# Dossier zur Nutzenbewertung gemäß § 35a SGB V

*Nivolumab (OPDIVO®)*

Bristol-Myers Squibb GmbH & Co. KGaA

**Modul 4 X**

*Anhang 4-G*

*Adjuvante Behandlung des Melanoms im Stadium IIB oder IIC nach vollständiger Resektion*

Ergänzende Analysen

Stand: 18.09.2023

# 4 Modul 4 X– Anhang 4-G - Ergänzende Analysen

# Inhaltsverzeichnis Anhang 4-G

# Anhang 4-G: Ergänzende Analysen der RCT CA209-76K

## Anhang 4-G 1: Endpunkte Morbidität und Lebensqualität: Zusatzanalysen (MMRM)

### Anhang 4-G 1.1: Zusatzanalysen zum zeitlichen Verlauf (auf Basis des MMRM) für Endpunkte gemäß EORTC-QLQ-C30 aus CA209-76K

Zusatzanalyse: Zeitlicher Verlauf der Änderung gegenüber Studienbeginn der Endpunkte Fatigue, Übelkeit und Erbrechen, Schmerz, Dyspnoe, Schlaflosigkeit, Appetitminderung, Obstipation, Diarrhoe, globaler Gesundheitsstatus, körperliche Funktion, Rollenfunktion, emotionale Funktion, kognitive Funktion und soziale Funktion gemäß EORTC-QLQ-C30 aus CA209-76K.

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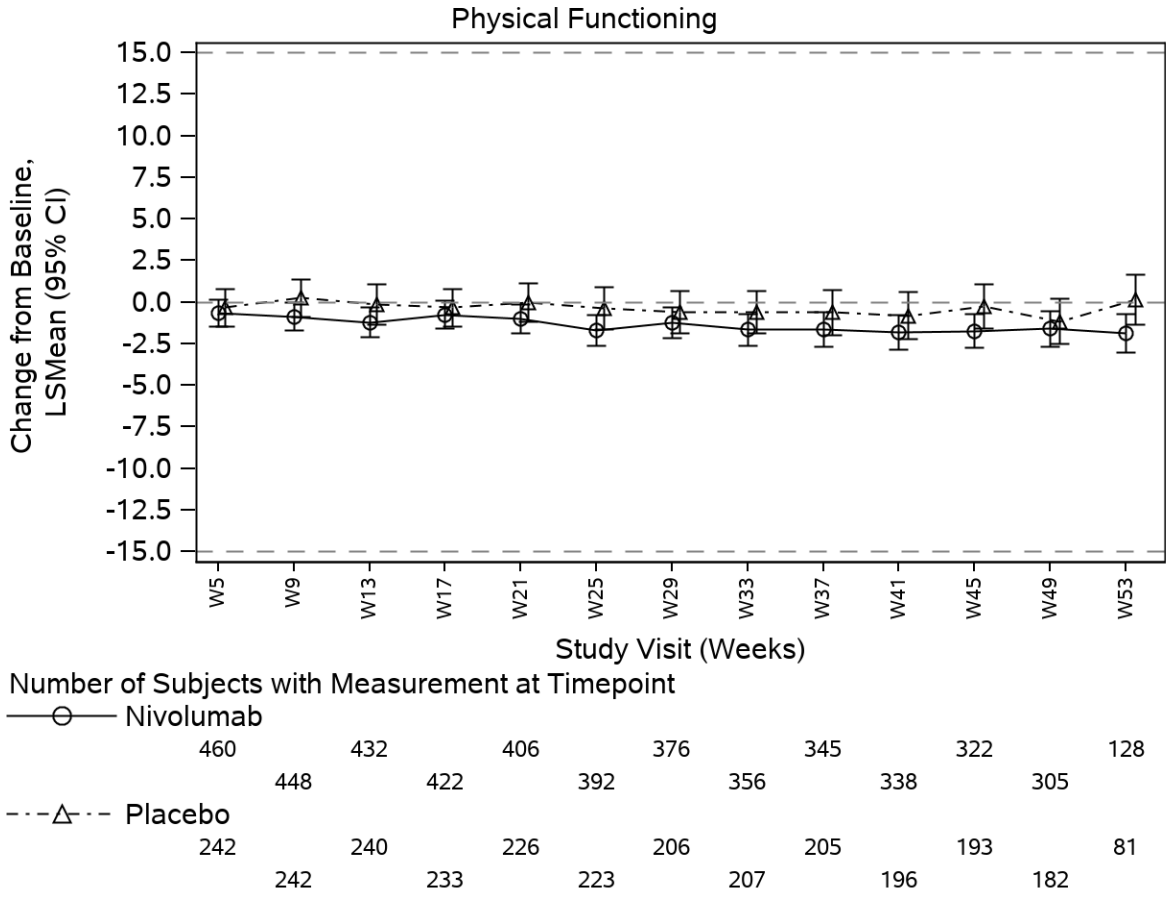
Figure 7.1:
Plot of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30 by Timepoint - All Randomized Subjects

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N = number of randomized subjects with non-missing baseline and Week t assessment timepoint.
MMRM model with chg from bsl as dependent variable, trt and trt*visit week
as fixed effects, baseline PRO score and AJCC T Stage at Study Entry as covariates, and visit week as repeated measure.
UN covariance matrix. If convergence issue, CS and then AR(1).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are includedin the analysis.
Functional scale/Global Health Status/QOL: Positive difference favors nivolumab, negative difference favors Placebo.
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Program Name: rg-sy-mmrm-ebr1575.sas 12JUL2023:11:00:36

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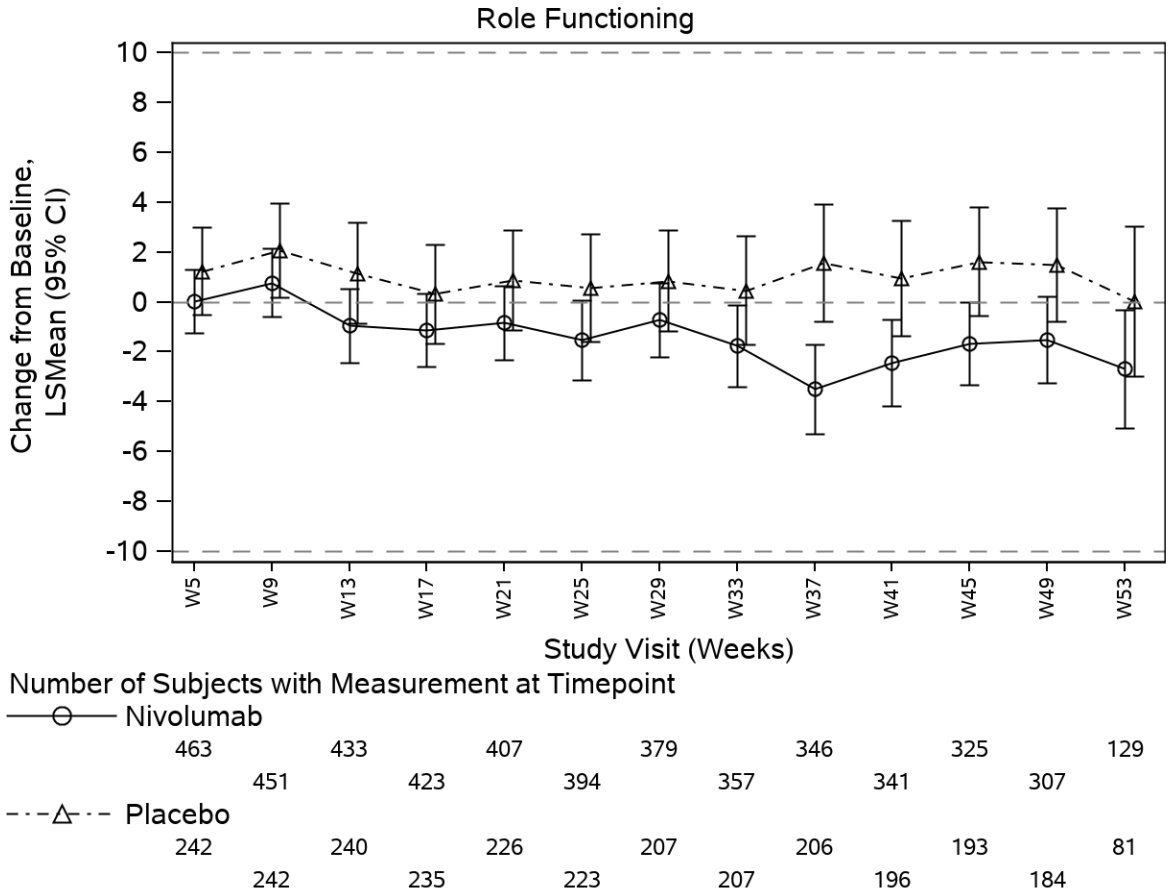


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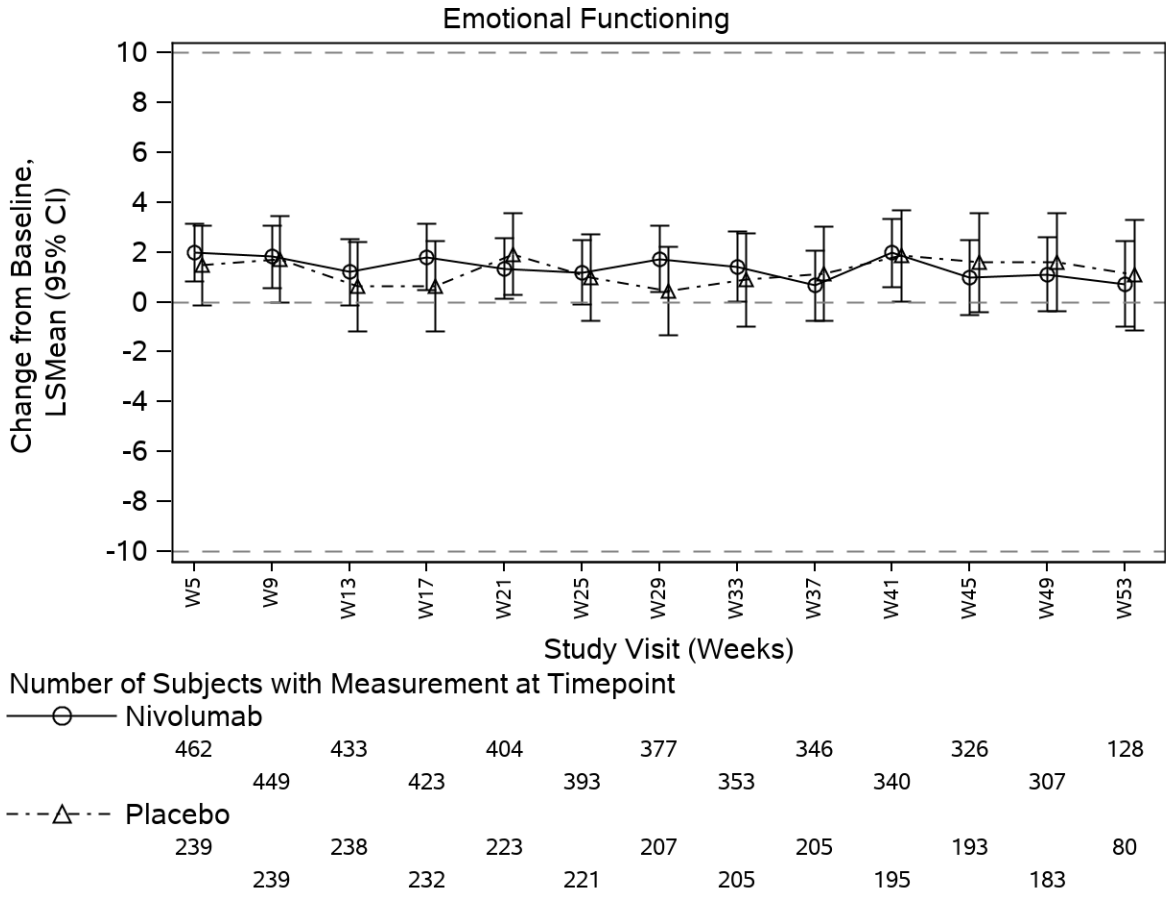


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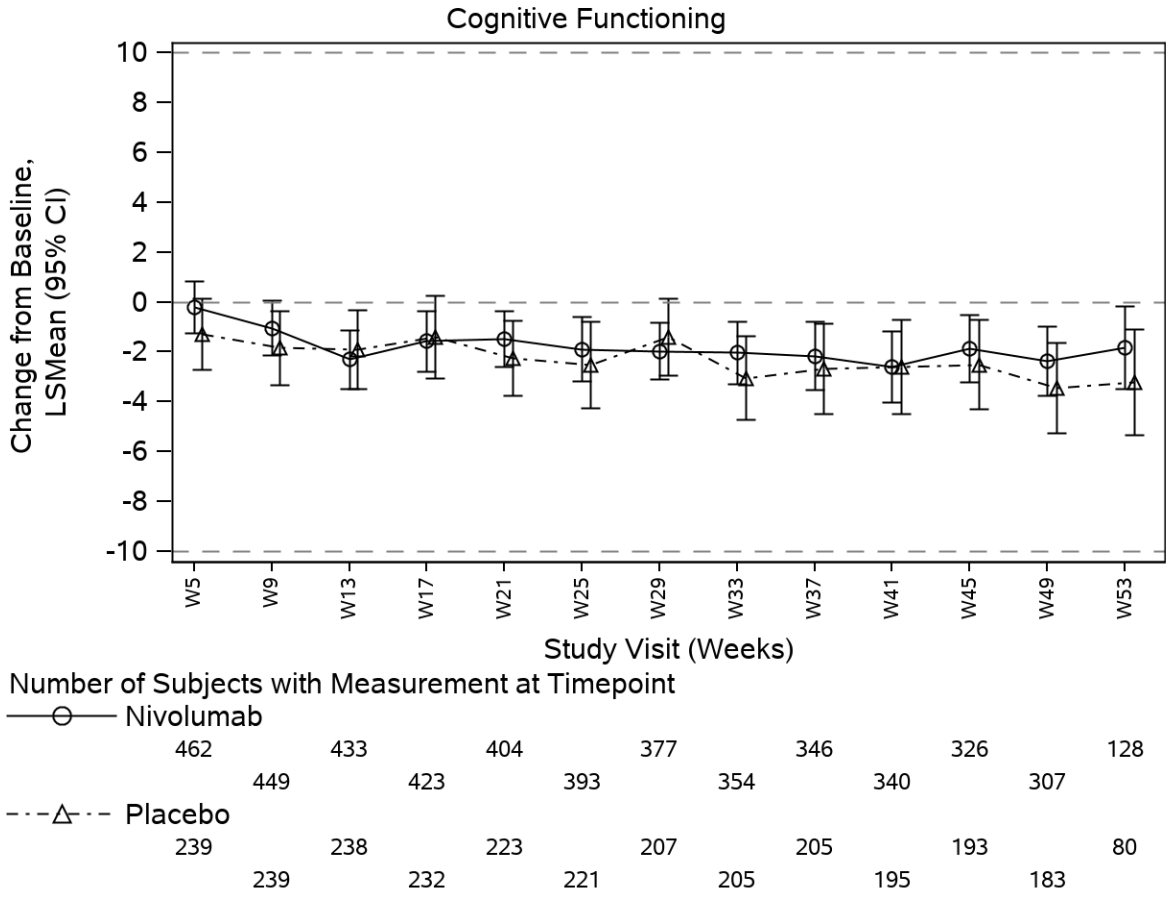


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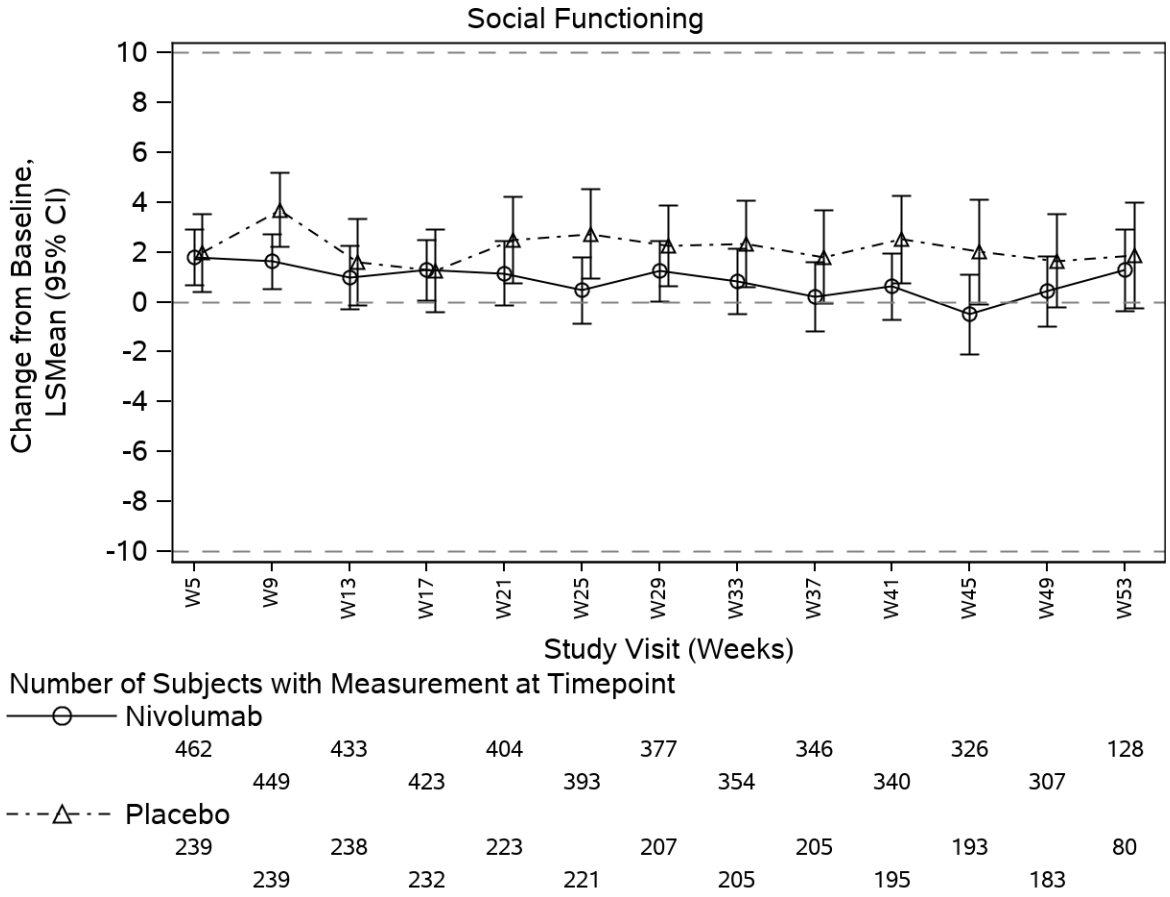


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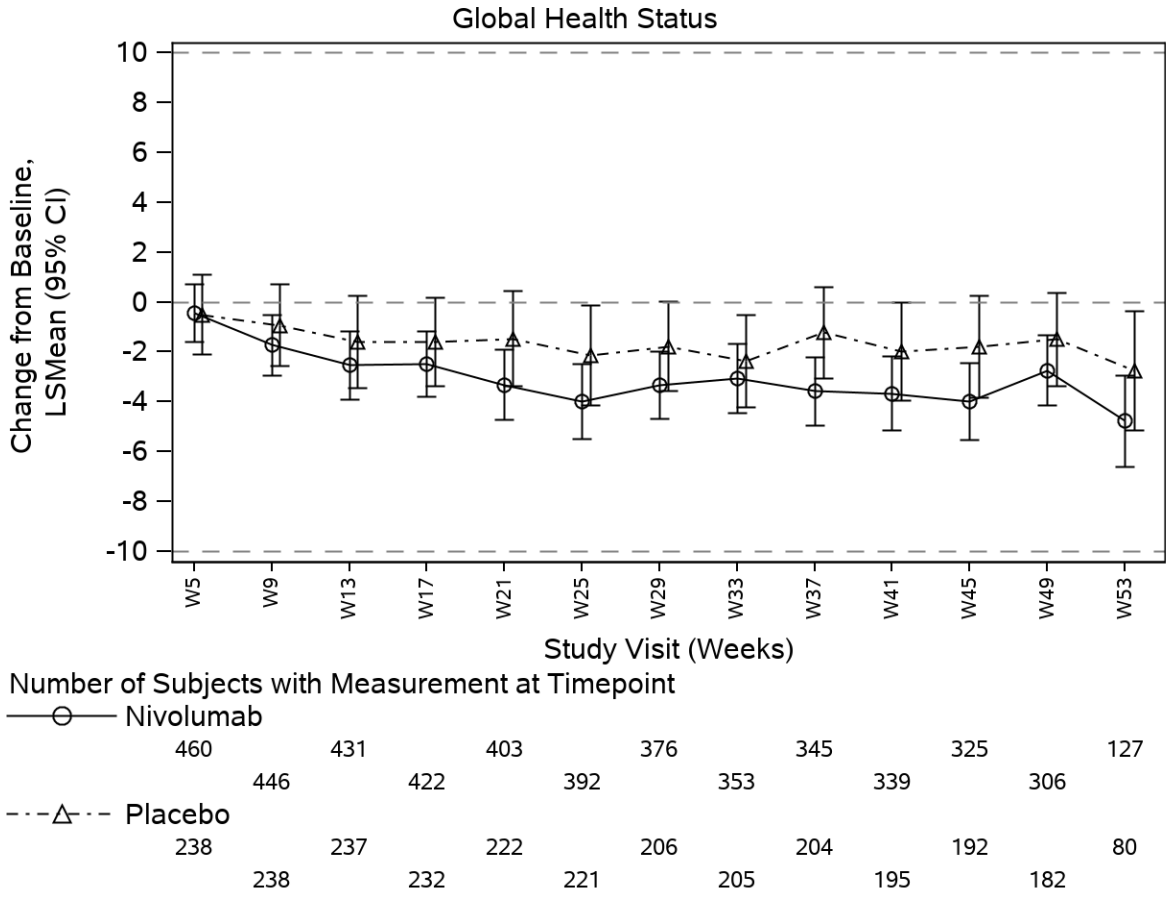


