al. Presented at SABCS 2023.

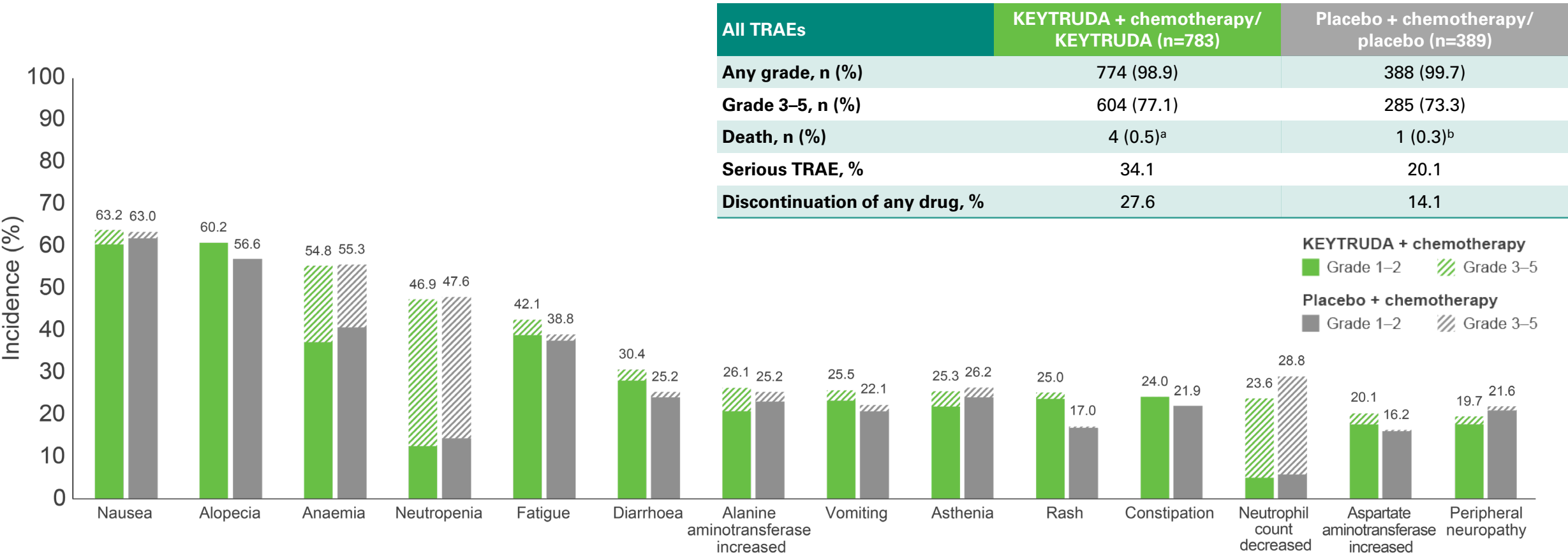
^aThere were no Grade 4 immune-mediated AEs or infusion reactions; ^bn=1 with pneumonitis (neoadjuvant phase), n=1 with autoimmune encephalitis (adjuvant phase); ^cDose reduction was not allowed for KEYTRUDA or placebo; ^dChemotherapy was administered during the neoadjuvant phase only; ^eDue to a severe skin reaction.
AE, adverse event.

Cortés J et al. Presented at the San Antonio Breast Cancer Symposium (SABCS) Congress 2023, 5–9 December, San Antonio, USA.

[UK Prescribing Information](#)



KEYNOTE-522: Summary of any-grade TRAEs occurring in ≥20% of patients in the combined neoadjuvant and adjuvant phases at 75-month follow-up^{1,2}



The tabular data for this plot is shown in the appendix. [Click here](#) to view.

Adapted from Schmid P et al. Presented at ESMO 2024.¹

Data cut-off: 22 March 2024. AEs were assessed during each phase of the study, as well as the study as a whole. Listed are AEs that occurred during the treatment period or within 30 days after the treatment period (or, for serious AEs, within 90 days) in patients who were randomised and received at least one trial drug or surgery. The severity of the AEs was graded according to the Common Terminology Criteria for Adverse Events v4.0 of the National Cancer Institute. Patients may have had more than one event.

^aGrade 5 AEs in the KEYTRUDA + chemotherapy arm were sepsis and multiple organ dysfunction syndrome (n=1) and pneumonitis, pulmonary embolism and autoimmune encephalitis (n=1 in each group);

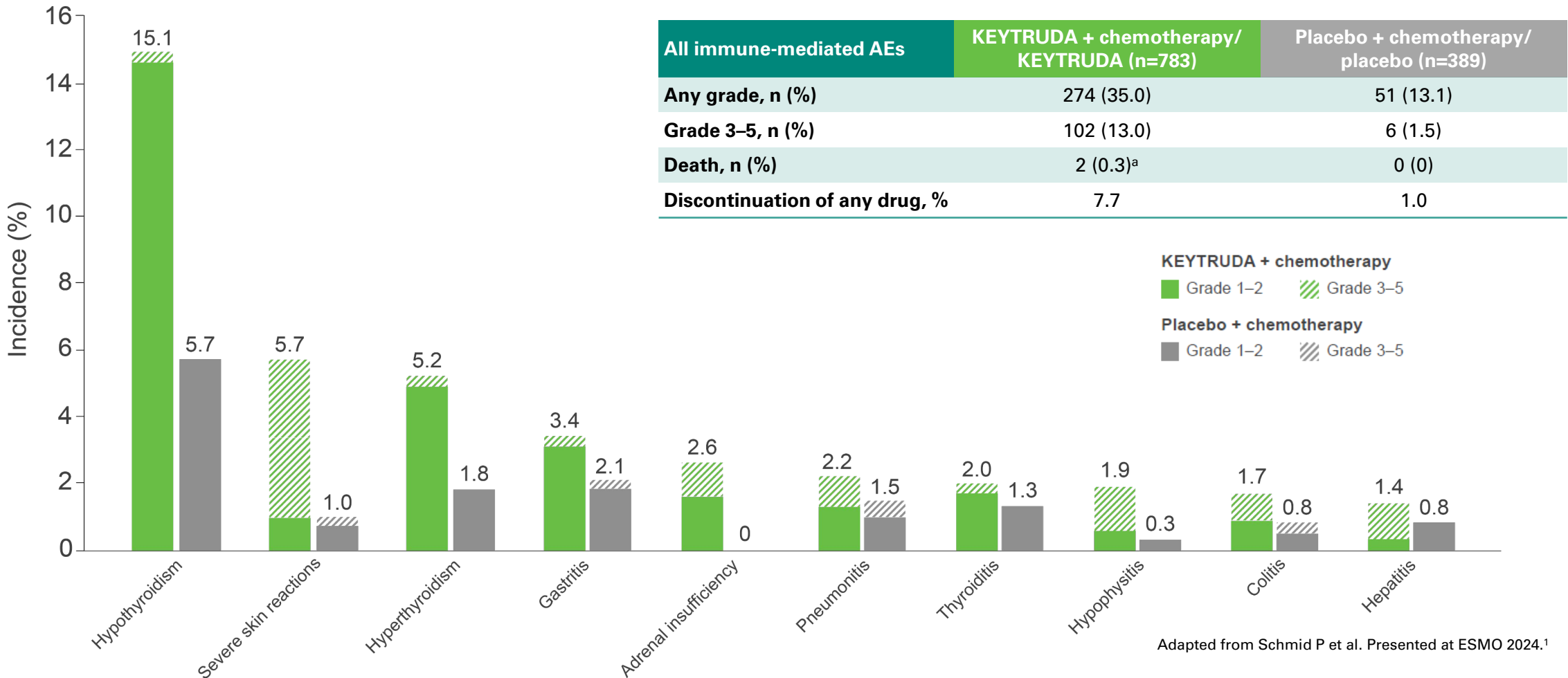
^bGrade 5 AEs in the placebo + chemotherapy arm were septic shock (n=1). AE, adverse event; TRAE, treatment-related adverse event.