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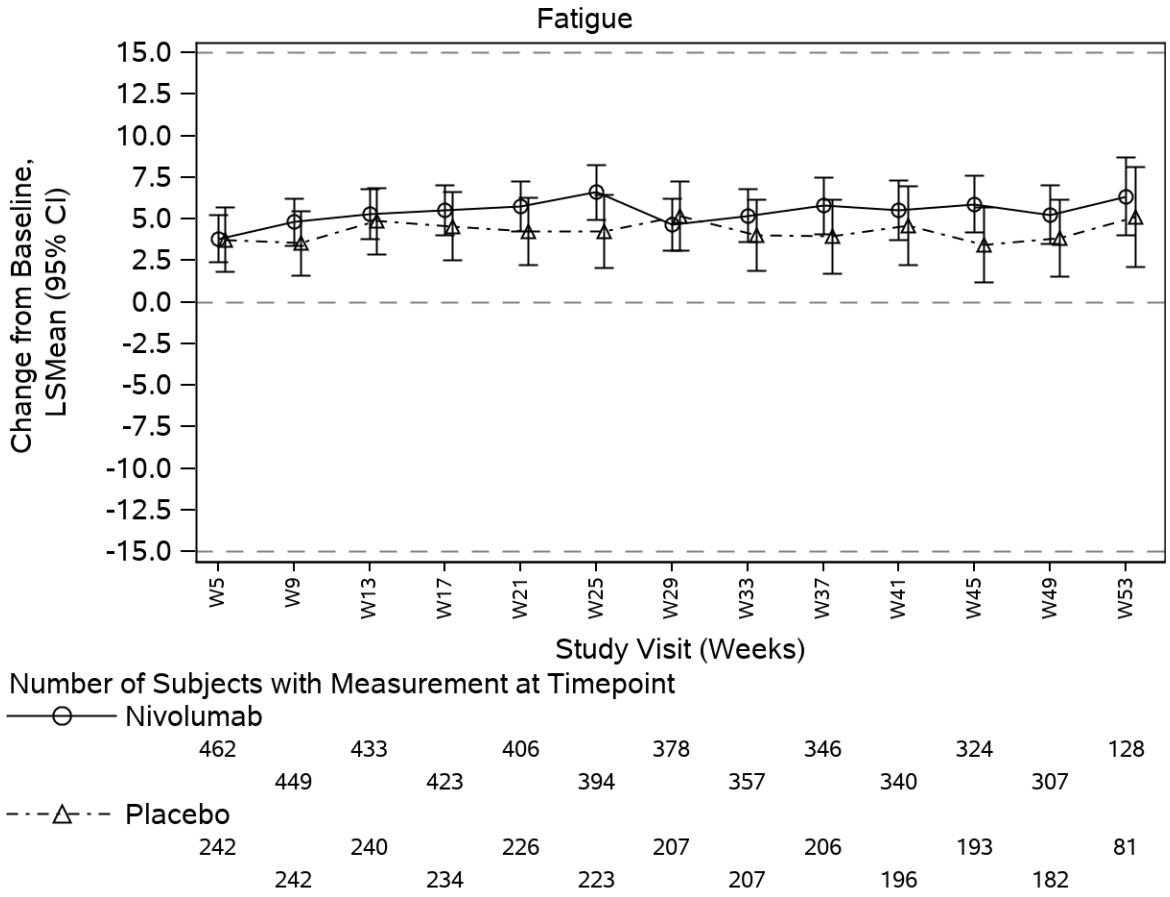


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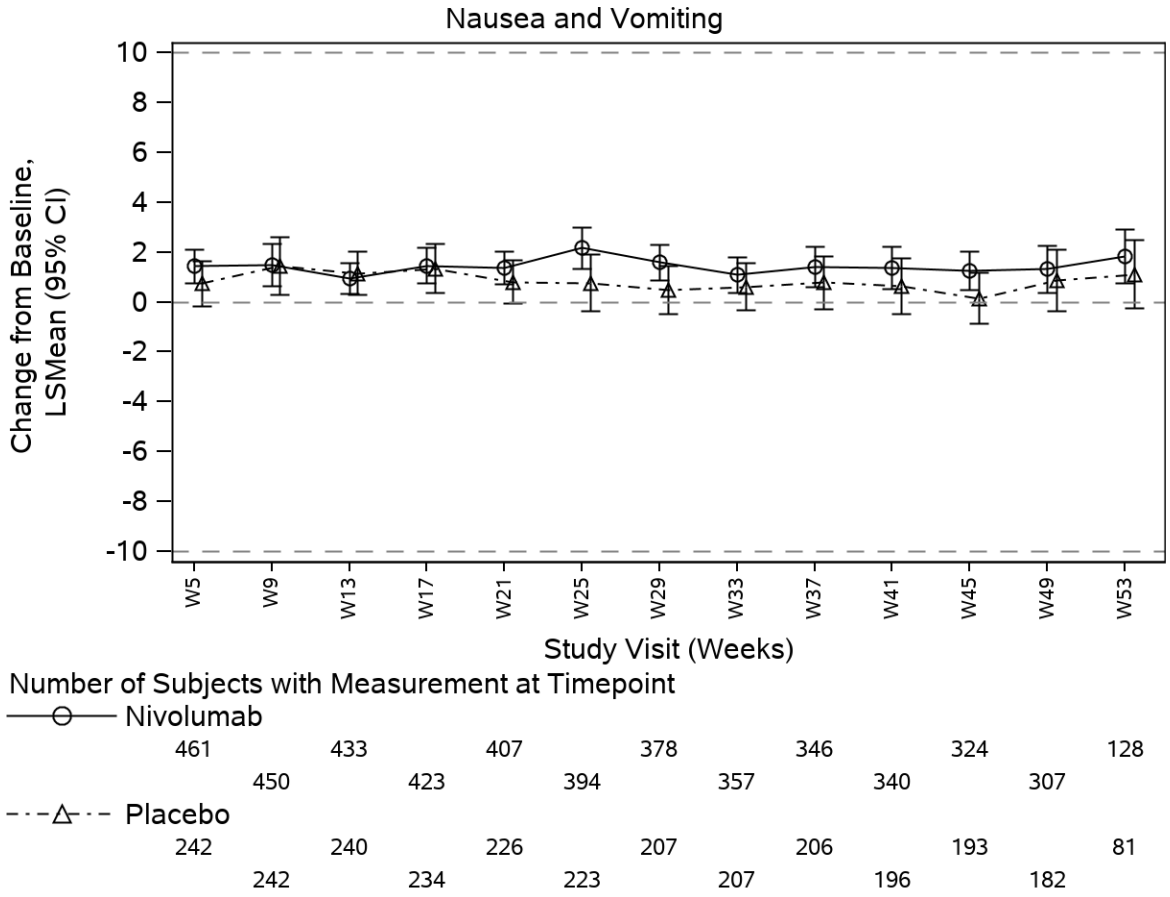


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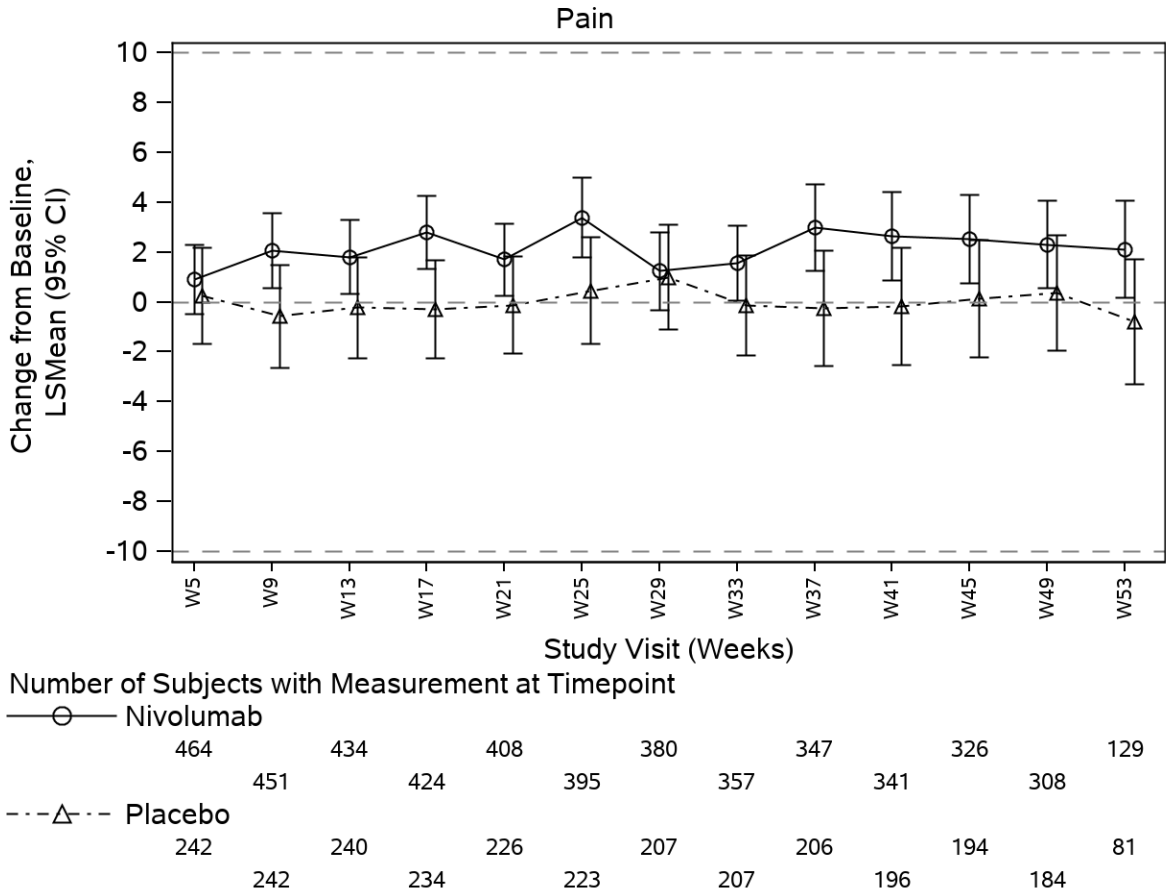


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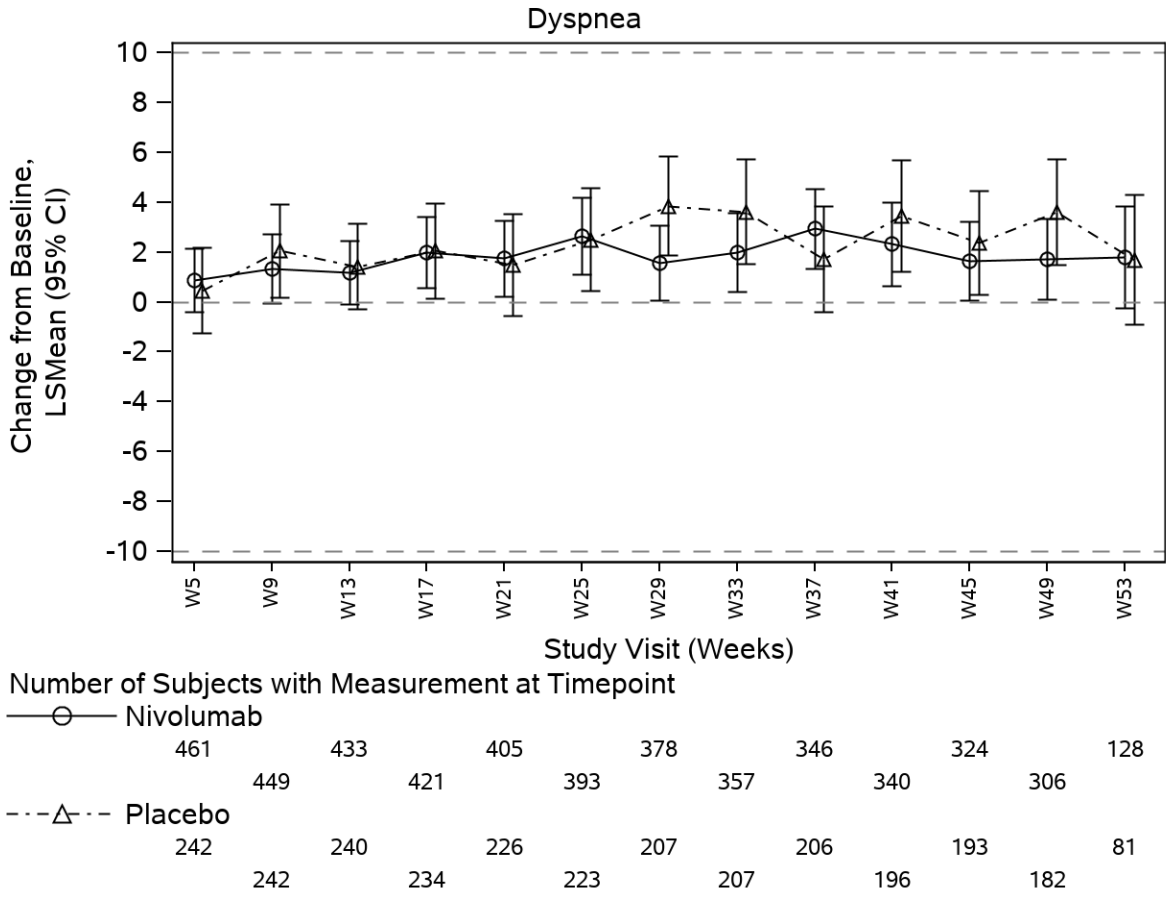


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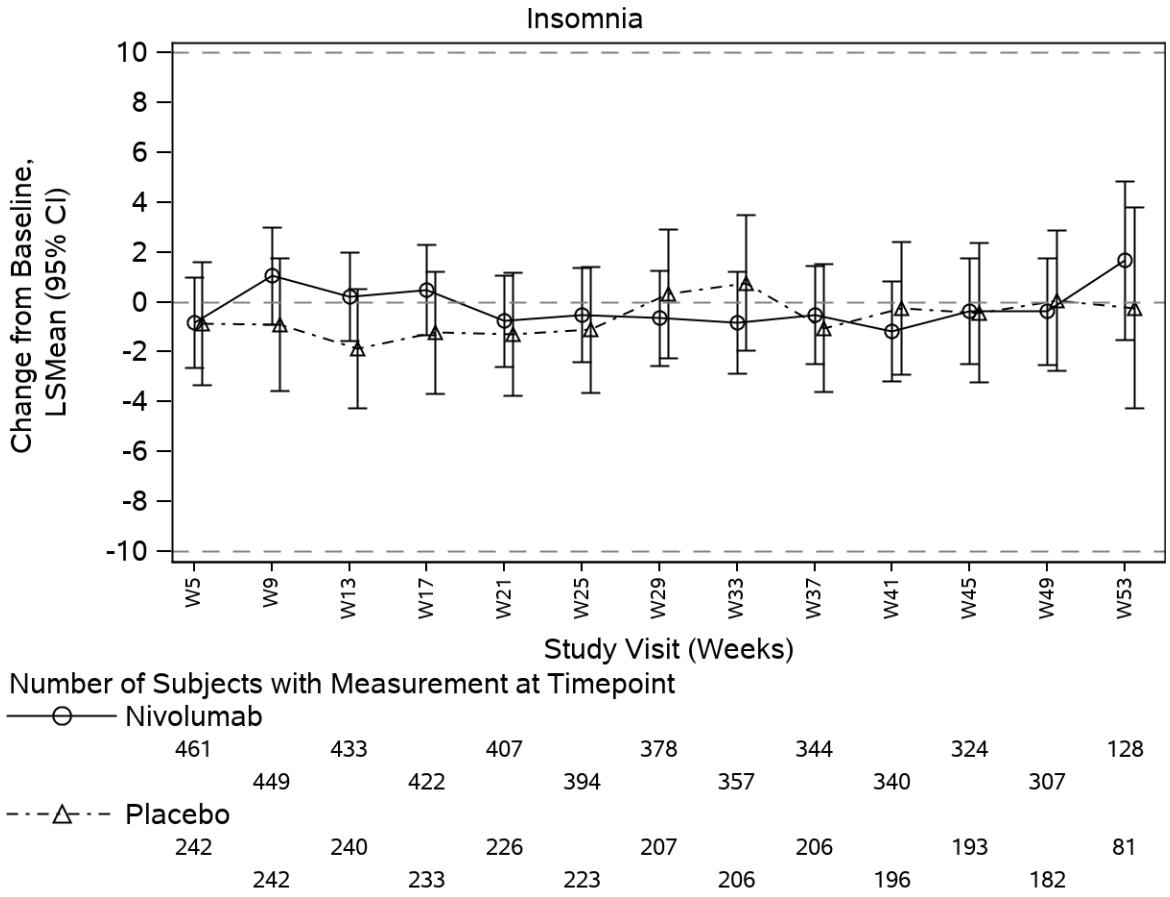


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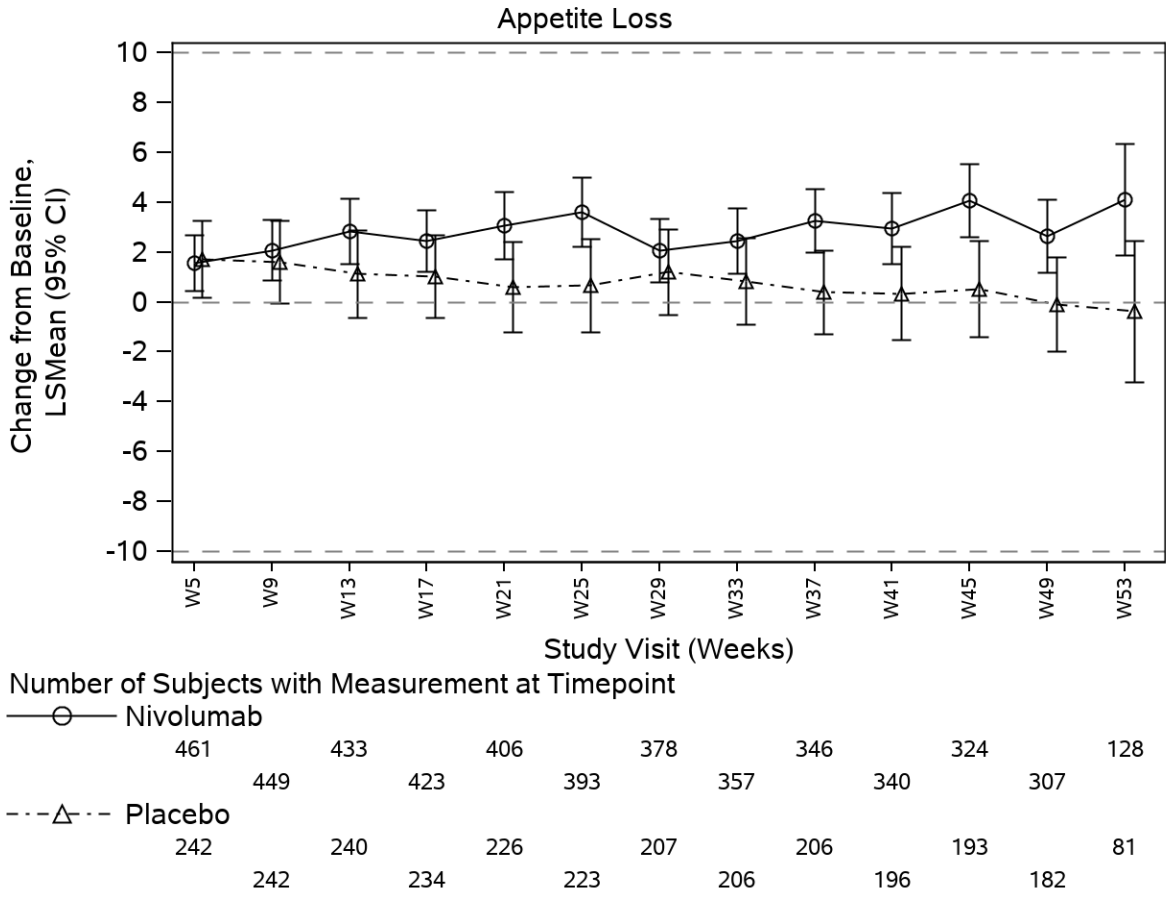


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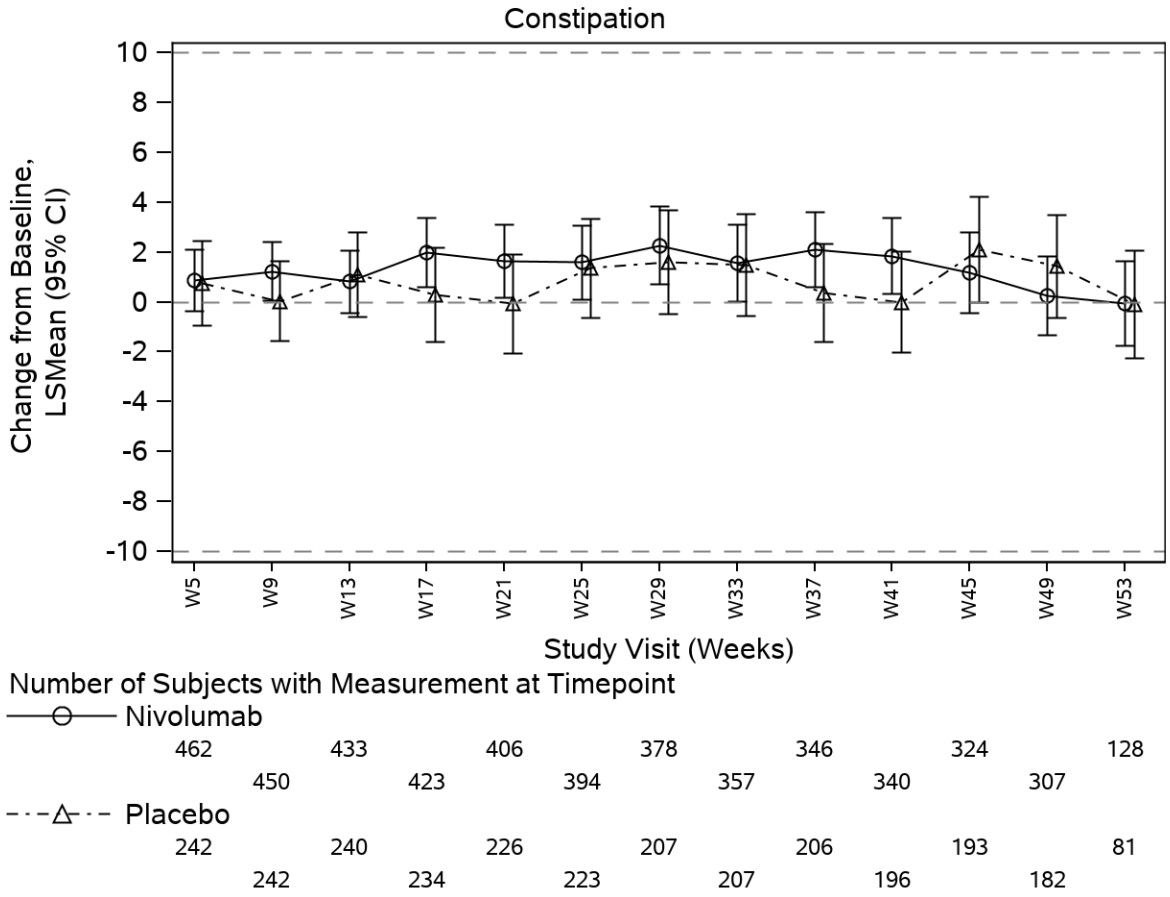