1. Schmid P et al. Presented at the European Society of Medical Oncology Congress 2024, 13–17 September, Barcelona, Spain;

2. Schmid P et al. *N Engl J Med* 2024;391:1981–1991.



KEYNOTE-522: Summary of immune-mediated AEs occurring in ≥10 patients in the combined neoadjuvant and adjuvant phases at 75-month follow-up^{1,2}

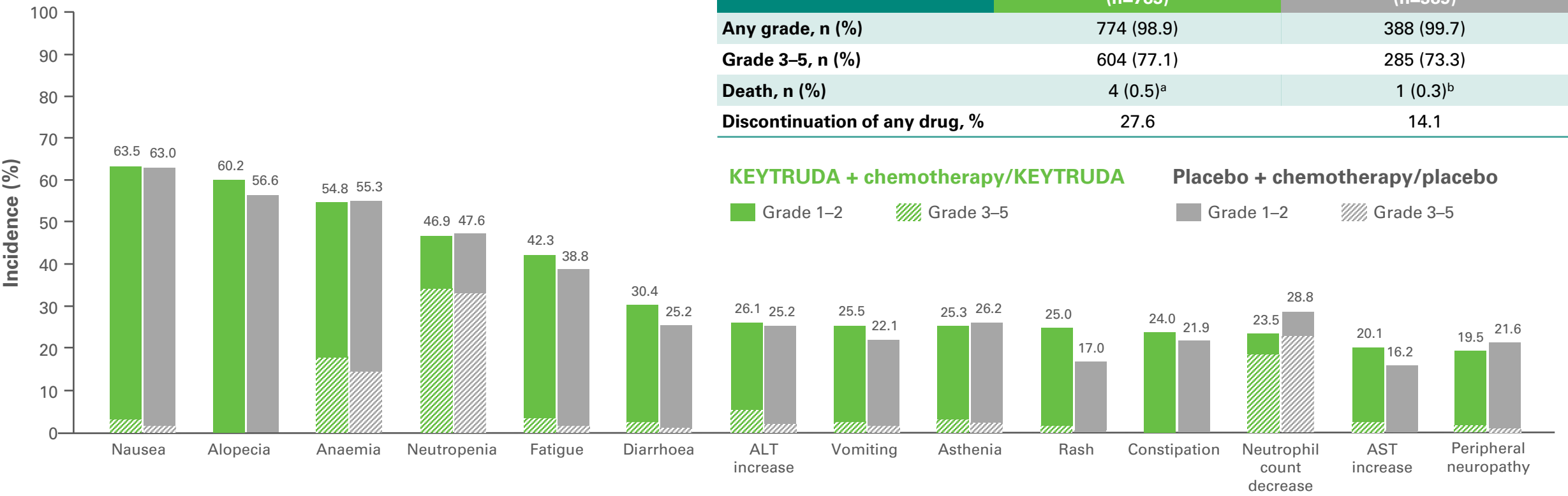


The tabular data for this plot is shown in the appendix. [Click here](#) to view.

Data cut-off: 22 March 2024. Data presented for AEs experienced by ≥10 patients.
^aOne patient from pneumonitis and one patient from autoimmune encephalitis. Considered regardless of attribution to treatment or immune-relatedness by the investigator. Related terms included in addition to preferred terms listed. AE, adverse event.
1. Schmid P et al. Presented at the European Society of Medical Oncology Congress 2024, 13–17 September, Barcelona, Spain;
2. Schmid P et al. *N Engl J Med* 2024;391:1981–1991.



KEYNOTE-522: Summary of any-grade TRAEs occurring in ≥20% of patients in the combined neoadjuvant and adjuvant phases at final analysis