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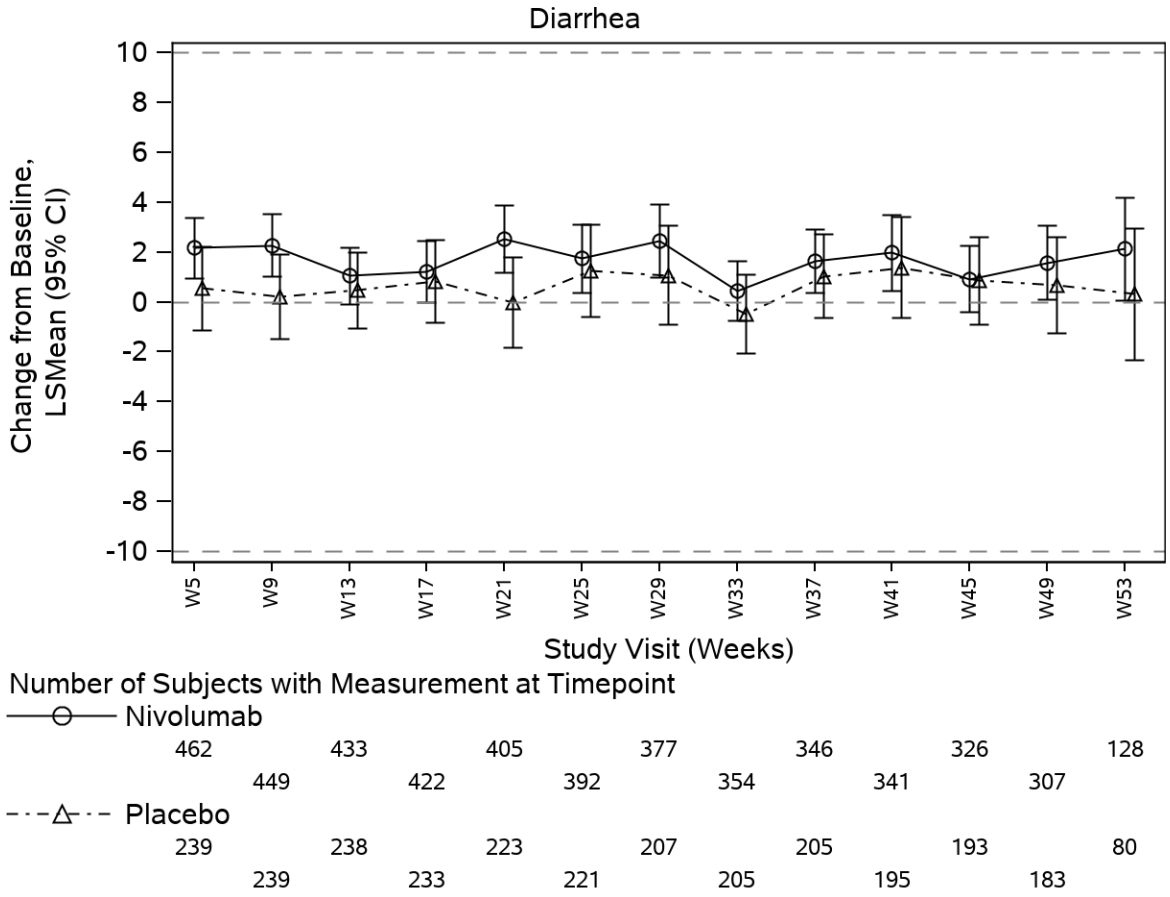


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## Anhang 4-G 1.2: Zusatzanalysen zum zeitlichen Verlauf (auf Basis des MMRM) für Endpunkt Gesundheitszustand gemäß EQ-5D-VAS aus CA209-76K

Zusatzanalyse: Zeitlicher Verlauf der Änderung gegenüber Studienbeginn des Endpunkts Gesundheitszustand gemäß EQ-5D-VAS aus CA209-76K.

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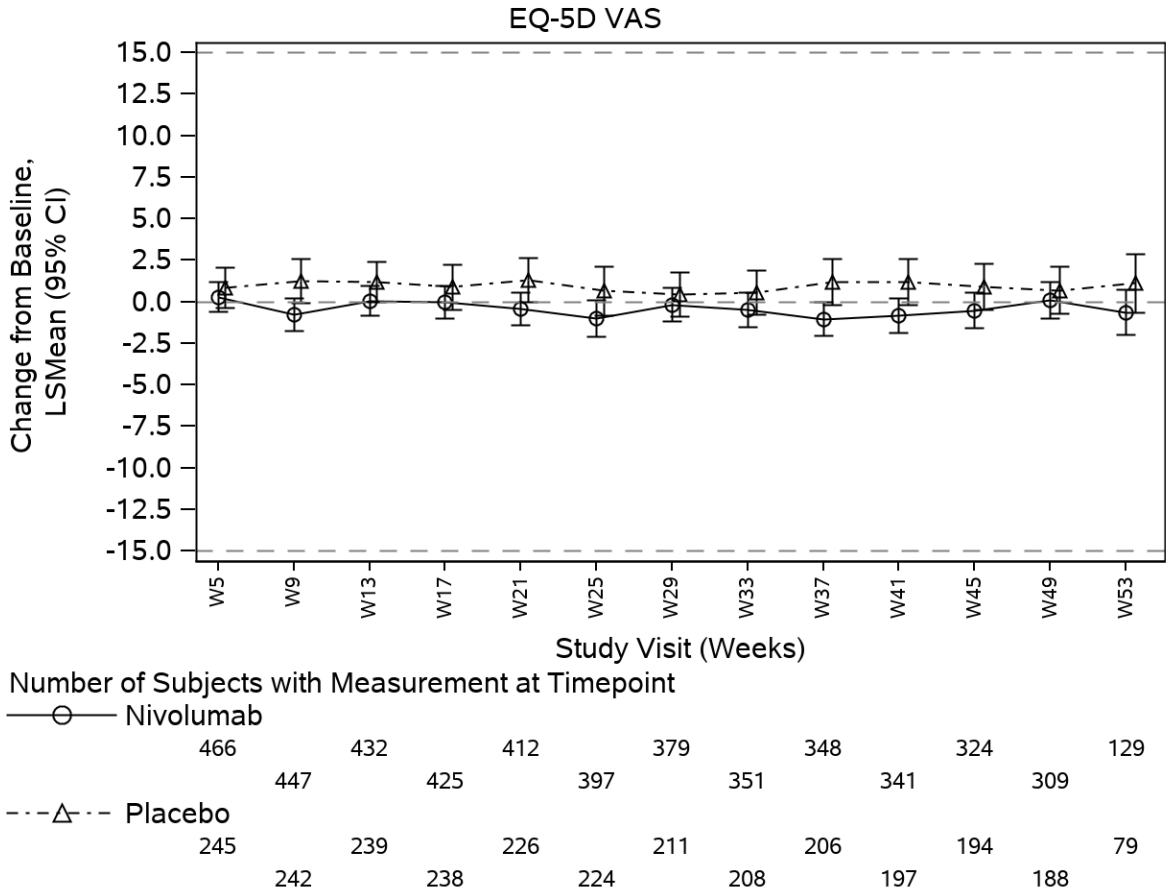
Figure 7.2:
Plot of Mixed Model Repeated Measures Analysis of EQ-5D-5L VAS by Timepoint - All Randomized Subjects

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Program Name: rg-sy-mmrm-ebr1575.sas 12JUL2023:09:54:41

## Anhang 4-G 2: Endpunkte Verträglichkeit

### Anhang 4-G 2.1: Sensitivitätsanalyse für die Endpunkte unerwünschte Ereignisse ohne Erfassung des Progresses der Grunderkrankung aus CA209-76K – Zeit bis zum ersten Auftreten des UE

Sensitivitätsanalyse: Endpunkte unerwünschte Ereignisse ohne Erfassung des Progresses der Grunderkrankung aus CA209-76K – Zeit bis zum ersten Auftreten des UE ohne Zensierung am Tag vor Beginn der Behandlung mit Nivolumab im unverblindeten Teil

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Table 22.2
Adverse Events: Time-Adjusted Analyses
Excluding Progression Terms
All Treated Subjects Censoring at Complete End of Safety Window

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Adverse Events (AE) | N | Subjects with Event n (%) | KME [95%CI] (mon) (1) | N | Subjects with Event n (%) | KME [95%CI] (mon) (1) | HR [95%CI] (2) | P-value (3) |
| SUBJECTS WITH ANY AES | 524 | 508 ( 96.9) | 0.95 ( 0.89, 0.95) | 264 | 233 ( 88.3) | 1.77 ( 1.12, 1.91) | 1.712 ( 1.462, 2.006) | <0.0001 |
| SUBJECTS WITH CTCAE GRADES >= 3 AES | 524 | 146 ( 27.9) | N.A. | 264 | 42 ( 15.9) | N.A. | 1.981 ( 1.405, 2.792) | <0.0001 |
| SUBJECTS WITH SAES | 524 | 98 ( 18.7) | N.A. | 264 | 34 ( 12.9) | N.A. | 1.602 ( 1.084, 2.367) | 0.0169 |
| SUBJECTS WITH AES LEADING TO DISCONTINUATION OF STUDY TREATMENT | 524 | 116 ( 22.1) | N.A. | 264 | 9 ( 3.4) | N.A. | 7.241 ( 3.675, 14.269) | <0.0001 |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days
after last dose of study therapy in the blinded phase.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not Meaningful Estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-aetahrx-ta-ebr1575b1.sas 19JUL2023:12:29:04

**Anhang 4-G 2.2: Ergebnisse für Endpunkte Unerwünschte Ereignisse von besonderem Interesse (UESI) aus CA209-76K – Zeit bis zum ersten Auftreten des UE**

**Anhang 4-G 2.2.1: Ergebnisse für Endpunkte spezifische immunvermittelte UE (imUE) aus CA209-76K – Zeit bis zum ersten Auftreten des UE**

**Anhang 4-G 2.2.1.1 Ergebnisse für Endpunkte jegliche spezifische immunvermittelte UE aus CA209-76K – Zeit bis zum ersten Auftreten des UE**

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Table 25.1
Immune-mediated Adverse Events: Time-Adjusted Analyses
On Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| | Nivolumab | | | | Placebo | | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|---|---|
| Immune-Mediated Adverse Events (IMAE) | N | Subjects with Event n (%) | Censored Subjects n (%) | KME [95%CI] (mon) (1) | N | Subjects with Event n (%) | Censored Subjects n (%) | KME [95%CI] (mon) (1) | HR [95%CI] (2) | P-value (3) |
| SUBJECTS WITH ANY IMAES | 524 | 186 ( 35.5) | 338 ( 64.5) | N.A. | 264 | 17 ( 6.4) | 247 ( 93.6) | N.A. | 6.899 ( 4.197, 11.340) | <0.0001 |
| SUBJECTS WITH PNEUMONITIS IMAES | 524 | 5 ( 1.0) | 519 ( 99.0) | N.A. | 264 | 2 ( 0.8) | 262 ( 99.2) | N.A. | 1.411 ( 0.274, 7.276) | 0.6793 |
| SUBJECTS WITH DIARRHEA/COLITIS IMAES | 524 | 26 ( 5.0) | 498 ( 95.0) | N.A. | 264 | 2 ( 0.8) | 262 ( 99.2) | N.A. | 7.044 ( 1.672, 29.684) | 0.0019 |
| SUBJECTS WITH HEPATITIS IMAES | 524 | 22 ( 4.2) | 502 ( 95.8) | N.A. | 264 | 1 ( 0.4) | 263 ( 99.6) | N.A. | 11.581 ( 1.561, 85.930) | 0.0024 |
| SUBJECTS WITH NEPHRITIS AND RENAL DYSFUNCTION IMAES | 524 | 4 ( 0.8) | 520 ( 99.2) | N.A. | 264 | 1 ( 0.4) | 263 ( 99.6) | N.A. | 2.060 ( 0.230, 18.437) | 0.5088 |
| SUBJECTS WITH RASH IMAES | 524 | 45 ( 8.6) | 479 ( 91.4) | N.A. | 264 | 4 ( 1.5) | 260 ( 98.5) | N.A. | 6.147 ( 2.210, 17.094) | <0.0001 |
| SUBJECTS WITH HYPERSENSITIVITY IMAES | 524 | 7 ( 1.3) | 517 ( 98.7) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.0572 |
| SUBJECTS WITH ADRENAL INSUFFICIENCY IMAES | 524 | 12 ( 2.3) | 512 ( 97.7) | N.A. | 264 | 3 ( 1.1) | 261 ( 98.9) | N.A. | 2.279 ( 0.643, 8.087) | 0.1897 |
| SUBJECTS WITH HYPOPHYSITIS IMAES | 524 | 9 ( 1.7) | 515 ( 98.3) | N.A. | 264 | 2 ( 0.8) | 262 ( 99.2) | N.A. | 2.404 ( 0.519, 11.129) | 0.2469 |
| SUBJECTS WITH HYPOTHYROIDISM/ THYROIDITIS IMAES | 524 | 68 ( 13.0) | 456 ( 87.0) | N.A. | 264 | 1 ( 0.4) | 263 ( 99.6) | N.A. | 38.365 ( 5.327,>99.999) | <0.0001 |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-timaetahrt-ebr1575.sas 20JUL2023:10:01:02

Protocol: CA20976K 

Table 25.1
Immune-mediated Adverse Events: Time-Adjusted Analyses
On Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| | Nivolumab | | | | Placebo | | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|---|---|
| Immune-Mediated Adverse Events (IMAE) | N | Subjects with Event n (%) | Censored Subjects n (%) | KME [95%CI] (mon) (1) | N | Subjects with Event n (%) | Censored Subjects n (%) | KME [95%CI] (mon) (1) | HR [95%CI] (2) | P-value (3) |
| SUBJECTS WITH HYPOTHYROIDISM IMAES | 524 | 64 ( 12.2) | 460 ( 87.8) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | <0.0001 |
| SUBJECTS WITH THYROIDITIS IMAES | 524 | 6 ( 1.1) | 518 ( 98.9) | N.A. | 264 | 1 ( 0.4) | 263 ( 99.6) | N.A. | 3.147 ( 0.379, 26.136) | 0.2625 |
| SUBJECTS WITH HYPERTHYROIDISM IMAES | 524 | 40 ( 7.6) | 484 ( 92.4) | N.A. | 264 | 3 ( 1.1) | 261 ( 98.9) | N.A. | 7.180 ( 2.221, 23.212) | 0.0001 |
| SUBJECTS WITH DIABETES MELLITUS IMAES | 524 | 3 ( 0.6) | 521 ( 99.4) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.2108 |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-timaetahrt-ebr1575.sas 20JUL2023:10:01:02

**Anhang 4-G 2.2.1.2 Ergebnisse für Endpunkte schwere spezifische immunvermittelte UE aus CA209-76K – Zeit bis zum ersten Auftreten des UE**

Protocol: CA20976K 

Table 25.3
Immune-mediated Adverse Events with CTCAE Grade 3-4-5: Time-Adjusted Analyses
On Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| | Nivolumab | | | | Placebo | | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|---|---|
| Immune-Mediated Adverse Events (IMAE) | N | Subjects with Event n (%) | Censored Subjects n (%) | KME [95%CI] (mon) (1) | N | Subjects with Event n (%) | Censored Subjects n (%) | KME [95%CI] (mon) (1) | HR [95%CI] (2) | P-value (3) |
| SUBJECTS WITH IMAES CTCAE GRADES >= 3 | 524 | 39 ( 7.4) | 485 ( 92.6) | N.A. | 264 | 1 ( 0.4) | 263 ( 99.6) | N.A. | 21.249 ( 2.919,>99.999) | <0.0001 |
| SUBJECTS WITH PNEUMONITIS IMAES | 524 | 1 ( 0.2) | 523 ( 99.8) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.4598 |
| SUBJECTS WITH DIARRHEA/COLITIS IMAES | 524 | 8 ( 1.5) | 516 ( 98.5) | N.A. | 264 | 1 ( 0.4) | 263 ( 99.6) | N.A. | 4.289 ( 0.536, 34.309) | 0.1344 |
| SUBJECTS WITH HEPATITIS IMAES | 524 | 14 ( 2.7) | 510 ( 97.3) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.0068 |
| SUBJECTS WITH NEPHRITIS AND RENAL DYSFUNCTION IMAES | 524 | 2 ( 0.4) | 522 ( 99.6) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.3105 |
| SUBJECTS WITH RASH IMAES | 524 | 5 ( 1.0) | 519 ( 99.0) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.0943 |
| SUBJECTS WITH HYPERSENSITIVITY IMAES | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH ADRENAL INSUFFICIENCY IMAES | 524 | 3 ( 0.6) | 521 ( 99.4) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.1784 |
| SUBJECTS WITH HYPOPHYSITIS IMAES | 524 | 5 ( 1.0) | 519 ( 99.0) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.1037 |
| SUBJECTS WITH HYPOTHYROIDISM/ THYROIDITIS IMAES | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-timaetahrt-ebr1575.sas 20JUL2023:10:01:44

Protocol: CA20976K 

Table 25.3
Immune-mediated Adverse Events with CTCAE Grade 3-4-5: Time-Adjusted Analyses
On Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| | Nivolumab | | | | Placebo | | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|---|---|
| Immune-Mediated Adverse Events (IMAE) | N | Subjects with Event n (%) | Censored Subjects n (%) | KME [95%CI] (mon) (1) | N | Subjects with Event n (%) | Censored Subjects n (%) | KME [95%CI] (mon) (1) | HR [95%CI] (2) | P-value (3) |
| SUBJECTS WITH HYPOTHYROIDISM IMAES | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH THYROIDITIS IMAES | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH HYPERTHYROIDISM IMAES | 524 | 1 ( 0.2) | 523 ( 99.8) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.4712 |
| SUBJECTS WITH DIABETES MELLITUS IMAES | 524 | 3 ( 0.6) | 521 ( 99.4) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.2108 |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-timaetahrt-ebr1575.sas 20JUL2023:10:01:44

**Anhang 4-G 2.2.1.3 Ergebnisse für Endpunkte schwerwiegende spezifische immunvermittelte UE aus CA209-76K – Zeit bis zum ersten Auftreten des UE**

Protocol: CA20976K 

Table 25.5
Serious Immune-mediated Adverse Events : Time-Adjusted Analyses
On Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| Immune-Mediated Adverse Events (IMAE) | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab Censored Subjects n (%) | Nivolumab KME [95%CI] (mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo Censored Subjects n (%) | Placebo KME [95%CI] (mon) (1) | Nivolumab vs. Placebo HR [95%CI] (2) | Nivolumab vs. Placebo P-value (3) |
|---|---|---|---|---|---|---|---|---|---|---|
| SUBJECTS WITH SERIOUS IMAES | 524 | 22 ( 4.2) | 502 ( 95.8) | N.A. | 264 | 3 ( 1.1) | 261 ( 98.9) | N.A. | 3.976 ( 1.190, 13.287) | 0.0153 |
| SUBJECTS WITH PNEUMONITIS IMAES | 524 | 1 ( 0.2) | 523 ( 99.8) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.4598 |
| SUBJECTS WITH DIARRHEA/COLITIS IMAES | 524 | 5 ( 1.0) | 519 ( 99.0) | N.A. | 264 | 2 ( 0.8) | 262 ( 99.2) | N.A. | 1.374 ( 0.266, 7.089) | 0.7027 |
| SUBJECTS WITH HEPATITIS IMAES | 524 | 7 ( 1.3) | 517 ( 98.7) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.0561 |
| SUBJECTS WITH NEPHRITIS AND RENAL DYSFUNCTION IMAES | 524 | 2 ( 0.4) | 522 ( 99.6) | N.A. | 264 | 1 ( 0.4) | 263 ( 99.6) | N.A. | 1.015 ( 0.092, 11.200) | 0.9901 |
| SUBJECTS WITH RASH IMAES | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH HYPERSENSITIVITY IMAES | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH ADRENAL INSUFFICIENCY IMAES | 524 | 3 ( 0.6) | 521 ( 99.4) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.1784 |
| SUBJECTS WITH HYPOPHYSITIS IMAES | 524 | 4 ( 0.8) | 520 ( 99.2) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.1481 |
| SUBJECTS WITH HYPOTHYROIDISM/ THYROIDITIS IMAES | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-timaetahrt-ebr1575.sas 20JUL2023:10:02:26

Protocol: CA20976K 

Table 25.5
Serious Immune-mediated Adverse Events : Time-Adjusted Analyses
On Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| Immune-Mediated Adverse Events (IMAE) | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab Censored Subjects n (%) | Nivolumab KME [95%CI] (mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo Censored Subjects n (%) | Placebo KME [95%CI] (mon) (1) | Nivolumab vs. Placebo HR [95%CI] (2) | Nivolumab vs. Placebo P-value (3) |
|---|---|---|---|---|---|---|---|---|---|---|
| SUBJECTS WITH HYPOTHYROIDISM IMAES | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH THYROIDITIS IMAES | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH HYPERTHYROIDISM IMAES | 524 | 1 ( 0.2) | 523 ( 99.8) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.4712 |
| SUBJECTS WITH DIABETES MELLITUS IMAES | 524 | 1 ( 0.2) | 523 ( 99.8) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.4594 |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-timaetahrt-ebr1575.sas 20JUL2023:10:02:26

**Anhang 4-G 2.2.2: Ergebnisse für Endpunkte spezifische UE (select UE) aus CA209-76K – Zeit bis zum ersten Auftreten des UE**

**Anhang 4-G 2.2.2.1 Ergebnisse für Endpunkte jegliche spezifische UE aus CA209-76K – Zeit bis zum ersten Auftreten des UE**

Protocol: CA20976K 

Table 24.1
Select Adverse Events: Time-Adjusted Analyses
On Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| Select Adverse Events (SLAE) | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME [95%CI] (mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME [95%CI] (mon) (1) | Nivolumab vs. Placebo HR [95%CI] (2) | Nivolumab vs. Placebo P-value (3) |
|---|---|---|---|---|---|---|---|---|
| SUBJECTS WITH ANY SELECT AES | 524 | 399 ( 76.1) | 2.86 ( 2.46, 3.65) | 264 | 131 ( 49.6) | 11.60 ( 8.94, N.A.) | 2.239 ( 1.836, 2.732) | <0.0001 |
| SUBJECTS WITH ENDOCRINE AES | 524 | 126 ( 24.0) | N.A. | 264 | 16 ( 6.1) | N.A. | 4.715 ( 2.802, 7.936) | <0.0001 |
| SUBJECTS WITH GASTROINTESTINAL AES | 524 | 132 ( 25.2) | N.A. | 264 | 46 ( 17.4) | N.A. | 1.556 ( 1.112, 2.176) | 0.0093 |
| SUBJECTS WITH HEPATIC AES | 524 | 93 ( 17.7) | N.A. | 264 | 38 ( 14.4) | N.A. | 1.327 ( 0.909, 1.935) | 0.1411 |
| SUBJECTS WITH PULMONARY AES | 524 | 11 ( 2.1) | N.A. | 264 | 3 ( 1.1) | N.A. | 2.016 ( 0.562, 7.231) | 0.2722 |
| SUBJECTS WITH RENAL AES | 524 | 33 ( 6.3) | N.A. | 264 | 12 ( 4.5) | N.A. | 1.494 ( 0.771, 2.893) | 0.2309 |
| SUBJECTS WITH SKIN AES | 524 | 224 ( 42.7) | N.A. (11.99, N.A.) | 264 | 68 ( 25.8) | N.A. | 1.994 ( 1.519, 2.616) | <0.0001 |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-slaetahrt-ebr1575-b4.sas 19JUL2023:14:09:42

Protocol: CA20976K 

Table 24.1
Select Adverse Events: Time-Adjusted Analyses
On Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Select Adverse Events (SLAE) | N | Subjects with Event n (%) | KME [95%CI] (mon) (1) | N | Subjects with Event n (%) | KME [95%CI] (mon) (1) | HR [95%CI] (2) | P-value (3) |
| SUBJECTS WITH HYPERSENSITIVITY/ INFUSION REACTION AES | 524 | 34 ( 6.5) | N.A. | 264 | 2 ( 0.8) | N.A. | 8.867 ( 2.131, 36.902) | 0.0003 |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-slaetahrt-ebr1575-b4.sas 19JUL2023:14:09:42

**Anhang 4-G 2.2.2.2 Ergebnisse für Endpunkte schwere spezifische UE aus CA209-76K – Zeit bis zum ersten Auftreten des UE**

Protocol: CA20976K 

Table 24.3
Select Adverse Events with CTCAE Grade 3-4-5: Time-Adjusted Analyses
On Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Select Adverse Events (SLAE) | N | Subjects with Event n (%) | KME [95%CI] (mon) (1) | N | Subjects with Event n (%) | KME [95%CI] (mon) (1) | HR [95%CI] (2) | P-value (3) |
| SUBJECTS WITH SELECT AES CTCAE GRADES >= 3 | 524 | 55 ( 10.5) | N.A. | 264 | 7 ( 2.7) | N.A. | 4.328 ( 1.971, 9.507) | <0.0001 |
| SUBJECTS WITH ENDOCRINE AES | 524 | 12 ( 2.3) | N.A. | 264 | 0 | N.E. | N.E. | 0.0105 |
| SUBJECTS WITH GASTROINTESTINAL AES | 524 | 11 ( 2.1) | N.A. | 264 | 1 ( 0.4) | N.A. | 5.839 ( 0.754, 45.234) | 0.0553 |
| SUBJECTS WITH HEPATIC AES | 524 | 24 ( 4.6) | N.A. | 264 | 4 ( 1.5) | N.A. | 3.208 ( 1.113, 9.247) | 0.0225 |
| SUBJECTS WITH PULMONARY AES | 524 | 2 ( 0.4) | N.A. | 264 | 0 | N.E. | N.E. | 0.3070 |
| SUBJECTS WITH RENAL AES | 524 | 2 ( 0.4) | N.A. | 264 | 1 ( 0.4) | N.A. | 1.031 ( 0.093, 11.369) | 0.9801 |
| SUBJECTS WITH SKIN AES | 524 | 7 ( 1.3) | N.A. | 264 | 2 ( 0.8) | N.A. | 2.005 ( 0.416, 9.665) | 0.3766 |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-slaetahrt-ebr1575-b4.sas 19JUL2023:14:10:11

Protocol: CA20976K 

Table 24.3
Select Adverse Events with CTCAE Grade 3-4-5: Time-Adjusted Analyses
On Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Select Adverse Events (SLAE) | N | Subjects with Event n (%) | KME [95%CI] (mon) (1) | N | Subjects with Event n (%) | KME [95%CI] (mon) (1) | HR [95%CI] (2) | P-value (3) |
| SUBJECTS WITH HYPERSENSITIVITY/ INFUSION REACTION AES | 524 | 0 | N.E. | 264 | 0 | N.E. | N.E. | N.E. |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-slaetahrt-ebr1575-b4.sas 19JUL2023:14:10:11

**Anhang 4-G 2.2.2.3 Ergebnisse für Endpunkte schwerwiegende spezifische UE aus CA209-76K – Zeit bis zum ersten Auftreten des UE**

Protocol: CA20976K 

Table 24.5
Serious Select Adverse Events : Time-Adjusted Analyses
On Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Select Adverse Events (SLAE) | N | Subjects with Event n (%) | KME [95%CI] (mon) (1) | N | Subjects with Event n (%) | KME [95%CI] (mon) (1) | HR [95%CI] (2) | P-value (3) |
| SUBJECTS WITH SERIOUS SELECT AES | 524 | 29 ( 5.5) | N.A. | 264 | 7 ( 2.7) | N.A. | 2.252 ( 0.986, 5.144) | 0.0477 |
| SUBJECTS WITH ENDOCRINE AES | 524 | 9 ( 1.7) | N.A. | 264 | 0 | N.E. | N.E. | 0.0257 |
| SUBJECTS WITH GASTROINTESTINAL AES | 524 | 7 ( 1.3) | N.A. | 264 | 2 ( 0.8) | N.A. | 1.896 ( 0.394, 9.131) | 0.4172 |
| SUBJECTS WITH HEPATIC AES | 524 | 11 ( 2.1) | N.A. | 264 | 2 ( 0.8) | N.A. | 2.943 ( 0.652, 13.283) | 0.1409 |
| SUBJECTS WITH PULMONARY AES | 524 | 2 ( 0.4) | N.A. | 264 | 1 ( 0.4) | N.A. | 1.047 ( 0.095, 11.546) | 0.9700 |
| SUBJECTS WITH RENAL AES | 524 | 3 ( 0.6) | N.A. | 264 | 2 ( 0.8) | N.A. | 0.766 ( 0.128, 4.584) | 0.7694 |
| SUBJECTS WITH SKIN AES | 524 | 0 | N.E. | 264 | 1 ( 0.4) | N.A. | N.E. | 0.2281 |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-slaetahrt-ebr1575-b4.sas 19JUL2023:14:10:36

Protocol: CA20976K 

Table 24.5
Serious Select Adverse Events : Time-Adjusted Analyses
On Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Select Adverse Events (SLAE) | N | Subjects with Event n (%) | KME [95%CI] (mon) (1) | N | Subjects with Event n (%) | KME [95%CI] (mon) (1) | HR [95%CI] (2) | P-value (3) |
| SUBJECTS WITH HYPERSENSITIVITY/ INFUSION REACTION AES | 524 | 0 | N.E. | 264 | 0 | N.E. | N.E. | N.E. |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-slaetahrt-ebr1575-b4.sas 19JUL2023:14:10:36

**Anhang 4-G 2.2.3: Ergebnisse für Endpunkte weitere UE von speziellem Interesse (OESI) aus CA209-76K – Zeit bis zum ersten Auftreten des UE**

**Anhang 4-G 2.2.3.1 Ergebnisse für Endpunkte jegliche weitere UE von speziellem Interesse aus CA209-76K – Zeit bis zum ersten Auftreten des UE**

Protocol: CA20976K 

Table 26.1
Other Events of Special Interest: Time-Adjusted Analyses
On Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| Other Events of Special Interest (OESI) | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab Censored Subjects n (%) | Nivolumab KME (95%CI) (mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo Censored Subjects n (%) | Placebo KME (95%CI) (mon) (1) | Nivolumab vs. Placebo HR (95%CI) (2) | Nivolumab vs. Placebo P-value (3) |
|---|---|---|---|---|---|---|---|---|---|---|
| SUBJECTS WITH ANY OESIS | 524 | 17 ( 3.2) | 507 ( 96.8) | N.A. | 264 | 2 ( 0.8) | 262 ( 99.2) | N.A. | 4.557 ( 1.053, 19.729) | 0.0259 |
| SUBJECTS WITH MYASTHENIC SYNDROME | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH DEMYELINATION EVENT | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH GUILLAIN-BARRE SYNDROME | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH PANCREATITIS EVENT | 524 | 8 ( 1.5) | 516 ( 98.5) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.0368 |
| SUBJECTS WITH UVEITIS EVENT | 524 | 2 ( 0.4) | 522 ( 99.6) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.2926 |
| SUBJECTS WITH ENCEPHALITIS EVENT | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-toesi-tahr--ta-cens-ebr1575-b4.sas 01AUG2023:16:10:20

Protocol: CA20976K 

Table 26.1
Other Events of Special Interest: Time-Adjusted Analyses
On Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Other Events of Special Interest (OESI) | N | Subjects with Event n (%) | Censored Subjects n (%) | KME (95%CI) (mon) (1) | Subjects with Event n (%) | Censored Subjects n (%) | KME (95%CI) (mon) (1) | HR (95%CI) (2) | P-value (3) |
| SUBJECTS WITH MYOCARDITIS EVENT | 524 | 3 ( 0.6) | 521 ( 99.4) | N.A. | 264 0 | 264 (100.0) | N.E. | N.E. | 0.2212 |
| SUBJECTS WITH MYOSITIS/ RHABDOMYOLYSIS EVENT | 524 | 8 ( 1.5) | 516 ( 98.5) | N.A. | 264 2 ( 0.8) | 262 ( 99.2) | N.A. | 2.073 ( 0.440, 9.763) | 0.3459 |
| SUBJECTS WITH GRAFT VERSUS HOST DISEASE | 524 | 0 | 524 (100.0) | N.E. | 264 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH AUTOIMMUNE CYTOPENIA | 524 | 0 | 524 (100.0) | N.E. | 264 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH AUTOIMMUNE EYE DISORDER | 524 | 0 | 524 (100.0) | N.E. | 264 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH IMMUNE MEDIATED ARTHRITIS | 524 | 0 | 524 (100.0) | N.E. | 264 0 | 264 (100.0) | N.E. | N.E. | N.E. |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-toesi-tahr--ta-cens-ebr1575-b4.sas 01AUG2023:16:10:20

**Anhang 4-G 2.2.3.2 Ergebnisse für Endpunkte schwere weitere UE von speziellem Interesse aus CA209-76K – Zeit bis zum ersten Auftreten des UE**

Protocol: CA20976K 

Table 26.3
Other Events of Special Interest with CTCAE Grade 3-4-5: Time-Adjusted Analyses
On Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| | Nivolumab | | | | Placebo | | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|---|---|
| Other Events of Special Interest (OESI) | N | Subjects with Event n (%) | Censored Subjects n (%) | KME (95%CI) (mon) (1) | N | Subjects with Event n (%) | Censored Subjects n (%) | KME (95%CI) (mon) (1) | HR (95%CI) (2) | P-value (3) |
| SUBJECTS WITH ANY OESIS | 524 | 7 ( 1.3) | 517 ( 98.7) | N.A. | 264 | 1 ( 0.4) | 263 ( 99.6) | N.A. | 3.660 ( 0.450, 29.749) | 0.1934 |
| SUBJECTS WITH MYASTHENIC SYNDROME | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH DEMYELINATION EVENT | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH GUILLAIN-BARRE SYNDROME | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH PANCREATITIS EVENT | 524 | 2 ( 0.4) | 522 ( 99.6) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.3076 |
| SUBJECTS WITH UVEITIS EVENT | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH ENCEPHALITIS EVENT | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-toesi-tahr--ta-cens-ebr1575-b4.sas 01AUG2023:16:10:50

Protocol: CA20976K 

Table 26.3
Other Events of Special Interest with CTCAE Grade 3-4-5: Time-Adjusted Analyses
On Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| | Nivolumab | | | | Placebo | | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|---|---|
| Other Events of Special Interest (OESI) | N | Subjects with Event n (%) | Censored Subjects n (%) | KME (95%CI) (mon) (1) | N | Subjects with Event n (%) | Censored Subjects n (%) | KME (95%CI) (mon) (1) | HR (95%CI) (2) | P-value (3) |
| SUBJECTS WITH MYOCARDITIS EVENT | 524 | 2 ( 0.4) | 522 ( 99.6) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.3170 |
| SUBJECTS WITH MYOSITIS/ RHABDOMYOLYSIS EVENT | 524 | 5 ( 1.0) | 519 ( 99.0) | N.A. | 264 | 1 ( 0.4) | 263 ( 99.6) | N.A. | 2.617 ( 0.305, 22.415) | 0.3618 |
| SUBJECTS WITH GRAFT VERSUS HOST DISEASE | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH AUTOIMMUNE CYTOPENIA | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH AUTOIMMUNE EYE DISORDER | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH IMMUNE MEDIATED ARTHRITIS | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-toesi-tahr--ta-cens-ebr1575-b4.sas 01AUG2023:16:10:50

**Anhang 4-G 2.2.3.3 Ergebnisse für Endpunkte schwerwiegende weitere UE von speziellem Interesse aus CA209-76K – Zeit bis zum ersten Auftreten des UE**

Protocol: CA20976K 

Table 26.5
Serious Other Events of Special Interest: Time-Adjusted Analyses
On Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Other Events of Special Interest (OESI) | N Subjects with Event n (%) | Censored Subjects n (%) | KME (95%CI) (mon) (1) | N Subjects with Event n (%) | Censored Subjects n (%) | KME (95%CI) (mon) (1) | HR (95%CI) (2) | P-value (3) |
| SUBJECTS WITH ANY OESIS | 524 8 ( 1.5) | 516 ( 98.5) | N.A. | 264 1 ( 0.4) | 263 ( 99.6) | N.A. | 4.108 ( 0.514, 32.847) | 0.1483 |
| SUBJECTS WITH MYASTHENIC SYNDROME | 524 0 | 524 (100.0) | N.E. | 264 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH DEMYELINATION EVENT | 524 0 | 524 (100.0) | N.E. | 264 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH GUILLAIN-BARRE SYNDROME | 524 0 | 524 (100.0) | N.E. | 264 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH PANCREATITIS EVENT | 524 3 ( 0.6) | 521 ( 99.4) | N.A. | 264 0 | 264 (100.0) | N.E. | N.E. | 0.2118 |
| SUBJECTS WITH UVEITIS EVENT | 524 1 ( 0.2) | 523 ( 99.8) | N.A. | 264 0 | 264 (100.0) | N.E. | N.E. | 0.4757 |
| SUBJECTS WITH ENCEPHALITIS EVENT | 524 0 | 524 (100.0) | N.E. | 264 0 | 264 (100.0) | N.E. | N.E. | N.E. |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-toesi-tahr--ta-cens-ebr1575-b4.sas 01AUG2023:16:11:20

Protocol: CA20976K 

Table 26.5
Serious Other Events of Special Interest: Time-Adjusted Analyses
On Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| | Nivolumab | | | | Placebo | | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|---|---|
| Other Events of Special Interest (OESI) | N | Subjects with Event n (%) | Censored Subjects n (%) | KME (95%CI) (mon) (1) | N | Subjects with Event n (%) | Censored Subjects n (%) | KME (95%CI) (mon) (1) | HR (95%CI) (2) | P-value (3) |
| SUBJECTS WITH MYOCARDITIS EVENT | 524 | 2 ( 0.4) | 522 ( 99.6) | N.A. | 264 | 0 | 264 (100.0) | N.E. | N.E. | 0.3170 |
| SUBJECTS WITH MYOSITIS/ RHABDOMYOLYSIS EVENT | 524 | 4 ( 0.8) | 520 ( 99.2) | N.A. | 264 | 1 ( 0.4) | 263 ( 99.6) | N.A. | 2.054 ( 0.230, 18.375) | 0.5108 |
| SUBJECTS WITH GRAFT VERSUS HOST DISEASE | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH AUTOIMMUNE CYTOPENIA | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH AUTOIMMUNE EYE DISORDER | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |
| SUBJECTS WITH IMMUNE MEDIATED ARTHRITIS | 524 | 0 | 524 (100.0) | N.E. | 264 | 0 | 264 (100.0) | N.E. | N.E. | N.E. |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-toesi-tahr--ta-cens-ebr1575-b4.sas 01AUG2023:16:11:20

**Anhang 4-G 2.3: Ergebnisse für Endpunkte häufige Unerwünschte Ereignisse auf SOC/PT-Ebene aus CA209-76K**

**Anhang 4-G 2.3.1: Ergebnisse für Endpunkte häufige jegliche UE auf SOC/PT-Ebene aus CA209-76K – Zeit bis zum ersten Auftreten des UE**

Protocol: CA20976K 

Table 23.1
Adverse Events: Time-Adjusted Analyses
by SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| System Organ Class (%) / Preferred Term (%) | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME [95%CI] (mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME [95%CI] (mon) (1) | Nivolumab vs. Placebo HR [95%CI] (2) | Nivolumab vs. Placebo P-value (3) |
|---|---|---|---|---|---|---|---|---|
| TOTAL SUBJECTS WITH AN EVENT | 524 | 508 ( 96.9) | 0.95 ( 0.89, 0.95) | 264 | 234 ( 88.6) | 1.77 ( 1.12, 1.91) | 1.700 ( 1.452, 1.991) | <0.0001 |
| SKIN AND SUBCUTANEOUS TISSUE DISORDERS | 524 | 271 ( 51.7) | 9.36 ( 6.47, 12.02) | 264 | 90 ( 34.1) | N.A. | 1.900 ( 1.496, 2.413) | <0.0001 |
| PRURITUS | 524 | 107 ( 20.4) | N.A. | 264 | 29 ( 11.0) | N.A. | 2.050 ( 1.360, 3.091) | 0.0005 |
| RASH | 524 | 70 ( 13.4) | N.A. | 264 | 26 ( 9.8) | N.A. | 1.447 ( 0.923, 2.271) | 0.1056 |
| RASH MACULO-PAPULAR | 524 | 28 ( 5.3) | N.A. | 264 | 7 ( 2.7) | N.A. | 2.140 ( 0.934, 4.901) | 0.0654 |
| ECZEMA | 524 | 24 ( 4.6) | N.A. | 264 | 6 ( 2.3) | N.A. | 2.143 ( 0.876, 5.244) | 0.0872 |
| DRY SKIN | 524 | 20 ( 3.8) | N.A. | 264 | 7 ( 2.7) | N.A. | 1.528 ( 0.646, 3.616) | 0.3306 |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-taesocpthrta-ebr1575-b4.sas 19JUL2023:12:32:15

Protocol: CA20976K 

Table 23.1
Adverse Events: Time-Adjusted Analyses
by SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| System Organ Class (%) / Preferred Term (%) | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME [95%CI] (mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME [95%CI] (mon) (1) | Nivolumab vs. Placebo HR [95%CI] (2) | Nivolumab vs. Placebo P-value (3) |
|---|---|---|---|---|---|---|---|---|
| RASH PRURITIC | 524 | 12 ( 2.3) | N.A. | 264 | 1 ( 0.4) | N.A. | 6.201 ( 0.806, 47.688) | 0.0448 |
| ERYTHEMA | 524 | 11 ( 2.1) | N.A. | 264 | 5 ( 1.9) | N.A. | 1.165 ( 0.405, 3.355) | 0.7764 |
| SKIN LESION | 524 | 11 ( 2.1) | N.A. | 264 | 8 ( 3.0) | N.A. | 0.747 ( 0.300, 1.859) | 0.5291 |
| GASTROINTESTINAL DISORDERS | 524 | 269 ( 51.3) | 9.23 ( 7.26, 14.98) | 264 | 112 ( 42.4) | N.A. (12.09, N.A.) | 1.341 ( 1.075, 1.672) | 0.0089 |
| DIARRHOEA | 524 | 128 ( 24.4) | N.A. | 264 | 44 ( 16.7) | N.A. | 1.575 ( 1.118, 2.219) | 0.0087 |
| NAUSEA | 524 | 81 ( 15.5) | N.A. | 264 | 30 ( 11.4) | N.A. | 1.435 ( 0.944, 2.183) | 0.0888 |
| CONSTIPATION | 524 | 50 ( 9.5) | N.A. | 264 | 17 ( 6.4) | N.A. | 1.582 ( 0.912, 2.744) | 0.0990 |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-taesocpthrta-ebr1575-b4.sas 19JUL2023:12:32:15