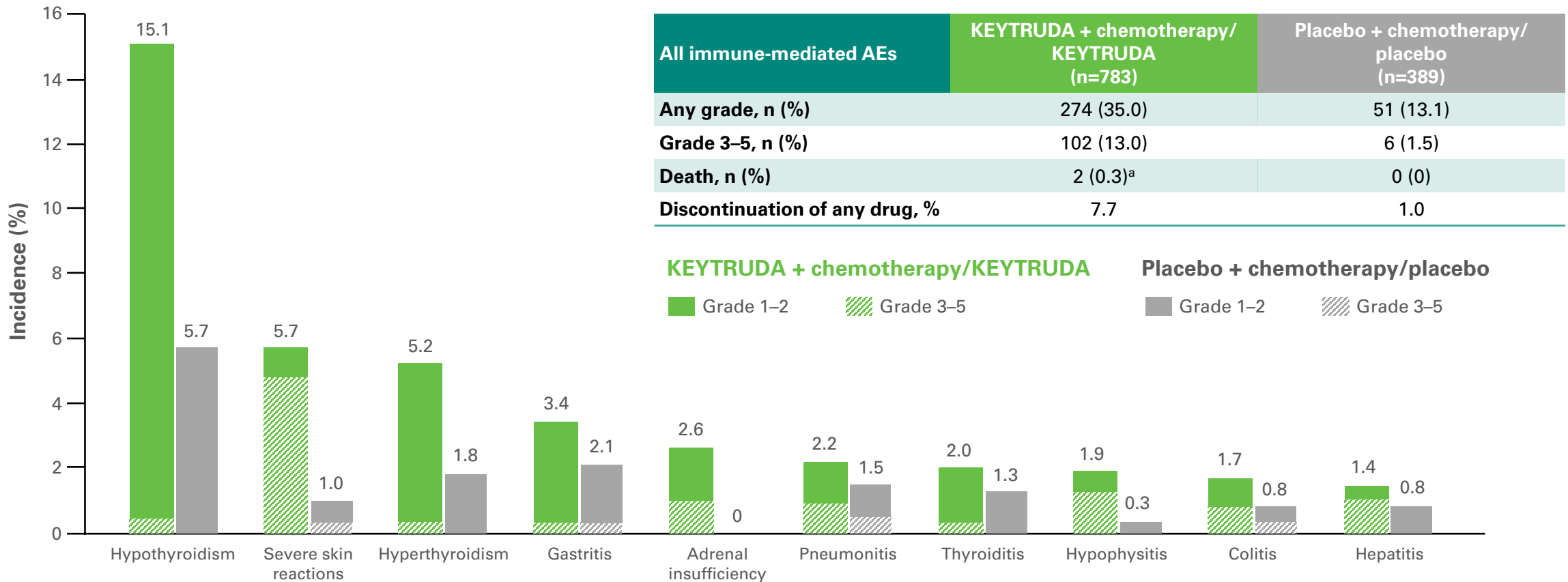
All TRAEs	KEYTRUDA + chemotherapy/ KEYTRUDA (n=783)	Placebo + chemotherapy/ placebo (n=389)
Any grade, n (%)	774 (98.9)	388 (99.7)
Grade 3–5, n (%)	604 (77.1)	285 (73.3)
Death, n (%)	4 (0.5) ^a	1 (0.3) ^b
Discontinuation of any drug, %	27.6	14.1

Adapted from Schmid P et al. Presented at ASCO 2026.

Data cutoff: 14 October 2025. Listed are AEs attributed to trial treatment by investigators; patients may have had more than one event.
^aGrade 5 AEs in the KEYTRUDA + chemotherapy/KEYTRUDA arm were sepsis and multiple organ dysfunction syndrome (n=1), and pneumonitis, pulmonary embolism and autoimmune encephalitis (n=1 each);
^bGrade 5 AEs in the placebo + chemotherapy/placebo arm were septic shock (n=1).
AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TRAE, treatment-related adverse event.
Schmid P et al. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2026, 29 May–2 June, Chicago, USA.



KEYNOTE-522: Summary of immune-mediated AEs occurring in ≥ 10 patients in the combined neoadjuvant and adjuvant phases at final analysis



Adapted from Schmid P et al. Presented at ASCO 2026.



Implementing KEYTRUDA + chemotherapy for early-stage TNBC



Click the links below to navigate to the section of interest

**KEYTRUDA dosing in
KEYNOTE-522**

**KEYTRUDA offers
flexibility of dosing**



KEYTRUDA dosing in KEYNOTE-522

First neoadjuvant phase¹



200 mg KEYTRUDA
+ paclitaxel^a and carboplatin^b



Q3W
up to 12 weeks



Second neoadjuvant phase¹



200 mg KEYTRUDA + doxorubicin^c
or epirubicin^d and
cyclophosphamide^e



Q3W
up to 12 weeks



Adjuvant cycle²



200 mg KEYTRUDA monotherapy
(radiation therapy concurrently or
2 weeks prior to adjuvant KEYTRUDA)



Q3W
up to 27 weeks

Patients should be treated with KEYTRUDA until disease progression or unacceptable toxicity³

Atypical responses (i.e. an initial transient increase in tumour size or new small lesions within the first few months, followed by tumour shrinkage) have been observed³

It is recommended to continue treatment in clinically stable patients with initial evidence of disease progression until disease progression is confirmed³

No dose reductions of KEYTRUDA are recommended. KEYTRUDA should be withheld or discontinued to manage AEs as described within the SmPC³

When administering KEYTRUDA in combination with IV chemotherapy, KEYTRUDA should be administered first³

Consult the full KEYTRUDA SmPC for guidance on dosing

^a80 mg/m² QW; ^bAUC of 5 mg/mm/min Q3W or 1.5 mg/mm/min QW; ^c60 mg/m² Q3W; ^d90 mg/m² Q3W; ^e600 mg/m² Q3W.

AE, adverse event; AUC, area under the curve; IV, intravenous; Q3W, every 3 weeks; QW, once a week; SmPC, Summary of Product Characteristics.

1. Schmid P et al. *N Engl J Med* 2020;382:810–821; 2. Schmid P et al. *N Engl J Med* 2022;386:556–567;

3. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: <https://www.medicines.org.uk/emc/product/2498/smpc>. Accessed August 2025.



KEYTRUDA offers flexibility of dosing

KEYTRUDA dosing:



**Administered
as an IV infusion**



**Over 30
minutes**



200 mg Q3W or 400 mg Q6W

Patients should be treated with KEYTRUDA until disease progression or unacceptable toxicity.

Atypical responses (i.e. an initial transient increase in tumour size or new small lesions within the first few months, followed by tumour shrinkage) have been observed.

It is recommended to continue treatment in clinically stable patients with suspected disease progression until disease progression is confirmed.

No dose reductions of KEYTRUDA are recommended. KEYTRUDA should be withheld or discontinued to manage AEs as described within the SmPC.

When administering KEYTRUDA in combination with IV chemotherapy, KEYTRUDA should be administered first.

Consult the full KEYTRUDA SmPC for guidance on dosing.

The KEYTRUDA 200 mg Q3W regimen has been assessed in Phase 2 and Phase 3 registration studies across a multitude of indications. An exposure–response evaluation (using modelling and simulation) led to the approval of the 400 mg Q6W dosing for monotherapy and combination therapy.