Protocol: CA20976K 

Table 23.1
Adverse Events: Time-Adjusted Analyses
by SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| System Organ Class (%) Preferred Term (%) | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME [95%CI] (mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME [95%CI] (mon) (1) | Nivolumab vs. Placebo HR [95%CI] (2) | Nivolumab vs. Placebo P-value (3) |
|---|---|---|---|---|---|---|---|---|
| DRY MOUTH | 524 | 41 ( 7.8) | N.A. | 264 | 13 ( 4.9) | N.A. | 1.639 ( 0.878, 3.059) | 0.1167 |
| ABDOMINAL PAIN | 524 | 24 ( 4.6) | N.A. | 264 | 14 ( 5.3) | N.A. | 0.910 ( 0.470, 1.760) | 0.7778 |
| VOMITING | 524 | 19 ( 3.6) | N.A. | 264 | 14 ( 5.3) | N.A. | 0.721 ( 0.361, 1.439) | 0.3517 |
| GASTROOESOPHAGEAL REFLUX DISEASE | 524 | 13 ( 2.5) | N.A. | 264 | 5 ( 1.9) | N.A. | 1.386 ( 0.494, 3.890) | 0.5330 |
| COLITIS | 524 | 12 ( 2.3) | N.A. | 264 | 2 ( 0.8) | N.A. | 3.239 ( 0.725, 14.477) | 0.1034 |
| DYSPEPSIA | 524 | 12 ( 2.3) | N.A. | 264 | 4 ( 1.5) | N.A. | 1.634 ( 0.527, 5.070) | 0.3901 |
| ABDOMINAL PAIN UPPER | 524 | 10 ( 1.9) | N.A. | 264 | 6 ( 2.3) | N.A. | 0.876 ( 0.318, 2.411) | 0.7980 |

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(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
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|---|---|---|---|---|---|---|---|---|
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | 524 | 268 ( 51.1) | 8.87 ( 6.67, N.A.) | 264 | 119 ( 45.1) | N.A. (10.15, N.A.) | 1.239 ( 0.998, 1.538) | 0.0510 |
| FATIGUE | 524 | 145 ( 27.7) | N.A. | 264 | 68 ( 25.8) | N.A. | 1.109 ( 0.831, 1.479) | 0.4795 |
| ASTHENIA | 524 | 65 ( 12.4) | N.A. | 264 | 26 ( 9.8) | N.A. | 1.331 ( 0.844, 2.098) | 0.2169 |
| PYREXIA | 524 | 35 ( 6.7) | N.A. | 264 | 12 ( 4.5) | N.A. | 1.576 ( 0.818, 3.038) | 0.1701 |
| OEDEMA PERIPHERAL | 524 | 25 ( 4.8) | N.A. | 264 | 6 ( 2.3) | N.A. | 2.253 ( 0.924, 5.494) | 0.0664 |
| INFLUENZA LIKE ILLNESS | 524 | 21 ( 4.0) | N.A. | 264 | 4 ( 1.5) | N.A. | 2.826 ( 0.969, 8.236) | 0.0466 |
| PAIN | 524 | 12 ( 2.3) | N.A. | 264 | 5 ( 1.9) | N.A. | 1.274 ( 0.449, 3.619) | 0.6481 |

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|---|---|---|---|---|---|---|---|---|
| MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS | 524 | 203 ( 38.7) | N.A. | 264 | 85 ( 32.2) | N.A. | 1.340 ( 1.040, 1.726) | 0.0230 |
| ARTHRALGIA | 524 | 89 ( 17.0) | N.A. | 264 | 32 ( 12.1) | N.A. | 1.533 ( 1.023, 2.296) | 0.0368 |
| MYALGIA | 524 | 41 ( 7.8) | N.A. | 264 | 17 ( 6.4) | N.A. | 1.278 ( 0.726, 2.250) | 0.3941 |
| BACK PAIN | 524 | 28 ( 5.3) | N.A. | 264 | 17 ( 6.4) | N.A. | 0.880 ( 0.481, 1.608) | 0.6767 |
| PAIN IN EXTREMITY | 524 | 25 ( 4.8) | N.A. | 264 | 11 ( 4.2) | N.A. | 1.223 ( 0.601, 2.486) | 0.5776 |
| ARTHRITIS | 524 | 13 ( 2.5) | N.A. | 264 | 1 ( 0.4) | N.A. | 7.085 ( 0.927, 54.181) | 0.0277 |
| MUSCLE SPASMS | 524 | 12 ( 2.3) | N.A. | 264 | 4 ( 1.5) | N.A. | 1.586 ( 0.511, 4.918) | 0.4202 |

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| System Organ Class (%) Preferred Term (%) | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME [95%CI] (mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME [95%CI] (mon) (1) | Nivolumab vs. Placebo HR [95%CI] (2) | Nivolumab vs. Placebo P-value (3) |
|---|---|---|---|---|---|---|---|---|
| INVESTIGATIONS | 524 | 197 ( 37.6) | N.A. | 264 | 87 ( 33.0) | N.A. | 1.249 ( 0.970, 1.607) | 0.0838 |
| BLOOD CREATINE PHOSPHOKINASE INCREASED | 524 | 58 ( 11.1) | N.A. | 264 | 32 ( 12.1) | N.A. | 0.951 ( 0.618, 1.465) | 0.8206 |
| ALANINE AMINOTRANSFERASE INCREASED | 524 | 53 ( 10.1) | N.A. | 264 | 19 ( 7.2) | N.A. | 1.488 ( 0.881, 2.513) | 0.1346 |
| ASPARTATE AMINOTRANSFERASE INCREASED | 524 | 43 ( 8.2) | N.A. | 264 | 8 ( 3.0) | N.A. | 2.930 ( 1.377, 6.234) | 0.0034 |
| BLOOD CREATININE INCREASED | 524 | 25 ( 4.8) | N.A. | 264 | 10 ( 3.8) | N.A. | 1.352 ( 0.649, 2.816) | 0.4189 |
| LIPASE INCREASED | 524 | 24 ( 4.6) | N.A. | 264 | 10 ( 3.8) | N.A. | 1.306 ( 0.624, 2.731) | 0.4776 |
| BLOOD ALKALINE PHOSPHATASE INCREASED | 524 | 17 ( 3.2) | N.A. | 264 | 2 ( 0.8) | N.A. | 4.621 ( 1.067, 20.008) | 0.0243 |

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|---|---|---|---|---|---|---|---|---|
| BLOOD BILIRUBIN INCREASED | 524 | 16 ( 3.1) | N.A. | 264 | 7 ( 2.7) | N.A. | 1.217 ( 0.500, 2.958) | 0.6643 |
| BLOOD THYROID STIMULATING HORMONE INCREASED | 524 | 15 ( 2.9) | N.A. | 264 | 6 ( 2.3) | N.A. | 1.302 ( 0.505, 3.356) | 0.5846 |
| GAMMA-GLUTAMYLTRANSFERASE INCREASED | 524 | 14 ( 2.7) | N.A. | 264 | 2 ( 0.8) | N.A. | 3.762 ( 0.855, 16.556) | 0.0596 |
| AMYLASE INCREASED | 524 | 13 ( 2.5) | N.A. | 264 | 6 ( 2.3) | N.A. | 1.150 ( 0.437, 3.028) | 0.7768 |
| WEIGHT DECREASED | 524 | 13 ( 2.5) | N.A. | 264 | 4 ( 1.5) | N.A. | 1.739 ( 0.567, 5.335) | 0.3274 |
| BLOOD LACTATE DEHYDROGENASE INCREASED | 524 | 12 ( 2.3) | N.A. | 264 | 5 ( 1.9) | N.A. | 1.263 ( 0.445, 3.587) | 0.6600 |
| INFECTIONS AND INFESTATIONS | 524 | 192 ( 36.6) | N.A. | 264 | 76 ( 28.8) | N.A. | 1.439 ( 1.103, 1.877) | 0.0070 |

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|---|---|---|---|---|---|---|---|---|
| COVID-19 | 524 | 62 ( 11.8) | N.A. | 264 | 27 ( 10.2) | N.A. | 1.301 ( 0.828, 2.046) | 0.2520 |
| URINARY TRACT INFECTION | 524 | 16 ( 3.1) | N.A. | 264 | 2 ( 0.8) | N.A. | 4.494 ( 1.032, 19.558) | 0.0281 |
| NASOPHARYNGITIS | 524 | 15 ( 2.9) | N.A. | 264 | 6 ( 2.3) | N.A. | 1.368 ( 0.530, 3.534) | 0.5159 |
| METABOLISM AND NUTRITION DISORDERS | 524 | 139 ( 26.5) | N.A. | 264 | 50 ( 18.9) | N.A. | 1.529 ( 1.107, 2.114) | 0.0095 |
| DECREASED APPETITE | 524 | 42 ( 8.0) | N.A. | 264 | 8 ( 3.0) | N.A. | 2.877 ( 1.351, 6.130) | 0.0041 |
| HYPERGLYCAEMIA | 524 | 28 ( 5.3) | N.A. | 264 | 12 ( 4.5) | N.A. | 1.216 ( 0.618, 2.391) | 0.5713 |
| HYPOPHOSPHATAEMIA | 524 | 20 ( 3.8) | N.A. | 264 | 13 ( 4.9) | N.A. | 0.808 ( 0.402, 1.626) | 0.5505 |

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|---|---|---|---|---|---|---|---|---|
| HYPOKALAEMIA | 524 | 19 ( 3.6) | N.A. | 264 | 9 ( 3.4) | N.A. | 1.117 ( 0.505, 2.470) | 0.7851 |
| HYPONATRAEMIA | 524 | 10 ( 1.9) | N.A. | 264 | 6 ( 2.3) | N.A. | 0.891 ( 0.324, 2.453) | 0.8231 |
| NERVOUS SYSTEM DISORDERS | 524 | 136 ( 26.0) | N.A. | 264 | 63 ( 23.9) | N.A. | 1.118 ( 0.830, 1.508) | 0.4619 |
| HEADACHE | 524 | 65 ( 12.4) | N.A. | 264 | 34 ( 12.9) | N.A. | 1.004 ( 0.663, 1.520) | 0.9863 |
| DIZZINESS | 524 | 22 ( 4.2) | N.A. | 264 | 13 ( 4.9) | N.A. | 0.873 ( 0.440, 1.734) | 0.6985 |
| PARAESTHESIA | 524 | 14 ( 2.7) | N.A. | 264 | 7 ( 2.7) | N.A. | 1.032 ( 0.416, 2.557) | 0.9458 |
| SYNCOPE | 524 | 10 ( 1.9) | N.A. | 264 | 0 | N.E. | N.E. | 0.0204 |
| RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS | 524 | 117 ( 22.3) | N.A. | 264 | 41 ( 15.5) | N.A. | 1.585 ( 1.110, 2.262) | 0.0105 |

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|---|---|---|---|---|---|---|---|---|
| COUGH | 524 | 40 ( 7.6) | N.A. | 264 | 13 ( 4.9) | N.A. | 1.648 ( 0.881, 3.082) | 0.1134 |
| DYSPNOEA | 524 | 31 ( 5.9) | N.A. | 264 | 10 ( 3.8) | N.A. | 1.698 ( 0.832, 3.464) | 0.1411 |
| RHINITIS ALLERGIC | 524 | 10 ( 1.9) | N.A. | 264 | 4 ( 1.5) | N.A. | 1.344 ( 0.421, 4.288) | 0.6160 |
| ENDOCRINE DISORDERS | 524 | 114 ( 21.8) | N.A. | 264 | 10 ( 3.8) | N.A. | 6.795 ( 3.559, 12.974) | <0.0001 |
| HYPOTHYROIDISM | 524 | 67 ( 12.8) | N.A. | 264 | 0 | N.E. | N.E. | <0.0001 |
| HYPERTHYROIDISM | 524 | 42 ( 8.0) | N.A. | 264 | 4 ( 1.5) | N.A. | 5.655 ( 2.028, 15.774) | 0.0002 |
| ADRENAL INSUFFICIENCY | 524 | 12 ( 2.3) | N.A. | 264 | 3 ( 1.1) | N.A. | 2.279 ( 0.643, 8.087) | 0.1897 |
| INJURY, POISONING AND PROCEDURAL COMPLICATIONS | 524 | 67 ( 12.8) | N.A. | 264 | 28 ( 10.6) | N.A. | 1.301 ( 0.837, 2.023) | 0.2424 |

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|---|---|---|---|---|---|---|---|---|
| INFUSION RELATED REACTION | 524 | 28 ( 5.3) | N.A. | 264 | 2 ( 0.8) | N.A. | 7.228 ( 1.722, 30.341) | 0.0015 |
| NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) | 524 | 63 ( 12.0) | N.A. | 264 | 39 ( 14.8) | N.A. | 0.869 ( 0.583, 1.296) | 0.4903 |
| BASAL CELL CARCINOMA | 524 | 24 ( 4.6) | N.A. | 264 | 12 ( 4.5) | N.A. | 1.055 ( 0.528, 2.111) | 0.8777 |
| VASCULAR DISORDERS | 524 | 60 ( 11.5) | N.A. | 264 | 32 ( 12.1) | N.A. | 0.982 ( 0.640, 1.509) | 0.9360 |
| HYPERTENSION | 524 | 36 ( 6.9) | N.A. | 264 | 20 ( 7.6) | N.A. | 0.937 ( 0.542, 1.619) | 0.8151 |
| BLOOD AND LYMPHATIC SYSTEM DISORDERS | 524 | 59 ( 11.3) | N.A. | 264 | 23 ( 8.7) | N.A. | 1.372 ( 0.847, 2.222) | 0.1970 |
| ANAEMIA | 524 | 25 ( 4.8) | N.A. | 264 | 9 ( 3.4) | N.A. | 1.458 ( 0.680, 3.123) | 0.3301 |

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|---|---|---|---|---|---|---|---|---|
| EOSINOPHILIA | 524 | 19 ( 3.6) | N.A. | 264 | 2 ( 0.8) | N.A. | 5.089 ( 1.185, 21.851) | 0.0148 |
| EYE DISORDERS | 524 | 48 ( 9.2) | N.A. | 264 | 13 ( 4.9) | N.A. | 2.009 ( 1.088, 3.709) | 0.0229 |
| DRY EYE | 524 | 18 ( 3.4) | N.A. | 264 | 3 ( 1.1) | N.A. | 3.263 ( 0.961, 11.083) | 0.0446 |
| PSYCHIATRIC DISORDERS | 524 | 48 ( 9.2) | N.A. | 264 | 32 ( 12.1) | N.A. | 0.772 ( 0.493, 1.208) | 0.2555 |
| INSOMNIA | 524 | 16 ( 3.1) | N.A. | 264 | 15 ( 5.7) | N.A. | 0.543 ( 0.268, 1.098) | 0.0839 |
| CARDIAC DISORDERS | 524 | 37 ( 7.1) | N.A. | 264 | 13 ( 4.9) | N.A. | 1.505 ( 0.800, 2.832) | 0.2018 |
| RENAL AND URINARY DISORDERS | 524 | 32 ( 6.1) | N.A. | 264 | 11 ( 4.2) | N.A. | 1.554 ( 0.783, 3.084) | 0.2031 |

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Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-taesocpthrta-ebr1575-b4.sas 19JUL2023:12:32:15

Protocol: CA20976K 

Table 23.1
Adverse Events: Time-Adjusted Analyses
by SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| System Organ Class (%) Preferred Term (%) | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME [95%CI] (mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME [95%CI] (mon) (1) | Nivolumab vs. Placebo HR [95%CI] (2) | Nivolumab vs. Placebo P-value (3) |
|---|---|---|---|---|---|---|---|---|
| HEPATOBILIARY DISORDERS | 524 | 25 ( 4.8) | N.A. | 264 | 11 ( 4.2) | N.A. | 1.199 ( 0.590, 2.437) | 0.6168 |
| EAR AND LABYRINTH DISORDERS | 524 | 23 ( 4.4) | N.A. | 264 | 11 ( 4.2) | N.A. | 1.126 ( 0.549, 2.311) | 0.7458 |
| VERTIGO | 524 | 11 ( 2.1) | N.A. | 264 | 4 ( 1.5) | N.A. | 1.478 ( 0.470, 4.642) | 0.5010 |
| REPRODUCTIVE SYSTEM AND BREAST DISORDERS | 524 | 23 ( 4.4) | N.A. | 264 | 9 ( 3.4) | N.A. | 1.369 ( 0.633, 2.960) | 0.4223 |
| IMMUNE SYSTEM DISORDERS | 524 | 16 ( 3.1) | N.A. | 264 | 6 ( 2.3) | N.A. | 1.421 ( 0.556, 3.633) | 0.4607 |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-taesocpthrta-ebr1575-b4.sas 19JUL2023:12:32:15

**Anhang 4-G 2.3.2: Ergebnisse für Endpunkte häufige schwere UE auf SOC/PT-Ebene aus CA209-76K – Zeit bis zum ersten Auftreten des UE**

Protocol: CA20976K 

Table 23.3
Adverse Events with CTCAE Grade 3-4-5: Time-Adjusted Analyses
by SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| System Organ Class (%)<br>Preferred Term (%) | N | Subjects with Event n (%) | KME [95%CI] (mon) (1) | N | Subjects with Event n (%) | KME [95%CI] (mon) (1) | HR [95%CI] (2) | P-value (3) |
| TOTAL SUBJECTS WITH AN EVENT | 524 | 148 ( 28.2) | N.A. | 264 | 48 ( 18.2) | N.A. | 1.738 ( 1.255, 2.407) | 0.0008 |
| INVESTIGATIONS | 524 | 43 ( 8.2) | N.A. | 264 | 9 ( 3.4) | N.A. | 2.590 ( 1.262, 5.314) | 0.0071 |
| ALANINE AMINOTRANSFERASE INCREASED | 524 | 12 ( 2.3) | N.A. | 264 | 1 ( 0.4) | N.A. | 6.489 ( 0.843, 49.920) | 0.0385 |
| BLOOD CREATINE PHOSPHOKINASE INCREASED | 524 | 11 ( 2.1) | N.A. | 264 | 2 ( 0.8) | N.A. | 2.925 ( 0.648, 13.202) | 0.1432 |
| INFECTIONS AND INFESTATIONS | 524 | 19 ( 3.6) | N.A. | 264 | 3 ( 1.1) | N.A. | 3.397 ( 1.005, 11.484) | 0.0364 |
| GASTROINTESTINAL DISORDERS | 524 | 16 ( 3.1) | N.A. | 264 | 4 ( 1.5) | N.A. | 2.158 ( 0.721, 6.459) | 0.1586 |
| METABOLISM AND NUTRITION DISORDERS | 524 | 16 ( 3.1) | N.A. | 264 | 2 ( 0.8) | N.A. | 4.383 ( 1.007, 19.070) | 0.0313 |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-taesocpthrta-ebr1575-b4.sas 19JUL2023:12:32:47

Protocol: CA20976K 

Table 23.3
Adverse Events with CTCAE Grade 3-4-5: Time-Adjusted Analyses
by SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| System Organ Class (%) Preferred Term (%) | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME [95%CI] (mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME [95%CI] (mon) (1) | Nivolumab vs. Placebo HR [95%CI] (2) | Nivolumab vs. Placebo P-value (3) |
|---|---|---|---|---|---|---|---|---|
| VASCULAR DISORDERS | 524 | 15 ( 2.9) | N.A. | 264 | 1 ( 0.4) | N.A. | 7.957 ( 1.051, 60.241) | 0.0169 |
| HYPERTENSION | 524 | 11 ( 2.1) | N.A. | 264 | 1 ( 0.4) | N.A. | 5.821 ( 0.751, 45.092) | 0.0557 |
| NERVOUS SYSTEM DISORDERS | 524 | 13 ( 2.5) | N.A. | 264 | 4 ( 1.5) | N.A. | 1.742 ( 0.568, 5.347) | 0.3258 |
| MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS | 524 | 12 ( 2.3) | N.A. | 264 | 3 ( 1.1) | N.A. | 2.188 ( 0.617, 7.759) | 0.2135 |
| CARDIAC DISORDERS | 524 | 10 ( 1.9) | N.A. | 264 | 2 ( 0.8) | N.A. | 2.634 ( 0.577, 12.025) | 0.1938 |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-taesocpthrta-ebr1575-b4.sas 19JUL2023:12:32:47

**Anhang 4-G 2.3.3: Ergebnisse für Endpunkte häufige SUE auf SOC/PT-Ebene aus CA209-76K – Zeit bis zum ersten Auftreten des UE**

Protocol: CA20976K 

Table 23.5
Serious Adverse Events: Time-Adjusted Analyses
by SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| System Organ Class (%)<br>Preferred Term (%) | N | Subjects with Event n (%) | KME [95%CI] (mon) (1) | N | Subjects with Event n (%) | KME [95%CI] (mon) (1) | HR [95%CI] (2) | P-value (3) |
| TOTAL SUBJECTS WITH AN EVENT | 524 | 101 ( 19.3) | N.A. | 264 | 40 ( 15.2) | N.A. | 1.387<br>( 0.962, 2.001) | 0.0786 |
| INFECTIONS AND INFESTATIONS | 524 | 23 ( 4.4) | N.A. | 264 | 2 ( 0.8) | N.A. | 6.044<br>( 1.425, 25.640) | 0.0054 |
| GASTROINTESTINAL DISORDERS | 524 | 13 ( 2.5) | N.A. | 264 | 4 ( 1.5) | N.A. | 1.777<br>( 0.579, 5.451) | 0.3083 |
| MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS | 524 | 11 ( 2.1) | N.A. | 264 | 5 ( 1.9) | N.A. | 1.174<br>( 0.408, 3.380) | 0.7660 |
| CARDIAC DISORDERS | 524 | 10 ( 1.9) | N.A. | 264 | 1 ( 0.4) | N.A. | 5.268<br>( 0.674, 41.169) | 0.0763 |
| RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS | 524 | 10 ( 1.9) | N.A. | 264 | 2 ( 0.8) | N.A. | 2.686<br>( 0.588, 12.267) | 0.1843 |
| NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) | 524 | 7 ( 1.3) | N.A. | 264 | 12 ( 4.5) | N.A. | 0.317<br>( 0.125, 0.805) | 0.0107 |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.E. = Not estimable.
(1) KME of median time to first AE.
(2) Stratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Log-rank test stratified by AJCC T Stage at Study Entry, as entered in IRT.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-taesocpthrta-ebr1575-b4.sas 19JUL2023:12:33:04

**Anhang 4-G 2.3.4: Ergebnisse für Endpunkte zum Therapieabbruch führende UE auf SOC/PT-Ebene aus CA209-76K – Inzidenzen**