KEYNOTE-522: Summary



Click the links below to navigate to the section of interest

Summary: Efficacy

Summary: Safety



Summary: Efficacy (1)



KEYTRUDA, in combination with chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment after surgery, is indicated in the treatment of adults with locally advanced or early-stage TNBC at high risk of recurrence¹

- There was a statistically significant improvement in pCR rates with KEYTRUDA + chemotherapy (neoadjuvant treatment) vs placebo + chemotherapy (neoadjuvant treatment) in the primary analysis (64.8% vs 51.2%, respectively; $p < 0.001$) and in the prespecified final analysis of KEYNOTE-522 (64.0% vs 54.7%, respectively; $p = 0.00221$)¹
- KEYTRUDA + chemotherapy in the neoadjuvant setting, followed by KEYTRUDA monotherapy as adjuvant treatment, resulted in a statistically significant improvement in EFS compared with placebo + chemotherapy followed by placebo at the 36-month analysis (HR, 0.63; 95% CI, 0.48–0.82 [$p < 0.001$])^{a,b,2} and numerically higher EFS at the 75-month (HR, 0.65; 95% CI: 0.51–0.83)^{a,3} and 84-month follow ups (HR, 0.68; 95% CI, 0.54–0.86)^{a,4}
 - At 36-, 75- and 84-month follow ups, the percentages of patients who experienced an event were 15.7%, 20.3% and 21.9% in the KEYTRUDA + chemotherapy group, and 23.8%, 29.2% and 30.3% in the placebo + chemotherapy group, respectively^{2–4}
- An exploratory analysis of EFS in key subgroups, including disease stage, nodal status and T2N0 status, suggested a benefit for patients treated with KEYTRUDA + chemotherapy vs placebo + chemotherapy^{2,4,5}

^aHR (CI) analysed based on a Cox regression model with treatment as a covariate stratified by the randomisation stratification factors;^{2–4} ^bPrespecified p-value boundary of 0.00517 was crossed.

CI, confidence interval; EFS, event-free survival; HR, hazard ratio; pCR, pathologic complete response; TNBC, triple-negative breast cancer.

1. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: <https://www.medicines.org.uk/emc/product/2498/smpc>. Accessed August 2025;

2. Schmid P et al. *N Engl J Med* 2022;386:556–567; 3. Schmid P et al. Presented at the European Society of Medical Oncology (ESMO) Congress 2024, 13–17 September, Barcelona, Spain;

4. Schmid P et al. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2026, 29 May–2 June, Chicago, USA;

5. Schmid P et al. Presented at the San Antonio Breast Cancer Symposium (SABCS) Congress 2023, 5–9 December, San Antonio, USA.



Summary: Efficacy (2)



KEYTRUDA, in combination with chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment after surgery, is indicated in the treatment of adults with locally advanced or early-stage TNBC at high risk of recurrence¹

- An exploratory analysis of EFS by pCR (ypT0/Tis ypN0) suggested a benefit for KEYTRUDA + chemotherapy vs placebo + chemotherapy regardless of pCR outcome at 36 months of follow up, with the difference maintained at the 84-month final analysis^{2,3}
- KEYTRUDA + chemotherapy in the neoadjuvant setting, followed by KEYTRUDA monotherapy as adjuvant treatment, resulted in a statistically significant and clinically meaningful improvement in OS (key secondary endpoint) at 75-month follow up (HR, 0.66; 95% CI, 0.50–0.87 [p=0.00150])^a compared with neoadjuvant placebo + chemotherapy followed by placebo in patients with previously untreated, high-risk, early-stage TNBC³
 - This trend in OS improvement was maintained at the 84-month final analysis (HR, 0.64; 95% CI, 0.49–0.85)^{b,2}
 - OS was numerically higher for patients treated with KEYTRUDA + chemotherapy vs placebo + chemotherapy in an exploratory analysis of key subgroups, including nodal status, tumour size T1/T2 vs T3/T4 and patients with baseline T2N0 disease^{2–4}

^aWith 200 events (67.3% information fraction), the observed p-value crossed the prespecified nominal boundary of 0.00503 (one-sided) at this interim analysis;

^bHR (CI) analysed based on a Cox regression model with treatment as a covariate stratified by the randomisation stratification factors.

CI, confidence interval; EFS, event-free survival; HR, hazard ratio; OS, overall survival; pCR, pathologic complete response; TNBC, triple-negative breast cancer.

1. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: <https://www.medicines.org.uk/emc/product/2498/smpc>. Accessed August 2025;

2. Schmid P et al. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2026, 29 May–2 June, Chicago, IL; 3. Schmid P et al. Presented at the European Society for Medical Oncology (ESMO) Congress 2024, 13–17 September, Barcelona, Spain; 4. Dent R et al. Presented at the San Antonio Breast Cancer Symposium 2024, 10–13 December, San Antonio, USA.



Summary: Safety



KEYTRUDA, in combination with chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment after surgery, is indicated in the treatment of adults with locally advanced or early-stage TNBC at high risk of recurrence¹

- The safety data for KEYTRUDA + chemotherapy as neoadjuvant treatment, followed by KEYTRUDA monotherapy as adjuvant treatment, are consistent with the known AE profiles of each regimen, being generally manageable in both phases^{2–6}
- No indication-specific immune-mediated AEs were identified at the 36-month analysis⁴
 - At 36 months, most immune-mediated AEs and infusion reactions were Grade 1–2 in severity, manageable with corticosteroids, treatment interruption and/or hormone replacement, and did not result in treatment discontinuation⁴
- At the 84-month final analysis, immune-mediated AEs of any grade were reported in 35.0% vs 13.1% of patients treated with KEYTRUDA + chemotherapy vs placebo + chemotherapy, respectively⁵
 - Most immune-mediated AEs were Grade 1–2 in severity⁵
 - Immune-mediated AEs resulted in discontinuation in 7.7% of patients treated with KEYTRUDA + chemotherapy compared with 1.0% of patients treated with placebo + chemotherapy⁵
- The safety profile remained consistent with the previous analyses and the established safety profiles of KEYTRUDA + chemotherapy.⁵ No new safety concerns were identified at the 75-month follow up or at the 84-month final analysis^{5,6}

AE, adverse event; TNBC, triple-negative breast cancer.

1. KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available at: <https://www.medicines.org.uk/emc/product/2498/smpc>. Accessed August 2025; 2. Schmid P et al. *N Engl J Med* 2022;386:556–567; 3. Schmid P et al. *N Engl J Med* 2020;382:810–821; 4. Cortés J et al. Presented at the San Antonio Breast Cancer Symposium (SABCS) Congress 2023, 5–9 December, San Antonio, USA; 5. Schmid P et al. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2026, 29 May–2 June, Chicago, USA; 6. Schmid P et al. Presented at the European Society of Medical Oncology Congress 2024, 13–17 September, Barcelona, Spain.



Appendix

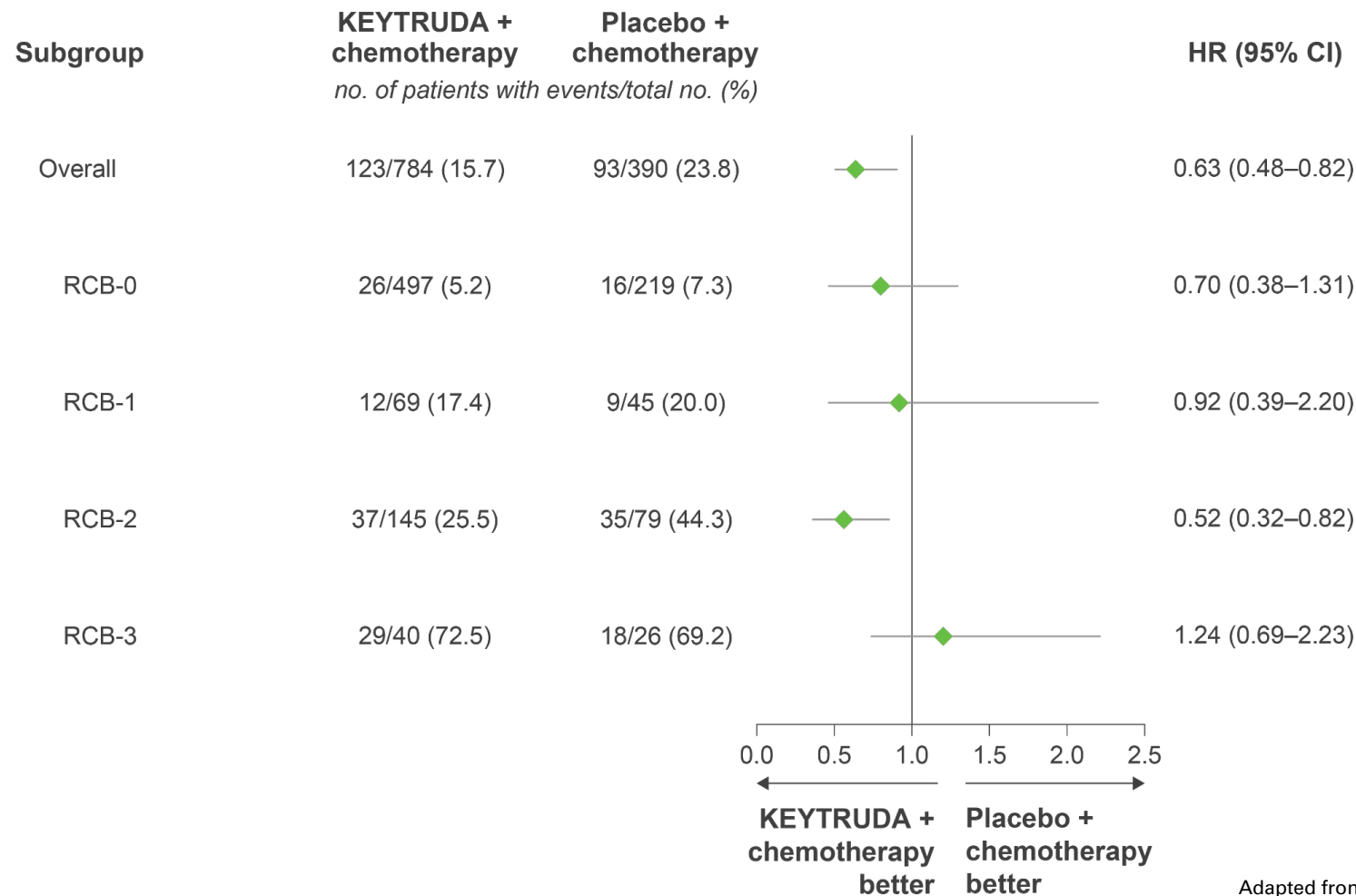


Click the links below to navigate to the section of interest

Efficacy	Safety	
EFS by RCB category	Summary of any-grade AEs in the neoadjuvant phase (primary analysis)	Immune-mediated AEs and infusion reactions in the adjuvant phase (36 months)
First EFS events by RCB category	AEs of interest in the neoadjuvant phase (1/2) (primary analysis)	Any-grade AEs in the combined phase (75-month follow-up)
pCR by PD-L1 expression level	AEs of interest in the neoadjuvant phase (2/2) (primary analysis)	Immune-mediated AEs in the combined phase (75-month follow-up)
	TRAEs in the adjuvant phase (36 months)	



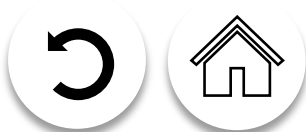
KEYNOTE-522: Exploratory analysis – EFS by RCB category



Adapted from Pusztai L et al. Presented at ASCO 2022.

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Data cutoff: 23 March 2021.
EFS in the overall population is based on a stratified Cox model; EFS by RCB is based on an unstratified Cox model.
CI, confidence interval; EFS, event-free survival; HR, hazard ratio; RCB, residual cancer burden.
Pusztai L et al. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2022, 3–7 June, Chicago, USA.



KEYNOTE-522: Exploratory analysis – First EFS events by RCB category

Event, %	RCB-0		RCB-1		RCB-2		RCB-3	
	KEYTRUDA + chemo (n=497)	Placebo + chemo (n=219)	KEYTRUDA + chemo (n=69)	Placebo + chemo (n=45)	KEYTRUDA + chemo (n=145)	Placebo + chemo (n=79)	KEYTRUDA + chemo (n=40)	Placebo + chemo (n=26)
Any EFS event	5.2	7.3	17.4	20.0	25.5	44.3	72.5	69.2
Secondary primary malignancy	0.2	0	1.4	2.2	1.4	3.8	2.5	0
PD precluded definitive surgery	0	0	1.4	2.2	1.4	5.1	10.0	7.7
Local recurrence	0.6	1.4	4.3	6.7	6.9	8.9	25.0	7.7
Distant recurrence	3.2	5.5	8.7	8.9	15.2	22.8	35.0	53.8
Death	1.2	0.5	1.4	0	0.7	3.8	0	0

Adapted from Pusztai L et al. Presented at ASCO 2022.