Protocol: CA20976K 

Table 27.1
Adverse Events Leading to Discontinuation of Study Treatment Summary
by Worst CTC Grade (Any Grade, Grade 3-4, Grade 5)
All Treated Subjects Censoring at Open-Label Nivolumab

| System Organ Class (%) Preferred Term (%) | Nivolumab N = 524 | | | Placebo N = 264 | | |
|---|---|---|---|---|---|---|
| | Any Grade | Grade 3-4 | Grade 5 | Any Grade | Grade 3-4 | Grade 5 |
| TOTAL SUBJECTS WITH AN EVENT | 118 ( 22.5) | 47 ( 9.0) | 0 | 10 ( 3.8) | 3 ( 1.1) | 0 |
| Musculoskeletal and connective tissue disorders | 22 ( 4.2) | 4 ( 0.8) | 0 | 1 ( 0.4) | 1 ( 0.4) | 0 |
| Arthralgia | 10 ( 1.9) | 0 | 0 | 0 | 0 | 0 |
| Myalgia | 4 ( 0.8) | 0 | 0 | 0 | 0 | 0 |
| Myositis | 3 ( 0.6) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Rhabdomyolysis | 2 ( 0.4) | 2 ( 0.4) | 0 | 1 ( 0.4) | 1 ( 0.4) | 0 |
| Arthritis | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Arthropathy | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Autoimmune myositis | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Immune-mediated myositis | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Muscle spasms | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Musculoskeletal pain | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Polyarthritis | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Gastrointestinal disorders | 21 ( 4.0) | 5 ( 1.0) | 0 | 0 | 0 | 0 |
| Colitis | 8 ( 1.5) | 2 ( 0.4) | 0 | 0 | 0 | 0 |
| Diarrhoea | 5 ( 1.0) | 2 ( 0.4) | 0 | 0 | 0 | 0 |
| Pancreatitis | 3 ( 0.6) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Autoimmune enteropathy | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Autoimmune pancreatitis | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Dry mouth | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Duodenitis | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Immune-mediated enterocolitis | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Nausea | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |

Apr 2023 DBL Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-aeltd-cat--ta-ebr1575.sas 22JUN2023:20:24:12

Protocol: CA20976K 

Table 27.1
Adverse Events Leading to Discontinuation of Study Treatment Summary
by Worst CTC Grade (Any Grade, Grade 3-4, Grade 5)
All Treated Subjects Censoring at Open-Label Nivolumab

| System Organ Class (%) Preferred Term (%) | Nivolumab N = 524 | | | Placebo N = 264 | | |
|---|---|---|---|---|---|---|
| | Any Grade | Grade 3-4 | Grade 5 | Any Grade | Grade 3-4 | Grade 5 |
| Investigations | 17 ( 3.2) | 9 ( 1.7) | 0 | 3 ( 1.1) | 1 ( 0.4) | 0 |
| Alanine aminotransferase increased | 7 ( 1.3) | 4 ( 0.8) | 0 | 2 ( 0.8) | 0 | 0 |
| Aspartate aminotransferase increased | 6 ( 1.1) | 4 ( 0.8) | 0 | 2 ( 0.8) | 1 ( 0.4) | 0 |
| Blood alkaline phosphatase increased | 3 ( 0.6) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Blood creatine phosphokinase increased | 3 ( 0.6) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Blood creatinine increased | 2 ( 0.4) | 0 | 0 | 1 ( 0.4) | 0 | 0 |
| Gamma-glutamyltransferase increased | 2 ( 0.4) | 0 | 0 | 0 | 0 | 0 |
| Hepatic enzyme increased | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Liver function test increased | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Platelet count decreased | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Red blood cell count decreased | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Troponin T increased | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Troponin increased | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| White blood cell count decreased | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Endocrine disorders | 13 ( 2.5) | 4 ( 0.8) | 0 | 1 ( 0.4) | 0 | 0 |
| Adrenal insufficiency | 5 ( 1.0) | 2 ( 0.4) | 0 | 0 | 0 | 0 |
| Hypophysitis | 2 ( 0.4) | 2 ( 0.4) | 0 | 1 ( 0.4) | 0 | 0 |
| Adrenocorticotropic hormone deficiency | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Hyperthyroidism | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Hypopituitarism | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Hypothyroidism | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Lymphocytic hypophysitis | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Thyroiditis | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | 11 ( 2.1) | 4 ( 0.8) | 0 | 1 ( 0.4) | 0 | 0 |

Apr 2023 DBL Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-aeltd-cat--ta-ebr1575.sas 22JUN2023:20:24:12

Protocol: CA20976K 

Table 27.1
Adverse Events Leading to Discontinuation of Study Treatment Summary
by Worst CTC Grade (Any Grade, Grade 3-4, Grade 5)
All Treated Subjects Censoring at Open-Label Nivolumab

| System Organ Class (%) Preferred Term (%) | Nivolumab N = 524 | | | Placebo N = 264 | | |
|---|---|---|---|---|---|---|
| | Any Grade | Grade 3-4 | Grade 5 | Any Grade | Grade 3-4 | Grade 5 |
| Cough | 3 ( 0.6) | 0 | 0 | 0 | 0 | 0 |
| Pneumonitis | 3 ( 0.6) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Acute respiratory failure | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Dyspnoea | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Interstitial lung disease | 1 ( 0.2) | 0 | 0 | 1 ( 0.4) | 0 | 0 |
| Pulmonary embolism | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Respiratory failure | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | 11 ( 2.1) | 4 ( 0.8) | 0 | 0 | 0 | 0 |
| Rash | 5 ( 1.0) | 3 ( 0.6) | 0 | 0 | 0 | 0 |
| Dermatitis psoriasiform | 2 ( 0.4) | 0 | 0 | 0 | 0 | 0 |
| Pruritus | 2 ( 0.4) | 0 | 0 | 0 | 0 | 0 |
| Lichenoid keratosis | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Pemphigoid | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Rash maculo-papular | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Nervous system disorders | 8 ( 1.5) | 5 ( 1.0) | 0 | 1 ( 0.4) | 0 | 0 |
| Ageusia | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Cerebrovascular disorder | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Dysarthria | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Embolic stroke | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Headache | 1 ( 0.2) | 0 | 0 | 1 ( 0.4) | 0 | 0 |
| Peripheral sensorimotor neuropathy | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Peripheral sensory neuropathy | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Polyneuropathy | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Hepatobiliary disorders | 7 ( 1.3) | 6 ( 1.1) | 0 | 1 ( 0.4) | 1 ( 0.4) | 0 |

Apr 2023 DBL Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-aeltd-cat--ta-ebr1575.sas 22JUN2023:20:24:12

Protocol: CA20976K 

Table 27.1
Adverse Events Leading to Discontinuation of Study Treatment Summary
by Worst CTC Grade (Any Grade, Grade 3-4, Grade 5)
All Treated Subjects Censoring at Open-Label Nivolumab

| System Organ Class (%) Preferred Term (%) | Nivolumab N = 524 | | | Placebo N = 264 | | |
|---|---|---|---|---|---|---|
| | Any Grade | Grade 3-4 | Grade 5 | Any Grade | Grade 3-4 | Grade 5 |
| Hepatitis | 4 ( 0.8) | 3 ( 0.6) | 0 | 1 ( 0.4) | 1 ( 0.4) | 0 |
| Autoimmune hepatitis | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Hepatic cytolysis | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Hepatotoxicity | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Infections and infestations | 6 ( 1.1) | 2 ( 0.4) | 0 | 0 | 0 | 0 |
| COVID-19 | 2 ( 0.4) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Conjunctivitis | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Herpes simplex encephalitis | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Pneumonia | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Rash pustular | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Cardiac disorders | 3 ( 0.6) | 2 ( 0.4) | 0 | 1 ( 0.4) | 0 | 0 |
| Myocarditis | 2 ( 0.4) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Acute myocardial infarction | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Atrial fibrillation | 0 | 0 | 0 | 1 ( 0.4) | 0 | 0 |
| General disorders and administration site conditions | 3 ( 0.6) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Fatigue | 2 ( 0.4) | 0 | 0 | 0 | 0 | 0 |
| Generalised oedema | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Non-cardiac chest pain | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Renal and urinary disorders | 3 ( 0.6) | 3 ( 0.6) | 0 | 0 | 0 | 0 |
| Acute kidney injury | 2 ( 0.4) | 2 ( 0.4) | 0 | 0 | 0 | 0 |
| Nephropathy toxic | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |

Apr 2023 DBL Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-aeltd-cat--ta-ebr1575.sas 22JUN2023:20:24:12

Protocol: CA20976K 

Table 27.1
Adverse Events Leading to Discontinuation of Study Treatment Summary
by Worst CTC Grade (Any Grade, Grade 3-4, Grade 5)
All Treated Subjects Censoring at Open-Label Nivolumab

| System Organ Class (%) Preferred Term (%) | Nivolumab N = 524 | | | Placebo N = 264 | | |
|---|---|---|---|---|---|---|
| | Any Grade | Grade 3-4 | Grade 5 | Any Grade | Grade 3-4 | Grade 5 |
| Metabolism and nutrition disorders | 2 ( 0.4) | 2 ( 0.4) | 0 | 0 | 0 | 0 |
| Diabetes mellitus | 2 ( 0.4) | 2 ( 0.4) | 0 | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 2 ( 0.4) | 1 ( 0.2) | 0 | 1 ( 0.4) | 1 ( 0.4) | 0 |
| Melanoma recurrent | 1 ( 0.2) | 1 ( 0.2) | 0 | 1 ( 0.4) | 1 ( 0.4) | 0 |
| Metastatic malignant melanoma | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Blood and lymphatic system disorders | 1 ( 0.2) | 0 | 0 | 1 ( 0.4) | 0 | 0 |
| Leukopenia | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Lymphocytic infiltration | 0 | 0 | 0 | 1 ( 0.4) | 0 | 0 |
| Congenital, familial and genetic disorders | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Fanconi syndrome | 1 ( 0.2) | 1 ( 0.2) | 0 | 0 | 0 | 0 |
| Eye disorders | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Uveitis | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Pregnancy, puerperium and perinatal conditions | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |
| Pregnancy | 1 ( 0.2) | 0 | 0 | 0 | 0 | 0 |

Apr 2023 DBL Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
MedDRA Version: 25.1; CTC Version 5.0
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-aeltd-cat--ta-ebr1575.sas 22JUN2023:20:24:12

**Anhang 4-G 3: Subgruppenanalysen**

**Anhang 4-G 3.1: Subgruppenanalysen zu Endpunkten des Hauptteils aus CA209-76K**

**Anhang 4-G 3.1.1: Subgruppenanalysen für Endpunkte Morbidität und Lebensqualität aus CA209-76K**

**Anhang 4-G 3.1.1.1: Subgruppenanalysen für Endpunkt Rezidivfreies Überleben (RFS) aus CA209-76K**

Protocol: CA20976K 

Table 10.20.1
Subgroup Analyses of Recurrence Free Survival per Investigator
All Randomized Subjects

| Subgroup | Nivolumab N | Nivolumab Patients with event n (%) | Nivolumab KME [95% CI](mon) (1) | Placebo N | Placebo Patients with event n (%) | Placebo KME [95% CI](mon) (1) | Nivolumab vs. Placebo HR [95% CI] p-value (2)(3) | Test for interaction p-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 526 | 102 ( 19.4) | N.A. | 264 | 84 ( 31.8) | 36.14 (24.77, N.A.) | 0.535 ( 0.401, 0.715) <0.0001 | |
| AGE CATEGORY I | | | | | | | | 0.4295 |
| < 65 | 305 | 51 ( 16.7) | N.A. | 155 | 48 ( 31.0) | 36.14 (36.14, N.A.) | 0.472 ( 0.318, 0.701) 0.0001 | |
| >= 65 | 221 | 51 ( 23.1) | N.A. | 109 | 36 ( 33.0) | N.A. (23.03, N.A.) | 0.625 ( 0.408, 0.959) 0.0297 | |
| AGE CATEGORY II | | | | | | | | 0.8398 |
| >= 18 AND < 65 | 305 | 51 ( 16.7) | N.A. | 155 | 48 ( 31.0) | 36.14 (36.14, N.A.) | 0.472 ( 0.318, 0.701) 0.0001 | |
| >= 65 AND < 75 | 140 | 27 ( 19.3) | N.A. | 77 | 23 ( 29.9) | N.A. (23.79, N.A.) | 0.599 ( 0.344, 1.046) 0.0683 | |
| >= 75 AND < 85 | 77 | 23 ( 29.9) | N.A. | 30 | 12 ( 40.0) | 23.62 (10.28, N.A.) | 0.611 ( 0.303, 1.230) 0.1635 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified Log-rank test
(4) Unstratified Cox proportional hazard model with treatment, subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) A p-value of <0.05 is indicated by 1 asterisk (indicates potential effect modification).
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ef-ossub-ebr1575.sas 22JUN2023:14:39:52

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Table 10.20.1
Subgroup Analyses of Recurrence Free Survival per Investigator
All Randomized Subjects

| Subgroup | Nivolumab N | Nivolumab Patients with event n (%) | Nivolumab KME [95% CI](mon) (1) | Placebo N | Placebo Patients with event n (%) | Placebo KME [95% CI](mon) (1) | Nivolumab vs. Placebo HR [95% CI] p-value (2)(3) | Test for interaction p-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| SEX | | | | | | | | 0.0778 |
| MALE | 322 | 63 ( 19.6) | N.A. (30.23, N.A.) | 161 | 60 ( 37.3) | 36.14 (23.62, N.A.) | 0.439 ( 0.308, 0.626) <0.0001 | |
| FEMALE | 204 | 39 ( 19.1) | N.A. | 103 | 24 ( 23.3) | N.A. | 0.775 ( 0.466, 1.290) 0.3265 | |
| DISEASE STAGE CATEGORY | | | | | | | | 0.4890 |
| STAGE IIB | 316 | 47 ( 14.9) | N.A. | 162 | 46 ( 28.4) | 36.14 (24.77, N.A.) | 0.472 ( 0.314, 0.709) 0.0002 | |
| STAGE IIC | 210 | 55 ( 26.2) | N.A. (30.23, N.A.) | 102 | 38 ( 37.3) | N.A. (19.81, N.A.) | 0.589 ( 0.389, 0.891) 0.0115 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified Log-rank test
(4) Unstratified Cox proportional hazard model with treatment, subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) A p-value of <0.05 is indicated by 1 asterisk (indicates potential effect modification).
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ef-ossub-ebr1575.sas 22JUN2023:14:39:52

Protocol: CA20976K 

Table 10.20.1
Subgroup Analyses of Recurrence Free Survival per Investigator
All Randomized Subjects

| Subgroup | Nivolumab N | Nivolumab Patients with event n (%) | Nivolumab KME [95% CI](mon) (1) | Placebo N | Placebo Patients with event n (%) | Placebo KME [95% CI](mon) (1) | Nivolumab vs. Placebo HR [95% CI] p-value (2)(3) | Test for interaction p-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| T STAGE (SOURCE: ECRF) | | | | | | | | 0.7503 |
| T3B | 204 | 26 ( 12.7) | N.A. | 104 | 28 ( 26.9) | 36.14 (24.77, N.A.) | 0.450 ( 0.264, 0.769) 0.0027 | |
| T4A | 112 | 21 ( 18.8) | N.A. | 58 | 18 ( 31.0) | N.A. (23.03, N.A.) | 0.490 ( 0.260, 0.921) 0.0239 | |
| T4B | 210 | 55 ( 26.2) | N.A. (30.23, N.A.) | 102 | 38 ( 37.3) | N.A. (19.81, N.A.) | 0.589 ( 0.389, 0.891) 0.0115 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified Log-rank test
(4) Unstratified Cox proportional hazard model with treatment, subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) A p-value of <0.05 is indicated by 1 asterisk (indicates potential effect modification).
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ef-ossub-ebr1575.sas 22JUN2023:14:39:52

Protocol: CA20976K 

Table 10.20.1
Subgroup Analyses of Recurrence Free Survival per Investigator
All Randomized Subjects

| Subgroup | Nivolumab N | Nivolumab Patients with event n (%) | Nivolumab KME [95% CI](mon) (1) | Placebo N | Placebo Patients with event n (%) | Placebo KME [95% CI](mon) (1) | Nivolumab vs. Placebo HR [95% CI] p-value (2)(3) | Test for interaction p-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.6988 |
| US AND CANADA | 97 | 16 ( 16.5) | N.A. (25.00, N.A.) | 46 | 11 ( 23.9) | N.A. (23.03, N.A.) | 0.654 ( 0.304, 1.410) 0.2768 | |
| WESTERN EUROPE | 303 | 63 ( 20.8) | N.A. | 160 | 56 ( 35.0) | 36.14 (23.62, N.A.) | 0.494 ( 0.344, 0.708) <0.0001 | |
| EASTERN EUROPE | 58 | 9 ( 15.5) | N.A. | 28 | 10 ( 35.7) | N.A. (21.62, N.A.) | 0.441 ( 0.179, 1.085) 0.0667 | |
| AUSTRALIA | 68 | 14 ( 20.6) | N.A. (25.00, N.A.) | 30 | 7 ( 23.3) | N.A. | 0.803 ( 0.324, 1.992) 0.6359 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified Log-rank test
(4) Unstratified Cox proportional hazard model with treatment, subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) A p-value of <0.05 is indicated by 1 asterisk (indicates potential effect modification).
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ef-ossub-ebr1575.sas 22JUN2023:14:39:52

**Anhang 4-G 3.1.1.2: Subgruppenanalysen für Endpunkt Fernmetastasenfreies Überleben (DMFS) aus CA209-76K**

Protocol: CA20976K 

Table 10.20.3
Subgroup Analyses of Distant Metastasis Free Survival per Investigator
All Randomized Subjects

| Subgroup | Nivolumab N | Nivolumab Patients with event n (%) | Nivolumab KME [95% CI](mon) (1) | Placebo N | Placebo Patients with event n (%) | Placebo KME [95% CI](mon) (1) | Nivolumab vs. Placebo HR [95% CI] p-value (2)(3) | Test for interaction p-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 526 | 69 ( 13.1) | N.A. | 264 | 51 ( 19.3) | 36.14 (32.85, N.A.) | 0.628 ( 0.437, 0.902) 0.0111 | |
| AGE CATEGORY I | | | | | | | | 0.5980 |
| < 65 | 305 | 35 ( 11.5) | N.A. | 155 | 29 ( 18.7) | 36.14 (32.85, N.A.) | 0.575 ( 0.351, 0.941) 0.0260 | |
| >= 65 | 221 | 34 ( 15.4) | N.A. | 109 | 22 ( 20.2) | N.A. | 0.727 ( 0.425, 1.243) 0.2421 | |
| AGE CATEGORY II | | | | | | | | 0.9055 |
| >= 18 AND < 65 | 305 | 35 ( 11.5) | N.A. | 155 | 29 ( 18.7) | 36.14 (32.85, N.A.) | 0.575 ( 0.351, 0.941) 0.0260 | |
| >= 65 AND < 75 | 140 | 19 ( 13.6) | N.A. | 77 | 14 ( 18.2) | N.A. | 0.705 ( 0.353, 1.406) 0.3179 | |
| >= 75 AND < 85 | 77 | 14 ( 18.2) | N.A. | 30 | 7 ( 23.3) | N.A. (23.62, N.A.) | 0.723 ( 0.291, 1.791) 0.4797 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified Log-rank test
(4) Unstratified Cox proportional hazard model with treatment, subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) A p-value of <0.05 is indicated by 1 asterisk (indicates potential effect modification).
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ef-ossub-ebr1575.sas 14JUN2023:14:15:51

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Table 10.20.3
Subgroup Analyses of Distant Metastasis Free Survival per Investigator
All Randomized Subjects

| Subgroup | Nivolumab N | Nivolumab Patients with event n (%) | Nivolumab KME [95% CI](mon) (1) | Placebo N | Placebo Patients with event n (%) | Placebo KME [95% CI](mon) (1) | Nivolumab vs. Placebo HR [95% CI] p-value (2)(3) | Test for interaction p-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| SEX | | | | | | | | 0.1412 |
| MALE | 322 | 40 ( 12.4) | N.A. | 161 | 35 ( 21.7) | 36.14 (36.14, N.A.) | 0.511 ( 0.325, 0.806) 0.0032 | |
| FEMALE | 204 | 29 ( 14.2) | N.A. | 103 | 16 ( 15.5) | N.A. (32.85, N.A.) | 0.908 ( 0.493, 1.673) 0.7564 | |
| DISEASE STAGE CATEGORY | | | | | | | | 0.7454 |
| STAGE IIB | 316 | 31 ( 9.8) | N.A. | 162 | 26 ( 16.0) | 36.14 (32.85, N.A.) | 0.571 ( 0.339, 0.963) 0.0333 | |
| STAGE IIC | 210 | 38 ( 18.1) | N.A. | 102 | 25 ( 24.5) | N.A. | 0.658 ( 0.397, 1.091) 0.1026 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified Log-rank test
(4) Unstratified Cox proportional hazard model with treatment, subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) A p-value of <0.05 is indicated by 1 asterisk (indicates potential effect modification).
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ef-ossub-ebr1575.sas 14JUN2023:14:15:51

Protocol: CA20976K 

Table 10.20.3
Subgroup Analyses of Distant Metastasis Free Survival per Investigator
All Randomized Subjects

| Subgroup | Nivolumab N | Nivolumab Patients with event n (%) | Nivolumab KME [95% CI](mon) (1) | Placebo N | Placebo Patients with event n (%) | Placebo KME [95% CI](mon) (1) | Nivolumab vs. Placebo HR [95% CI] p-value (2)(3) | Test for interaction p-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| T STAGE (SOURCE: ECRF) | | | | | | | | 0.4626 |
| T3B | 204 | 16 ( 7.8) | N.A. | 104 | 18 ( 17.3) | 36.14 (32.85, N.A.) | 0.437 ( 0.222, 0.858) 0.0133 | |
| T4A | 112 | 15 ( 13.4) | N.A. | 58 | 8 ( 13.8) | N.A. | 0.867 ( 0.367, 2.047) 0.7459 | |
| T4B | 210 | 38 ( 18.1) | N.A. | 102 | 25 ( 24.5) | N.A. | 0.658 ( 0.397, 1.091) 0.1026 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified Log-rank test
(4) Unstratified Cox proportional hazard model with treatment, subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) A p-value of <0.05 is indicated by 1 asterisk (indicates potential effect modification).
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ef-ossub-ebr1575.sas 14JUN2023:14:15:51