Data cutoff: 23 March 2021.

The treatment regimen in each arm included chemotherapy. Among all patients (N=1174), 54 (4.6%) patients had missing RCB categorical data: 33 (4.2%) in the KEYTRUDA + chemotherapy group and 21 (5.4%) in the placebo + chemotherapy group.

EFS, event-free survival; PD, progressive disease; RCB, residual cancer burden.

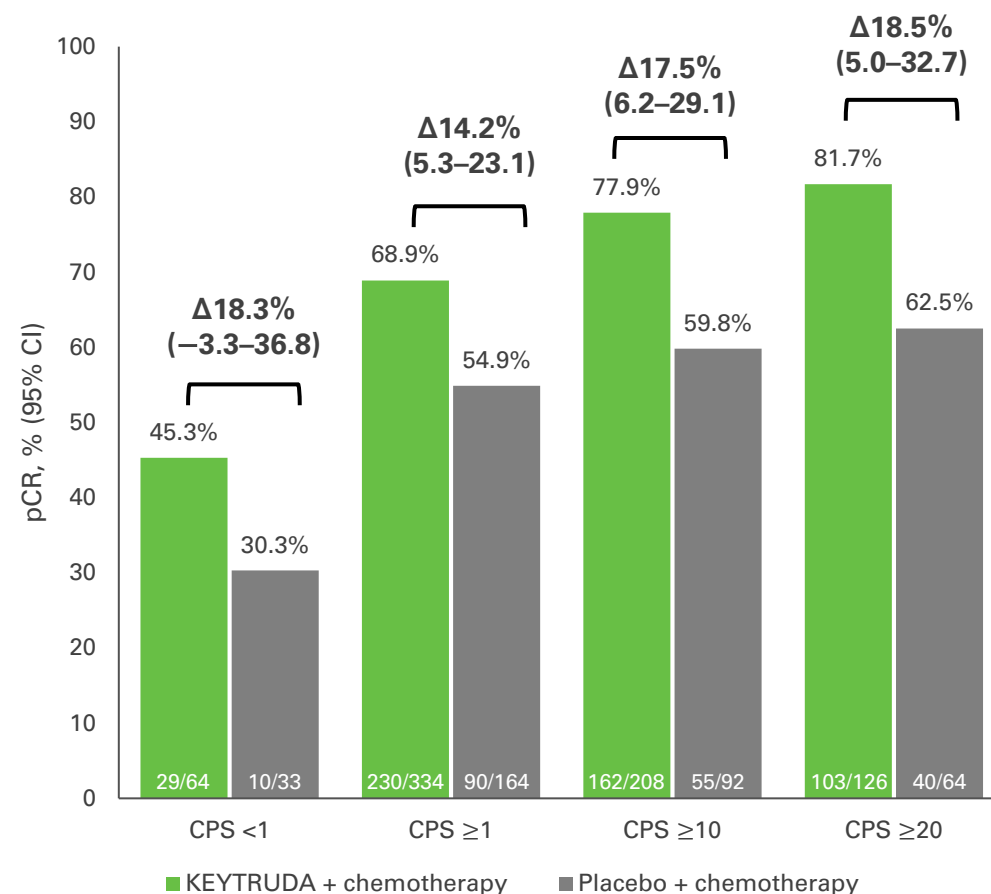
Pusztai L et al. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2022, 3–7 June, Chicago, USA.

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KEYNOTE-522: Exploratory analysis – pCR by PD-L1 expression level

Similar pCR^a benefits were observed in PD-L1–positive and PD-L1–negative patients treated with KEYTRUDA + chemotherapy



Adapted from Schmid P et al. Presented at SABCS 2019.

This was an exploratory analysis; significance was not tested and no statistical conclusions can be drawn

Data cutoff: 24 September 2018.

^aEstimated treatment difference based on Miettinen and Nurminen method stratified by nodal status (+ vs –), tumour size (T1/T2 vs T3/T4) and frequency of carboplatin administration (Q3W vs QW).

CI, confidence interval; CPS, combined positive score; pCR, pathologic complete response; PD-L1, programmed death ligand-1; Q3W, every 3 weeks; QW, once a week.

Schmid P et al. Presented at the San Antonio Breast Cancer Symposium 2019, 11–14 December, San Antonio, USA.

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KEYNOTE-522: Summary of any-grade AEs occurring in ≥20% of patients in the neoadjuvant phase at primary analysis

AE, n (%)	KEYTRUDA + chemotherapy (n=781)		Placebo + chemotherapy (n=389)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any AE	777 (99.2)	633 (81.0)	389 (100.0)	295 (75.8)
Treatment-related AE^a	773 (99.0)	600 (76.8)	388 (99.7)	281 (72.2)
Nausea	490 (62.7)	26 (3.3)	246 (63.2)	5 (1.3)
Alopecia	471 (60.3)	14 (1.8)	220 (56.6)	8 (2.1)
Anaemia	430 (55.1)	142 (18.2)	215 (55.3)	58 (14.9)
Neutropenia	365 (46.7)	270 (34.6)	183 (47.0)	129 (33.2)
Fatigue	321 (41.1)	27 (3.5)	147 (37.8)	6 (1.5)
Diarrhoea	230 (29.4)	17 (2.2)	92 (23.7)	5 (1.3)
Alanine aminotransferase increased	199 (25.5)	41 (5.2)	96 (24.7)	9 (2.3)
Vomiting	199 (25.5)	18 (2.3)	85 (21.9)	6 (1.5)
Asthenia	191 (24.5)	25 (3.2)	99 (25.4)	9 (2.3)
Constipation	185 (23.7)	0	82 (21.1)	0
Decreased neutrophil count	185 (23.7)	146 (18.7)	112 (28.8)	90 (23.1)
Rash	170 (21.8)	7 (0.9)	59 (15.2)	1 (0.3)
Peripheral neuropathy	154 (19.7)	15 (1.9)	82 (21.1)	4 (1.0)

Adapted from Schmid P et al. 2020.