Protocol: CA20976K 

Table 10.20.3
Subgroup Analyses of Distant Metastasis Free Survival per Investigator
All Randomized Subjects

| Subgroup | Nivolumab N | Nivolumab Patients with event n (%) | Nivolumab KME [95% CI](mon) (1) | Placebo N | Placebo Patients with event n (%) | Placebo KME [95% CI](mon) (1) | Nivolumab vs. Placebo HR [95% CI] p-value (2)(3) | Test for interaction p-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.3532 |
| US AND CANADA | 97 | 12 ( 12.4) | N.A. | 46 | 9 ( 19.6) | N.A. | 0.632 ( 0.266, 1.501) 0.2956 | |
| WESTERN EUROPE | 303 | 43 ( 14.2) | N.A. | 160 | 34 ( 21.3) | 36.14 (32.85, N.A.) | 0.599 ( 0.382, 0.940) 0.0243 | |
| EASTERN EUROPE | 58 | 6 ( 10.3) | N.A. | 28 | 7 ( 25.0) | N.A. (23.95, N.A.) | 0.407 ( 0.137, 1.212) 0.0950 | |
| AUSTRALIA | 68 | 8 ( 11.8) | N.A. | 30 | 1 ( 3.3) | N.A. | 3.335 ( 0.417, 26.666) 0.2280 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified Log-rank test
(4) Unstratified Cox proportional hazard model with treatment, subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) A p-value of <0.05 is indicated by 1 asterisk (indicates potential effect modification).
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ef-ossub-ebr1575.sas 14JUN2023:14:15:51

**Anhang 4-G 3.1.1.3: Subgruppenanalysen für Endpunkte gemäß EORTC-QLQ-C30 aus CA209-76K**

Subgruppenanalysen für die Endpunkte Fatigue, Übelkeit und Erbrechen, Schmerz, Dyspnoe, Schlaflosigkeit, Appetitminderung, Obstipation, Diarrhoe, globaler Gesundheitsstatus, körperliche Funktion, Rollenfunktion, emotionale Funktion, kognitive Funktion und soziale Funktion gemäß EORTC-QLQ-C30 aus CA209-76K – Änderung zu Studienbeginn (MMRM)