Listed are AEs that occurred during the treatment period or within 30 days after the treatment period (or, for serious AEs, within 90 days) in patients who were randomised and received at least one trial drug or surgery. The severity of the AEs was graded according to the Common Terminology Criteria for Adverse Events, v4.0, of the National Cancer Institute. Patients may have had more than one event.

AE, adverse event.
Schmid P et al. *N Engl J Med* 2020;382:810–821.



KEYNOTE-522: AEs of interest in the neoadjuvant phase at primary analysis (1/2)

AE, n (%)	KEYTRUDA + chemotherapy (n=781)		Placebo + chemotherapy (n=389)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any AE	777 (99.5)	633 (81.0)	389 (100.0)	295 (75.8)
Treatment-related AE^a	773 (99.0)	600 (76.8)	388 (99.7)	281 (72.2)
AE of interest^b	304 (38.9)	101 (12.9)	71 (18.3)	7 (1.8)
Infusion reaction	132 (16.9)	20 (2.6)	43 (11.1)	4 (1.0)
Hypothyroidism	107 (13.7)	3 (0.4)	13 (3.3)	0
Hyperthyroidism	36 (4.6)	2 (0.3)	4 (1.0)	0
Severe skin reaction	34 (4.4)	30 (3.8)	4 (1.0)	1 (0.3)
Adrenal insufficiency	18 (2.3)	10 (1.3)	0	0
Hypophysitis	14 (1.8)	8 (1.0)	1 (0.3)	0
Colitis	13 (1.7)	7 (0.9)	3 (0.8)	1 (0.3)
Thyroiditis	13 (1.7)	2 (0.3)	3 (0.8)	0
Hepatitis	11 (1.4)	9 (1.2)	2 (0.5)	0

Adapted from Schmid P et al. 2020.

Listed are AEs that occurred during the treatment period or within 30 days after the treatment period (or, for serious AEs, within 90 days) in patients who underwent randomisation and received at least one trial drug or surgery. The severity of the AEs was graded according to the Common Terminology Criteria for Adverse Events, v4.0, of the National Cancer Institute. Patients may have had more than one event.

^aTreatment-related AEs were events occurring in ≥20% of patients or considered medically relevant by the investigator; ^bAEs of interest were determined according to a list of terms specified by the sponsor, regardless of attribution to any trial treatment by the investigators.

AE, adverse event.

Schmid P et al. *N Engl J Med* 2020;382:810–821.



KEYNOTE-522: AEs of interest in the neoadjuvant phase at primary analysis (2/2)

AE, n (%)	KEYTRUDA + chemotherapy (n=781)		Placebo + chemotherapy (n=389)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any AE	777 (99.5)	633 (81.0)	389 (100.0)	295 (75.8)
Treatment-related AE^a	773 (99.0)	600 (76.8)	388 (99.7)	281 (72.2)
AE of interest^b	304 (38.9)	101 (12.9)	71 (18.3)	7 (1.8)
Pneumonitis	10 (1.3)	3 (0.4)	5 (1.3)	1 (0.3)
Nephritis	7 (0.9)	7 (0.9)	0	0
Pancreatitis	4 (0.5)	4 (0.5)	0	0
Myocarditis	3 (0.4)	2 (0.3)	0	0
Myositis	3 (0.4)	0	0	0
Type 1 diabetes mellitus	2 (0.3)	2 (0.3)	0	0
Uveitis	2 (0.3)	0	0	0
Encephalitis	1 (0.1)	1 (0.1)	0	0
Sarcoidosis	1 (0.1)	0	0	0

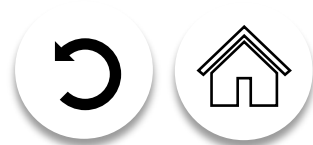
Adapted from Schmid P et al. 2020.

Listed are AEs that occurred during the treatment period or within 30 days after the treatment period (or, for serious AEs, within 90 days) in patients who were randomised and received at least one trial drug or surgery. The severity of the AEs was graded according to the Common Terminology Criteria for Adverse Events, v4.0, of the National Cancer Institute. Patients may have had more than one event.

^aTreatment-related AEs were events occurring in ≥20% of patients or considered medically relevant by the investigator; ^bAEs of interest were determined according to a list of terms specified by the sponsor, regardless of attribution to any trial treatment by the investigators.

AE, adverse event.

Schmid P et al. *N Engl J Med* 2020;382:810–821.



KEYNOTE-522: TRAEs occurring in $\geq 2\%$ of patients in the adjuvant phase at 36 months

AE, n (%) ^a	KEYTRUDA + chemotherapy (n=588)	Placebo + chemotherapy (n=331)
Any grade	316	286
Arthralgia	50 (8.5)	41 (6.9)
Rash	35 (6.0)	14 (2.4)
Pruritus	30 (5.1)	12 (2.1)
Asthenia	27 (4.6)	30 (5.1)
Diarrhoea	24 (4.1)	19 (3.3)
Fatigue	20 (3.4)	28 (4.8)
Aspartate aminotransferase increased	17 (2.9)	7 (1.2)
Hypothyroidism	16 (2.7)	19 (3.3)
Neutropenia	16 (2.7)	23 (3.9)
Alanine aminotransferase increased	13 (2.2)	11 (1.8)
Myalgia	13 (2.2)	7 (1.2)
Nausea	13 (2.2)	14 (2.4)
Dry mouth	12 (2.0)	5 (0.9)
Anaemia	9 (1.5)	16 (2.7)
Lymphopenia	9 (1.5)	14 (2.4)
Headache	5 (0.9)	14 (2.4)

Adapted from Schmid P et al. Presented at ESMO 2021.

Listed are AEs that occurred during the treatment period or within 30 days after the treatment period (or, for serious AEs, within 90 days) in patients who were randomised and received at least one trial drug or surgery. The severity of the AEs was graded according to the Common Terminology Criteria for Adverse Events, v4.0, of the National Cancer Institute. Patients may have had more than one event.

^an numbers for each AE have been calculated from provided percentages.

AE, adverse event; TRAE, treatment-related adverse event.

Schmid P et al. Presented at the European Society for Medical Oncology (ESMO) Virtual Plenary 2021, 16–21 September.

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KEYNOTE-522: Immune-mediated AEs and infusion reactions in the adjuvant phase at 36 months^a

AE, n (%) ^b	KEYTRUDA + chemotherapy (n=588)	Placebo + chemotherapy (n=331)
Any grade	60 (10.2)	35 (6.0)
Hypothyroidism	17 (2.9)	21 (3.6)
Infusion reactions	11 (1.9)	7 (1.2)
Severe skin reactions	11 (1.9)	0
Pneumonitis	7 (1.2)	4 (0.6)
Hyperthyroidism	5 (0.9)	4 (0.6)
Adrenal insufficiency	3 (0.5)	0
Colitis	2 (0.3)	0
Myocarditis	2 (0.3)	0

Adapted from Schmid P et al. Presented at ESMO 2021.

Listed are AEs that occurred during the treatment period or within 30 days after the treatment period (or, for serious AEs, within 90 days) in patients who were randomised and received at least one trial drug or surgery. The severity of the AEs was graded according to the Common Terminology Criteria for Adverse Events, v4.0, of the National Cancer Institute. Patients may have had more than one event.

^aImmune-mediated AEs were considered regardless of attribution to treatment or immune-relatedness by the investigator; ^bn numbers for each AE have been calculated from provided percentages.

AE, adverse event.

Schmid P et al. Presented at the European Society for Medical Oncology (ESMO) Virtual Plenary 2021, 16–21 September.

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KEYNOTE-522: Any-grade AEs in the combined neoadjuvant and adjuvant phases occurring in $\geq 20\%$ of patients at 75-month follow-up

AE, n (%)	KEYTRUDA + chemotherapy (n=783)		Placebo + chemotherapy (n=389)	
	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
Any AE	777 (99.2)	645 (82.4)	389 (100.0)	306 (78.7)
TRAE^a	774 (98.9)	604 (77.1)	388 (99.7)	285 (73.3)
Nausea	495 (63.2)	27 (3.4)	245 (63.0)	6 (1.5)
Alopecia	471 (60.2)	0	220 (56.6)	0
Anaemia	429 (54.8)	141 (18.0)	215 (55.3)	58 (14.9)
Neutropenia	367 (46.9)	270 (34.5)	185 (47.6)	130 (33.4)
Fatigue	330 (42.1)	28 (3.6)	151 (38.8)	7 (1.8)
Diarrhoea	238 (30.4)	20 (2.6)	98 (25.2)	5 (1.3)
Alanine aminotransferase increased	204 (26.1)	43 (5.5)	98 (25.2)	9 (2.3)
Vomiting	200 (25.5)	19 (2.4)	86 (22.1)	6 (1.5)
Asthenia	198 (25.3)	28 (3.6)	102 (26.2)	9 (2.3)
Rash	196 (25.0)	12 (1.5)	66 (17.0)	1 (0.3)
Constipation	188 (24.0)	0	85 (21.9)	0
Neutrophil count decreased	185 (23.6)	146 (18.6)	112 (28.8)	90 (23.1)
Aspartate aminotransferase increased	157 (20.1)	20 (2.6)	63 (16.2)	1 (0.3)
Peripheral neuropathy	154 (19.7)	15 (1.9)	84 (21.6)	4 (1.0)

Adapted from Schmid P et al.
Presented at ESMO 2024.

Listed are AEs that occurred during the treatment period or within 30 days after the treatment period (or, for serious AEs, within 90 days) in patients who were randomised and received at least one trial drug, underwent surgery, or both. The severity of the AEs was graded according to the Common Terminology Criteria for Adverse Events, v4.0, of the National Cancer Institute. Patients may have had more than one event.

^aGrade 5 TRAEs were sepsis and multiple organ dysfunction syndrome (n=1) and pneumonitis, pulmonary embolism and autoimmune encephalitis (n=1 in each group) in the KEYTRUDA + chemotherapy arm and septic shock (n=1) in the placebo + chemotherapy arm.

AE, adverse event; TRAE, treatment-related adverse event.

Schmid P et al. *N Engl J Med* 2024;391:1981–1991.



KEYNOTE-522: Immune-mediated AEs occurring in patients in the combined neoadjuvant and adjuvant phases at 75-month follow-up

AE, n (%)	KEYTRUDA + chemotherapy (n=783)		Placebo + chemotherapy (n=389)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any AE	777 (99.2)	645 (82.4)	389 (100.0)	306 (78.7)
TRAE ^a	774 (98.9)	604 (77.1)	388 (99.7)	285 (73.3)
Immune-mediated AE ^b	274 (35.0)	102 (13.0)	51 (13.1)	6 (1.5)
Hypothyroidism	118 (15.1)	4 (0.5)	22 (5.7)	0
Severe skin reaction	45 (5.7)	37 (4.7)	4 (1.0)	1 (0.3)
Hyperthyroidism	41 (5.2)	2 (0.3)	7 (1.8)	0
Gastritis	27 (3.4)	2 (0.3)	8 (2.1)	1 (0.3)
Adrenal insufficiency	20 (2.6)	8 (1.0)	0	0
Pneumonitis	17 (2.2)	7 (0.9)	6 (1.5)	2 (0.5)
Thyroiditis	16 (2.0)	2 (0.3)	5 (1.3)	0
Hypophysitis	15 (1.9)	10 (1.3)	1 (0.3)	0

Adapted from Schmid P et al. 2024.

Listed are AEs that occurred during, or 30 days after the treatment period (or, for serious AEs, within 90 days) in patients who were randomised and received ≥1 trial drug, underwent surgery, or both. The severity of the AEs was graded according to the Common Terminology Criteria for Adverse Events, v4.0, of the National Cancer Institute. Immune-mediated adverse events that occurred in ≥15 patients in either treatment group are reported. Patients may have had more than one event.

^aGrade 5 TRAEs were sepsis and multiple organ dysfunction syndrome (n=1) and pneumonitis, pulmonary embolism and autoimmune encephalitis (n=1 in each group) in the KEYTRUDA + chemotherapy arm and septic shock (n=1) in the placebo + chemotherapy arm; ^bImmune-mediated AEs were determined according to a list of terms determined by the sponsor, regardless of attribution to any trial treatment by the investigators. Grade 5 immune-mediated AEs were pulmonary embolism and autoimmune encephalitis (n=1 each) in the KEYTRUDA + chemotherapy group.

AE, adverse event.

Schmid P et al. *N Engl J Med* 2024;391:1981–1991.