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| PHYSICAL FUNCTIONING | | | | | | | | | |
| OVERALL | 482 | 92.7 (13.4) | -1.24 (-1.97, -0.52) | 253 | 91.8 (14.4) | -0.25 (-1.24, 0.74) | -0.99 (-2.22, 0.23) 0.1128 | -0.12 (-0.28, 0.03) | |
| AGE CATEGORY I | | | | | | | | | 0.2718 |
| < 65 | 290 | 93.8 (13.3) | -0.91 (-1.81, -0.01) | 151 | 92.7 (13.5) | 0.59 (-0.64, 1.81) | -1.50 (-3.02, 0.02) 0.0537 | -0.19 (-0.39, 0.00) | |
| >= 65 | 192 | 91.0 (13.3) | -1.75 (-2.83, -0.66) | 102 | 90.5 (15.6) | -1.52 (-3.01, -0.04) | -0.22 (-2.06, 1.61) 0.8111 | -0.03 (-0.27, 0.21) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain<br>Subgroup | Nivolumab 480 mg Q4W<br>N (1) | Nivolumab 480 mg Q4W<br>Baseline Mean (SD) | Nivolumab 480 mg Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W<br>N (1) | Placebo Q4W<br>Baseline Mean (SD) | Placebo Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | | 0.5590 |
| >= 18 AND < 65 | 290 | 93.8 (13.3) | -0.91 (-1.81, -0.02) | 151 | 92.7 (13.5) | 0.57 (-0.65, 1.79) | -1.48 (-3.00, 0.03) 0.0547 | -0.19 (-0.39, 0.00) | |
| >= 65 AND < 75 | 123 | 92.0 (11.7) | -1.21 (-2.53, 0.12) | 74 | 90.8 (16.4) | -0.85 (-2.57, 0.86) | -0.35 (-2.52, 1.81) 0.7483 | -0.05 (-0.34, 0.24) | |
| >= 75 AND < 85 | 66 | 89.8 (15.8) | -2.64 (-4.45, -0.83) | 26 | 90.3 (12.3) | -2.66 (-5.49, 0.18) | 0.02 (-3.34, 3.37) 0.9920 | 0.00 (-0.45, 0.46) | |
| SEX | | | | | | | | | 0.8626 |
| MALE | 295 | 93.6 (13.1) | -0.79 (-1.69, 0.10) | 156 | 94.3 (11.6) | 0.27 (-0.95, 1.48) | -1.06 (-2.57, 0.45) 0.1681 | -0.14 (-0.33, 0.06) | |
| FEMALE | 187 | 91.2 (13.6) | -1.95 (-3.04, -0.85) | 97 | 87.8 (17.3) | -1.09 (-2.61, 0.43) | -0.86 (-2.73, 1.01) 0.3678 | -0.11 (-0.36, 0.13) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | | 0.0809 |
| STAGE IIB | 294 | 92.9 (13.3) | -1.02 (-1.91, -0.12) | 160 | 93.2 (12.3) | -0.78 (-1.98, 0.41) | -0.23 (-1.73, 1.26) 0.7583 | -0.03 (-0.22, 0.16) | |
| STAGE IIC | 188 | 92.4 (13.5) | -1.60 (-2.69, -0.50) | 93 | 89.4 (17.3) | 0.70 (-0.86, 2.25) | -2.29 (-4.20, -0.39) 0.0183 | -0.30 (-0.55, -0.05) | |
| T STAGE | | | | | | | | | 0.0740 |
| T3B | 189 | 92.0 (13.2) | -1.03 (-2.13, 0.06) | 103 | 93.9 (12.0) | -0.04 (-1.50, 1.42) | -1.00 (-2.82, 0.82) 0.2821 | -0.13 (-0.37, 0.11) | |
| T4A | 105 | 94.4 (13.4) | -0.98 (-2.42, 0.46) | 57 | 91.8 (12.8) | -2.16 (-4.10, -0.22) | 1.18 (-1.24, 3.60) 0.3383 | 0.16 (-0.17, 0.48) | |
| T4B | 188 | 92.4 (13.5) | -1.60 (-2.70, -0.51) | 93 | 89.4 (17.3) | 0.70 (-0.86, 2.25) | -2.30 (-4.20, -0.40) 0.0180 | -0.30 (-0.55, -0.05) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain<br>Subgroup | Nivolumab 480 mg Q4W<br>N (1) | Nivolumab 480 mg Q4W<br>Baseline Mean (SD) | Nivolumab 480 mg Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W<br>N (1) | Placebo Q4W<br>Baseline Mean (SD) | Placebo Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | | 0.1516 |
| US AND CANADA | 89 | 93.3 (14.3) | -0.49<br>(-2.05, 1.07) | 44 | 93.8 (12.3) | -0.95<br>(-3.13, 1.24) | 0.45<br>(-2.23, 3.14)<br>0.7399 | 0.06<br>(-0.30, 0.42) | |
| WESTERN EUROPE | 281 | 93.0 (12.8) | -1.28<br>(-2.19, -0.37) | 152 | 92.1 (15.4) | 0.78<br>(-0.45, 2.02) | -2.06<br>(-3.60, -0.53)<br>0.0085 | -0.26<br>(-0.46, -0.07) | |
| EASTERN EUROPE | 51 | 88.5 (11.7) | -1.15<br>(-3.17, 0.87) | 27 | 85.9 (13.2) | -1.83<br>(-4.62, 0.95) | 0.69<br>(-2.75, 4.12)<br>0.6952 | 0.09<br>(-0.37, 0.56) | |
| AUSTRALIA | 61 | 93.6 (15.3) | -2.27<br>(-4.16, -0.39) | 30 | 92.7 (12.3) | -2.98<br>(-5.62, -0.35) | 0.71<br>(-2.53, 3.95)<br>0.6664 | 0.10<br>(-0.34, 0.53) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| ROLE FUNCTIONING | | | | | | | | | |
| OVERALL | 484 | 91.3 (18.9) | -1.36 (-2.51, -0.21) | 253 | 89.1 (21.1) | 1.04 (-0.53, 2.60) | -2.40 (-4.34, -0.46) 0.0156 | -0.19 (-0.34, -0.04) | |
| AGE CATEGORY I | | | | | | | | | 0.5754 |
| < 65 | 291 | 90.2 (21.0) | -0.78 (-2.21, 0.65) | 151 | 89.1 (21.7) | 1.21 (-0.74, 3.16) | -1.99 (-4.41, 0.43) 0.1066 | -0.16 (-0.36, 0.04) | |
| >= 65 | 193 | 92.8 (15.2) | -2.25 (-3.98, -0.52) | 102 | 89.2 (20.4) | 0.78 (-1.58, 3.14) | -3.03 (-5.96, -0.10) 0.0427 | -0.25 (-0.49, -0.01) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain<br>Subgroup | Nivolumab 480 mg Q4W<br>N (1) | Nivolumab 480 mg Q4W<br>Baseline Mean (SD) | Nivolumab 480 mg Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W<br>N (1) | Placebo Q4W<br>Baseline Mean (SD) | Placebo Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | | 0.0873 |
| >= 18 AND < 65 | 291 | 90.2 (21.0) | -0.85 (-2.26, 0.56) | 151 | 89.1 (21.7) | 1.17 (-0.76, 3.11) | -2.03 (-4.42, 0.37) 0.0973 | -0.17 (-0.36, 0.03) | |
| >= 65 AND < 75 | 124 | 92.5 (15.8) | -0.46 (-2.56, 1.64) | 74 | 90.8 (20.1) | 0.64 (-2.08, 3.35) | -1.10 (-4.53, 2.34) 0.5312 | -0.09 (-0.38, 0.20) | |
| >= 75 AND < 85 | 66 | 93.7 (13.9) | -5.29 (-8.16, -2.41) | 26 | 85.9 (20.4) | 2.63 (-1.87, 7.14) | -7.92 (-13.27, -2.57) 0.0038 | -0.67 (-1.13, -0.20) | |
| SEX | | | | | | | | | 0.6358 |
| MALE | 297 | 92.2 (17.9) | -0.41 (-1.82, 1.00) | 156 | 92.2 (18.3) | 1.63 (-0.29, 3.56) | -2.04 (-4.42, 0.34) 0.0935 | -0.17 (-0.36, 0.03) | |
| FEMALE | 187 | 89.8 (20.4) | -2.87 (-4.61, -1.12) | 97 | 84.2 (24.3) | 0.06 (-2.35, 2.46) | -2.92 (-5.89, 0.05) 0.0538 | -0.24 (-0.49, 0.01) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | | 0.5615 |
| STAGE IIB | 295 | 92.1 (17.1) | -1.23 (-2.65, 0.19) | 160 | 90.5 (20.1) | 1.55 (-0.35, 3.45) | -2.78 (-5.15, -0.41) 0.0218 | -0.22 (-0.42, -0.03) | |
| STAGE IIC | 189 | 89.9 (21.4) | -1.56 (-3.31, 0.18) | 93 | 86.7 (22.7) | 0.12 (-2.35, 2.60) | -1.69 (-4.71, 1.34) 0.2748 | -0.14 (-0.39, 0.11) | |
| T STAGE | | | | | | | | | 0.0919 |
| T3B | 190 | 91.6 (16.9) | -1.80 (-3.53, -0.07) | 103 | 92.2 (18.5) | 2.76 (0.45, 5.08) | -4.56 (-7.45, -1.67) 0.0020 | -0.38 (-0.62, -0.14) | |
| T4A | 105 | 93.2 (17.6) | -0.20 (-2.49, 2.10) | 57 | 87.4 (22.6) | -0.67 (-3.76, 2.42) | 0.48 (-3.38, 4.33) 0.8087 | 0.04 (-0.28, 0.36) | |
| T4B | 189 | 89.9 (21.4) | -1.56 (-3.30, 0.18) | 93 | 86.7 (22.7) | 0.09 (-2.38, 2.57) | -1.65 (-4.68, 1.37) 0.2834 | -0.14 (-0.38, 0.11) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
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Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain<br>Subgroup | Nivolumab 480 mg Q4W<br>N (1) | Nivolumab 480 mg Q4W<br>Baseline Mean (SD) | Nivolumab 480 mg Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W<br>N (1) | Placebo Q4W<br>Baseline Mean (SD) | Placebo Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | | 0.1111 |
| US AND CANADA | 89 | 90.8 (21.0) | -0.78<br>(-3.27, 1.71) | 44 | 89.8 (19.8) | 2.69<br>(-0.79, 6.18) | -3.47<br>(-7.76, 0.81)<br>0.1118 | -0.29<br>(-0.65, 0.07) | |
| WESTERN EUROPE | 283 | 91.8 (17.7) | -1.66<br>(-3.10, -0.22) | 152 | 88.8 (22.5) | 1.94<br>(-0.02, 3.89) | -3.60<br>(-6.03, -1.17)<br>0.0038 | -0.29<br>(-0.49, -0.09) | |
| EASTERN EUROPE | 51 | 85.6 (22.4) | -1.27<br>(-4.49, 1.95) | 27 | 87.7 (19.9) | -3.95<br>(-8.38, 0.48) | 2.67<br>(-2.80, 8.15)<br>0.3377 | 0.23<br>(-0.24, 0.69) | |
| AUSTRALIA | 61 | 94.3 (17.4) | -0.84<br>(-3.86, 2.17) | 30 | 91.1 (17.4) | -1.49<br>(-5.69, 2.72) | 0.65<br>(-4.53, 5.82)<br>0.8066 | 0.05<br>(-0.38, 0.49) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| EMOTIONAL FUNCTIONING | | | | | | | | | |
| OVERALL | 484 | 86.2 (16.9) | 1.38 (0.38, 2.38) | 251 | 87.5 (15.8) | 1.24 (-0.13, 2.61) | 0.14 (-1.55, 1.84) 0.8684 | 0.01 (-0.14, 0.17) | |
| AGE CATEGORY I | | | | | | | | | 0.9929 |
| < 65 | 290 | 85.5 (17.7) | 0.94 (-0.31, 2.20) | 149 | 87.1 (16.3) | 0.79 (-0.94, 2.52) | 0.15 (-1.98, 2.29) 0.8885 | 0.01 (-0.18, 0.21) | |
| >= 65 | 194 | 87.2 (15.7) | 2.04 (0.52, 3.57) | 102 | 88.0 (15.0) | 1.91 (-0.17, 3.99) | 0.14 (-2.44, 2.72) 0.9164 | 0.01 (-0.23, 0.25) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain<br>Subgroup | Nivolumab 480 mg Q4W<br>N (1) | Nivolumab 480 mg Q4W<br>Baseline Mean (SD) | Nivolumab 480 mg Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W<br>N (1) | Placebo Q4W<br>Baseline Mean (SD) | Placebo Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | | 0.9763 |
| >= 18 AND < 65 | 290 | 85.5 (17.7) | 0.92<br>(-0.33, 2.18) | 149 | 87.1 (16.3) | 0.76<br>(-0.97, 2.48) | 0.16<br>(-1.97, 2.30)<br>0.8795 | 0.02<br>(-0.18, 0.21) | |
| >= 65 AND < 75 | 125 | 86.7 (14.8) | 2.63<br>(0.76, 4.49) | 74 | 87.8 (16.1) | 2.40<br>(-0.03, 4.82) | 0.23<br>(-2.83, 3.29)<br>0.8830 | 0.02<br>(-0.27, 0.31) | |
| >= 75 AND < 85 | 66 | 89.3 (14.9) | 0.94<br>(-1.64, 3.51) | 26 | 88.8 (11.0) | 1.31<br>(-2.73, 5.34) | -0.37<br>(-5.16, 4.42)<br>0.8795 | -0.03<br>(-0.49, 0.42) | |
| SEX | | | | | | | | | 0.3250 |
| MALE | 298 | 88.0 (16.4) | 2.37<br>(1.13, 3.61) | 155 | 90.5 (13.4) | 1.61<br>(-0.10, 3.32) | 0.76<br>(-1.35, 2.87)<br>0.4804 | 0.07<br>(-0.12, 0.26) | |
| FEMALE | 186 | 83.1 (17.2) | -0.21<br>(-1.76, 1.34) | 96 | 82.5 (17.9) | 0.66<br>(-1.47, 2.79) | -0.87<br>(-3.49, 1.75)<br>0.5130 | -0.08<br>(-0.33, 0.16) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | | 0.8621 |
| STAGE IIB | 296 | 86.1 (17.1) | 1.87 (0.62, 3.11) | 159 | 87.7 (15.5) | 1.59 (-0.09, 3.26) | 0.28 (-1.80, 2.37) 0.7900 | 0.03 (-0.17, 0.22) | |
| STAGE IIC | 188 | 86.2 (16.5) | 0.61 (-0.93, 2.15) | 92 | 87.0 (16.4) | 0.62 (-1.57, 2.81) | -0.01 (-2.69, 2.67) 0.9955 | 0.00 (-0.25, 0.25) | |
| T STAGE | | | | | | | | | 0.3564 |
| T3B | 190 | 86.8 (15.0) | 1.46 (-0.07, 2.98) | 102 | 89.2 (14.0) | 2.26 (0.20, 4.31) | -0.80 (-3.36, 1.76) 0.5396 | -0.08 (-0.32, 0.17) | |
| T4A | 106 | 84.9 (20.4) | 2.60 (0.57, 4.62) | 57 | 85.1 (17.6) | 0.36 (-2.37, 3.10) | 2.24 (-1.17, 5.64) 0.1975 | 0.21 (-0.11, 0.53) | |
| T4B | 188 | 86.2 (16.5) | 0.62 (-0.92, 2.16) | 92 | 87.0 (16.4) | 0.62 (-1.57, 2.81) | 0.00 (-2.68, 2.67) 0.9974 | 0.00 (-0.25, 0.25) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain<br>Subgroup | Nivolumab 480 mg Q4W<br>N (1) | Nivolumab 480 mg Q4W<br>Baseline Mean (SD) | Nivolumab 480 mg Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W<br>N (1) | Placebo Q4W<br>Baseline Mean (SD) | Placebo Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | | 0.3718 |
| US AND CANADA | 89 | 87.3 (18.8) | 2.33<br>(0.11, 4.54) | 44 | 90.5 (11.9) | 0.01<br>(-3.09, 3.11) | 2.32<br>(-1.49, 6.13)<br>0.2331 | 0.22<br>(-0.14, 0.58) | |
| WESTERN EUROPE | 282 | 86.3 (16.3) | 1.02<br>(-0.25, 2.30) | 150 | 87.1 (16.5) | 2.02<br>(0.29, 3.76) | -1.00<br>(-3.15, 1.15)<br>0.3626 | -0.09<br>(-0.29, 0.11) | |
| EASTERN EUROPE | 51 | 79.9 (18.3) | 2.34<br>(-0.53, 5.22) | 27 | 83.3 (18.9) | 0.35<br>(-3.59, 4.29) | 1.99<br>(-2.87, 6.86)<br>0.4215 | 0.19<br>(-0.28, 0.66) | |
| AUSTRALIA | 62 | 89.2 (14.3) | 0.84<br>(-1.82, 3.50) | 30 | 88.6 (13.2) | -0.05<br>(-3.80, 3.69) | 0.90<br>(-3.69, 5.48)<br>0.7017 | 0.08<br>(-0.35, 0.52) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| COGNITIVE FUNCTIONING | | | | | | | | | |
| OVERALL | 484 | 93.2 (13.1) | -1.82 (-2.74, -0.90) | 251 | 95.2 (10.2) | -2.34 (-3.59, -1.08) | 0.51 (-1.04, 2.07) 0.5165 | 0.05 (-0.10, 0.20) | |
| AGE CATEGORY I | | | | | | | | | 0.8433 |
| < 65 | 290 | 93.9 (13.8) | -1.84 (-2.96, -0.72) | 149 | 96.6 (8.4) | -2.24 (-3.78, -0.70) | 0.40 (-1.50, 2.31) 0.6789 | 0.04 (-0.16, 0.24) | |
| >= 65 | 194 | 92.3 (11.9) | -1.80 (-3.14, -0.46) | 102 | 93.1 (12.0) | -2.48 (-4.30, -0.65) | 0.68 (-1.59, 2.94) 0.5563 | 0.07 (-0.17, 0.31) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain<br>Subgroup | Nivolumab 480 mg Q4W<br>N (1) | Nivolumab 480 mg Q4W<br>Baseline Mean (SD) | Nivolumab 480 mg Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W<br>N (1) | Placebo Q4W<br>Baseline Mean (SD) | Placebo Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | | 0.5208 |
| >= 18 AND < 65 | 290 | 93.9 (13.8) | -1.94 (-3.05, -0.82) | 149 | 96.6 (8.4) | -2.28 (-3.81, -0.75) | 0.34 (-1.55, 2.24) 0.7231 | 0.04 (-0.16, 0.23) | |
| >= 65 AND < 75 | 125 | 92.9 (11.6) | -0.92 (-2.54, 0.69) | 74 | 94.4 (11.5) | -2.21 (-4.30, -0.12) | 1.29 (-1.36, 3.93) 0.3399 | 0.14 (-0.15, 0.43) | |
| >= 75 AND < 85 | 66 | 91.9 (10.2) | -3.49 (-5.69, -1.29) | 26 | 91.0 (10.8) | -2.03 (-5.48, 1.42) | -1.46 (-5.54, 2.62) 0.4834 | -0.16 (-0.62, 0.29) | |
| SEX | | | | | | | | | 0.5645 |
| MALE | 298 | 93.3 (12.9) | -0.92 (-2.02, 0.18) | 155 | 96.0 (9.1) | -1.74 (-3.25, -0.23) | 0.82 (-1.05, 2.69) 0.3923 | 0.08 (-0.11, 0.28) | |
| FEMALE | 186 | 93.1 (13.5) | -3.28 (-4.64, -1.93) | 96 | 93.9 (11.6) | -3.29 (-5.14, -1.44) | 0.01 (-2.28, 2.30) 0.9946 | 0.00 (-0.25, 0.25) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | | 0.8300 |
| STAGE IIB | 296 | 93.5 (13.2) | -1.35 (-2.46, -0.24) | 159 | 95.5 (9.7) | -2.01 (-3.50, -0.51) | 0.65 (-1.21, 2.52) 0.4909 | 0.07 (-0.13, 0.26) | |
| STAGE IIC | 188 | 92.8 (13.0) | -2.56 (-3.92, -1.21) | 92 | 94.7 (11.0) | -2.91 (-4.83, -1.00) | 0.35 (-1.99, 2.69) 0.7696 | 0.04 (-0.21, 0.29) | |
| T STAGE | | | | | | | | | 0.9764 |
| T3B | 190 | 93.7 (11.7) | -1.55 (-2.89, -0.20) | 102 | 97.2 (7.8) | -2.24 (-4.04, -0.43) | 0.69 (-1.57, 2.94) 0.5487 | 0.07 (-0.17, 0.31) | |
| T4A | 106 | 93.1 (15.6) | -1.01 (-2.76, 0.74) | 57 | 92.4 (11.8) | -1.60 (-3.97, 0.78) | 0.58 (-2.36, 3.53) 0.6968 | 0.06 (-0.26, 0.39) | |
| T4B | 188 | 92.8 (13.0) | -2.56 (-3.92, -1.21) | 92 | 94.7 (11.0) | -2.91 (-4.83, -1.00) | 0.35 (-1.99, 2.70) 0.7677 | 0.04 (-0.21, 0.29) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | | 0.5815 |
| US AND CANADA | 89 | 91.4 (18.0) | -1.29 (-3.21, 0.62) | 44 | 93.2 (12.6) | -3.50 (-6.18, -0.83) | 2.21 (-1.08, 5.50) 0.1879 | 0.24 (-0.12, 0.60) | |
| WESTERN EUROPE | 282 | 94.8 (10.5) | -2.11 (-3.25, -0.97) | 150 | 97.0 (7.7) | -2.04 (-3.59, -0.49) | -0.07 (-1.99, 1.85) 0.9460 | -0.01 (-0.20, 0.19) | |
| EASTERN EUROPE | 51 | 88.6 (15.5) | -1.90 (-4.37, 0.57) | 27 | 92.6 (11.6) | -1.58 (-4.96, 1.80) | -0.32 (-4.50, 3.86) 0.8806 | -0.04 (-0.50, 0.43) | |
| AUSTRALIA | 62 | 92.5 (12.7) | -1.17 (-3.46, 1.12) | 30 | 91.7 (13.7) | -2.75 (-5.97, 0.47) | 1.59 (-2.36, 5.53) 0.4308 | 0.17 (-0.26, 0.61) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| SOCIAL FUNCTIONING | | | | | | | | | |
| OVERALL | 484 | 92.4 (16.7) | 0.88 (-0.05, 1.81) | 251 | 91.9 (18.2) | 2.17 (0.91, 3.44) | -1.29 (-2.86, 0.28) 0.1069 | -0.13 (-0.28, 0.03) | |
| AGE CATEGORY I | | | | | | | | | 0.5068 |
| < 65 | 290 | 91.4 (18.5) | 0.92 (-0.22, 2.06) | 149 | 91.6 (17.7) | 1.83 (0.27, 3.39) | -0.91 (-2.84, 1.02) 0.3564 | -0.09 (-0.29, 0.10) | |
| >= 65 | 194 | 93.9 (13.5) | 0.82 (-0.55, 2.19) | 102 | 92.3 (19.0) | 2.68 (0.82, 4.54) | -1.86 (-4.17, 0.45) 0.1139 | -0.19 (-0.43, 0.05) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain<br>Subgroup | Nivolumab 480 mg Q4W<br>N (1) | Nivolumab 480 mg Q4W<br>Baseline Mean (SD) | Nivolumab 480 mg Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W<br>N (1) | Placebo Q4W<br>Baseline Mean (SD) | Placebo Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | | 0.1784 |
| >= 18 AND < 65 | 290 | 91.4 (18.5) | 0.93<br>(-0.19, 2.04) | 149 | 91.6 (17.7) | 1.83<br>(0.30, 3.36) | -0.91<br>(-2.80, 0.99)<br>0.3477 | -0.09<br>(-0.29, 0.10) | |
| >= 65 AND < 75 | 125 | 93.9 (14.3) | 1.70<br>(0.08, 3.33) | 74 | 92.6 (20.7) | 2.60<br>(0.50, 4.71) | -0.90<br>(-3.56, 1.76)<br>0.5057 | -0.10<br>(-0.38, 0.19) | |
| >= 75 AND < 85 | 66 | 93.9 (12.3) | -0.46<br>(-2.69, 1.76) | 26 | 92.3 (13.5) | 4.52<br>(1.04, 8.00) | -4.98<br>(-9.11, -0.86)<br>0.0181 | -0.54<br>(-1.00, -0.08) | |
| SEX | | | | | | | | | 0.4170 |
| MALE | 298 | 93.3 (16.7) | 1.83<br>(0.71, 2.95) | 155 | 92.7 (18.7) | 2.67<br>(1.14, 4.20) | -0.84<br>(-2.74, 1.06)<br>0.3849 | -0.09<br>(-0.28, 0.11) | |
| FEMALE | 186 | 91.0 (16.6) | -0.64<br>(-2.02, 0.74) | 96 | 90.6 (17.4) | 1.37<br>(-0.52, 3.25) | -2.01<br>(-4.34, 0.33)<br>0.0919 | -0.21<br>(-0.46, 0.04) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | | 0.3113 |
| STAGE IIB | 296 | 93.1 (15.8) | 1.00 (-0.13, 2.13) | 159 | 93.3 (15.5) | 2.81 (1.30, 4.32) | -1.81 (-3.69, 0.08) 0.0602 | -0.18 (-0.38, 0.01) | |
| STAGE IIC | 188 | 91.4 (18.1) | 0.70 (-0.68, 2.08) | 92 | 89.5 (22.1) | 1.03 (-0.93, 2.98) | -0.33 (-2.72, 2.06) 0.7842 | -0.03 (-0.28, 0.21) | |
| T STAGE | | | | | | | | | 0.5935 |
| T3B | 190 | 92.8 (15.7) | 0.91 (-0.46, 2.27) | 102 | 95.8 (13.8) | 2.61 (0.78, 4.45) | -1.71 (-4.00, 0.58) 0.1433 | -0.18 (-0.42, 0.06) | |
| T4A | 106 | 93.6 (15.9) | 1.18 (-0.61, 2.96) | 57 | 88.9 (17.3) | 3.17 (0.75, 5.59) | -1.99 (-5.00, 1.02) 0.1948 | -0.21 (-0.53, 0.11) | |
| T4B | 188 | 91.4 (18.1) | 0.70 (-0.69, 2.08) | 92 | 89.5 (22.1) | 1.03 (-0.92, 2.99) | -0.34 (-2.73, 2.06) 0.7822 | -0.04 (-0.28, 0.21) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | | 0.0418** |
| US AND CANADA | 89 | 92.7 (16.8) | 1.61 (-0.33, 3.56) | 44 | 95.5 (11.6) | 0.47 (-2.23, 3.18) | 1.14 (-2.19, 4.47) 0.5026 | 0.12 (-0.24, 0.48) | |
| WESTERN EUROPE | 282 | 92.8 (16.6) | 0.58 (-0.57, 1.73) | 150 | 90.2 (21.0) | 3.51 (1.95, 5.07) | -2.93 (-4.87, -1.00) 0.0031 | -0.30 (-0.50, -0.10) | |
| EASTERN EUROPE | 51 | 87.9 (16.4) | -0.15 (-2.65, 2.34) | 27 | 92.0 (16.3) | -2.07 (-5.50, 1.36) | 1.91 (-2.32, 6.15) 0.3752 | 0.21 (-0.26, 0.68) | |
| AUSTRALIA | 62 | 93.8 (17.4) | 2.17 (-0.16, 4.50) | 30 | 95.0 (10.9) | 1.90 (-1.37, 5.16) | 0.27 (-3.74, 4.28) 0.8957 | 0.03 (-0.41, 0.46) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| GLOBAL HEALTH STATUS | | | | | | | | | |
| OVERALL | 483 | 81.5 (17.2) | -2.99 (-3.97, -2.02) | 250 | 82.4 (15.3) | -1.63 (-2.96, -0.31) | -1.36 (-3.00, 0.28) 0.1040 | -0.13 (-0.28, 0.03) | |
| AGE CATEGORY I | | | | | | | | | 0.9236 |
| < 65 | 289 | 81.0 (17.9) | -3.00 (-4.22, -1.79) | 148 | 82.8 (15.2) | -1.58 (-3.25, 0.09) | -1.42 (-3.49, 0.64) 0.1765 | -0.14 (-0.33, 0.06) | |
| >= 65 | 194 | 82.1 (16.3) | -2.98 (-4.45, -1.51) | 102 | 81.9 (15.3) | -1.71 (-3.72, 0.29) | -1.27 (-3.76, 1.21) 0.3158 | -0.12 (-0.36, 0.12) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain<br>Subgroup | Nivolumab 480 mg Q4W<br>N (1) | Nivolumab 480 mg Q4W<br>Baseline Mean (SD) | Nivolumab 480 mg Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W<br>N (1) | Placebo Q4W<br>Baseline Mean (SD) | Placebo Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | | 0.5669 |
| >= 18 AND < 65 | 289 | 81.0 (17.9) | -3.01 (-4.23, -1.80) | 148 | 82.8 (15.2) | -1.65 (-3.32, 0.02) | -1.36 (-3.43, 0.71) 0.1969 | -0.13 (-0.33, 0.07) | |
| >= 65 AND < 75 | 125 | 82.9 (15.3) | -2.60 (-4.40, -0.80) | 74 | 83.0 (15.3) | -1.79 (-4.12, 0.54) | -0.81 (-3.75, 2.14) 0.5914 | -0.08 (-0.37, 0.21) | |
| >= 75 AND < 85 | 66 | 81.1 (18.2) | -3.88 (-6.36, -1.41) | 26 | 78.8 (15.1) | -0.19 (-4.07, 3.69) | -3.69 (-8.29, 0.91) 0.1154 | -0.36 (-0.82, 0.10) | |
| SEX | | | | | | | | | 0.8474 |
| MALE | 297 | 82.0 (16.9) | -2.34 (-3.54, -1.14) | 154 | 85.4 (13.9) | -0.85 (-2.50, 0.80) | -1.49 (-3.53, 0.55) 0.1526 | -0.14 (-0.34, 0.05) | |
| FEMALE | 186 | 80.6 (17.8) | -4.05 (-5.54, -2.56) | 96 | 77.7 (16.2) | -2.87 (-4.92, -0.82) | -1.18 (-3.71, 1.34) 0.3590 | -0.11 (-0.36, 0.13) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | | 0.4182 |
| STAGE IIB | 296 | 81.9 (18.0) | -3.19 (-4.40, -1.99) | 159 | 83.6 (13.7) | -2.28 (-3.90, -0.67) | -0.91 (-2.92, 1.10) 0.3748 | -0.09 (-0.28, 0.11) | |
| STAGE IIC | 187 | 80.7 (16.0) | -2.68 (-4.17, -1.19) | 91 | 80.3 (17.5) | -0.46 (-2.59, 1.66) | -2.22 (-4.81, 0.38) 0.0940 | -0.21 (-0.46, 0.04) | |
| T STAGE | | | | | | | | | 0.1881 |
| T3B | 190 | 82.1 (17.1) | -3.77 (-5.25, -2.30) | 102 | 85.6 (13.6) | -1.66 (-3.64, 0.32) | -2.11 (-4.58, 0.36) 0.0939 | -0.21 (-0.45, 0.04) | |
| T4A | 106 | 81.4 (19.6) | -2.16 (-4.11, -0.21) | 57 | 80.1 (13.2) | -3.41 (-6.03, -0.78) | 1.24 (-2.03, 4.51) 0.4555 | 0.12 (-0.20, 0.44) | |
| T4B | 187 | 80.7 (16.0) | -2.68 (-4.17, -1.19) | 91 | 80.3 (17.5) | -0.47 (-2.59, 1.66) | -2.21 (-4.80, 0.38) 0.0949 | -0.21 (-0.46, 0.04) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | | 0.5482 |
| US AND CANADA | 89 | 82.2 (16.4) | -1.80 (-3.92, 0.32) | 44 | 86.7 (13.1) | -1.20 (-4.17, 1.77) | -0.59 (-4.25, 3.06) 0.7492 | -0.06 (-0.42, 0.30) | |
| WESTERN EUROPE | 281 | 81.5 (17.8) | -2.87 (-4.10, -1.64) | 149 | 82.3 (15.5) | -0.95 (-2.62, 0.73) | -1.92 (-4.00, 0.15) 0.0693 | -0.18 (-0.38, 0.02) | |
| EASTERN EUROPE | 51 | 75.3 (17.4) | -5.70 (-8.44, -2.95) | 27 | 76.9 (18.7) | -3.20 (-6.96, 0.57) | -2.50 (-7.15, 2.15) 0.2917 | -0.25 (-0.72, 0.22) | |
| AUSTRALIA | 62 | 85.1 (14.6) | -2.97 (-5.52, -0.42) | 30 | 81.9 (12.2) | -4.23 (-7.81, -0.65) | 1.26 (-3.14, 5.65) 0.5744 | 0.12 (-0.31, 0.56) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| FATIGUE | | | | | | | | | |
| OVERALL | 483 | 11.9 (16.7) | 5.35 (4.19, 6.51) | 253 | 11.9 (16.8) | 4.20 (2.62, 5.77) | 1.15 (-0.81, 3.11) 0.2487 | 0.09 (-0.06, 0.24) | |
| AGE CATEGORY I | | | | | | | | | 0.9137 |
| < 65 | 291 | 11.9 (17.6) | 6.13 (4.67, 7.58) | 151 | 12.2 (16.5) | 5.07 (3.08, 7.05) | 1.06 (-1.40, 3.52) 0.3981 | 0.08 (-0.11, 0.28) | |
| >= 65 | 192 | 11.9 (15.4) | 4.15 (2.38, 5.93) | 102 | 11.3 (17.3) | 2.89 (0.47, 5.30) | 1.27 (-1.73, 4.26) 0.4064 | 0.10 (-0.14, 0.34) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain<br>Subgroup | Nivolumab 480 mg Q4W<br>N (1) | Nivolumab 480 mg Q4W<br>Baseline Mean (SD) | Nivolumab 480 mg Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W<br>N (1) | Placebo Q4W<br>Baseline Mean (SD) | Placebo Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | | 0.9600 |
| >= 18 AND < 65 | 291 | 11.9 (17.6) | 6.17 (4.72, 7.62) | 151 | 12.2 (16.5) | 5.09 (3.10, 7.08) | 1.08 (-1.38, 3.55) 0.3888 | 0.09 (-0.11, 0.28) | |
| >= 65 AND < 75 | 123 | 10.8 (15.7) | 3.58 (1.39, 5.77) | 74 | 11.0 (17.7) | 2.15 (-0.67, 4.97) | 1.42 (-2.14, 4.99) 0.4337 | 0.11 (-0.17, 0.40) | |
| >= 75 AND < 85 | 66 | 13.0 (14.3) | 5.14 (2.13, 8.14) | 26 | 10.7 (13.1) | 4.66 (-0.04, 9.36) | 0.48 (-5.10, 6.06) 0.8667 | 0.04 (-0.42, 0.49) | |
| SEX | | | | | | | | | 0.5455 |
| MALE | 296 | 9.8 (15.1) | 4.17 (2.73, 5.61) | 156 | 9.0 (15.0) | 2.57 (0.62, 4.53) | 1.59 (-0.83, 4.02) 0.1971 | 0.13 (-0.07, 0.32) | |
| FEMALE | 187 | 15.2 (18.5) | 7.23 (5.45, 9.02) | 97 | 16.4 (18.6) | 6.80 (4.35, 9.25) | 0.44 (-2.58, 3.45) 0.7767 | 0.04 (-0.21, 0.28) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | | 0.8687 |
| STAGE IIB | 294 | 11.7 (17.3) | 5.51 (4.06, 6.96) | 160 | 10.1 (14.6) | 4.23 (2.30, 6.17) | 1.28 (-1.14, 3.70) 0.2992 | 0.10 (-0.09, 0.29) | |
| STAGE IIC | 189 | 12.3 (15.8) | 5.09 (3.30, 6.88) | 93 | 14.9 (19.8) | 4.14 (1.59, 6.68) | 0.96 (-2.15, 4.07) 0.5459 | 0.08 (-0.17, 0.32) | |
| T STAGE | | | | | | | | | 0.5464 |
| T3B | 189 | 12.0 (16.3) | 5.85 (4.06, 7.63) | 103 | 8.3 (13.1) | 3.61 (1.23, 5.99) | 2.24 (-0.74, 5.22) 0.1405 | 0.18 (-0.06, 0.42) | |
| T4A | 105 | 11.2 (19.0) | 4.90 (2.54, 7.27) | 57 | 13.3 (16.6) | 5.37 (2.19, 8.56) | -0.47 (-4.44, 3.50) 0.8168 | -0.04 (-0.36, 0.28) | |
| T4B | 189 | 12.3 (15.8) | 5.09 (3.30, 6.88) | 93 | 14.9 (19.8) | 4.13 (1.59, 6.68) | 0.96 (-2.15, 4.07) 0.5457 | 0.08 (-0.17, 0.32) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | | 0.5194 |
| US AND CANADA | 89 | 11.5 (16.5) | 4.21 (1.62, 6.79) | 44 | 8.3 (15.4) | 5.62 (2.02, 9.23) | -1.42 (-5.86, 3.02) 0.5304 | -0.11 (-0.48, 0.25) | |
| WESTERN EUROPE | 282 | 11.4 (16.9) | 5.63 (4.14, 7.11) | 152 | 11.3 (17.0) | 4.11 (2.11, 6.12) | 1.51 (-0.98, 4.00) 0.2340 | 0.12 (-0.08, 0.32) | |
| EASTERN EUROPE | 51 | 17.0 (17.0) | 4.63 (1.28, 7.97) | 27 | 20.2 (18.2) | 3.91 (-0.70, 8.52) | 0.72 (-4.95, 6.38) 0.8042 | 0.06 (-0.41, 0.52) | |
| AUSTRALIA | 61 | 10.6 (15.5) | 6.37 (3.24, 9.50) | 30 | 12.6 (14.8) | 2.73 (-1.63, 7.10) | 3.63 (-1.74, 9.00) 0.1849 | 0.29 (-0.15, 0.73) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
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Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain<br>Subgroup | Nivolumab 480 mg Q4W<br>N (1) | Nivolumab 480 mg Q4W<br>Baseline Mean (SD) | Nivolumab 480 mg Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W<br>N (1) | Placebo Q4W<br>Baseline Mean (SD) | Placebo Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| NAUSEA AND VOMITING | | | | | | | | | |
| OVERALL | 483 | 1.7 (9.1) | 1.40 (0.94, 1.87) | 253 | 0.7 (3.7) | 0.80 (0.17, 1.43) | 0.60 (-0.18, 1.38) 0.1295 | 0.12 (-0.03, 0.27) | |
| AGE CATEGORY I | | | | | | | | | 0.4825 |
| < 65 | 291 | 2.1 (9.9) | 1.84 (1.26, 2.41) | 151 | 1.0 (4.4) | 1.45 (0.67, 2.23) | 0.39 (-0.58, 1.36) 0.4292 | 0.08 (-0.12, 0.28) | |
| >= 65 | 192 | 1.1 (7.8) | 0.73 (0.03, 1.44) | 102 | 0.3 (2.3) | -0.18 (-1.13, 0.76) | 0.92 (-0.26, 2.10) 0.1280 | 0.19 (-0.05, 0.43) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | | 0.7623 |
| >= 18 AND < 65 | 291 | 2.1 (9.9) | 1.83 (1.26, 2.41) | 151 | 1.0 (4.4) | 1.42 (0.64, 2.20) | 0.41 (-0.56, 1.38) 0.4101 | 0.08 (-0.11, 0.28) | |
| >= 65 AND < 75 | 123 | 0.7 (3.3) | 1.01 (0.15, 1.87) | 74 | 0.5 (2.7) | 0.01 (-1.10, 1.11) | 1.00 (-0.40, 2.40) 0.1594 | 0.21 (-0.08, 0.50) | |
| >= 75 AND < 85 | 66 | 2.0 (12.6) | 0.10 (-1.10, 1.30) | 26 | 0.0 (0.0) | -0.73 (-2.59, 1.12) | 0.83 (-1.37, 3.04) 0.4591 | 0.17 (-0.28, 0.62) | |
| SEX | | | | | | | | | 0.2211 |
| MALE | 296 | 1.3 (9.1) | 0.40 (-0.16, 0.96) | 156 | 0.4 (3.3) | 0.14 (-0.62, 0.90) | 0.26 (-0.68, 1.20) 0.5859 | 0.05 (-0.14, 0.25) | |
| FEMALE | 187 | 2.3 (9.2) | 2.99 (2.30, 3.68) | 97 | 1.2 (4.3) | 1.83 (0.89, 2.76) | 1.16 (0.00, 2.33) 0.0507 | 0.24 (0.00, 0.49) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | | 0.5223 |
| STAGE IIB | 294 | 1.8 (9.6) | 1.36 (0.78, 1.94) | 160 | 0.7 (3.4) | 0.93 (0.17, 1.69) | 0.43 (-0.53, 1.38) 0.3823 | 0.09 (-0.11, 0.28) | |
| STAGE IIC | 189 | 1.5 (8.4) | 1.47 (0.76, 2.18) | 93 | 0.7 (4.2) | 0.56 (-0.45, 1.57) | 0.92 (-0.32, 2.15) 0.1454 | 0.18 (-0.06, 0.43) | |
| T STAGE | | | | | | | | | 0.6346 |
| T3B | 189 | 1.2 (5.6) | 1.32 (0.62, 2.03) | 103 | 0.6 (3.2) | 0.66 (-0.27, 1.59) | 0.66 (-0.51, 1.83) 0.2655 | 0.14 (-0.10, 0.38) | |
| T4A | 105 | 2.9 (14.1) | 1.42 (0.48, 2.36) | 57 | 0.9 (3.8) | 1.44 (0.19, 2.69) | -0.02 (-1.58, 1.55) 0.9805 | 0.00 (-0.33, 0.32) | |
| T4B | 189 | 1.5 (8.4) | 1.48 (0.76, 2.19) | 93 | 0.7 (4.2) | 0.56 (-0.45, 1.57) | 0.92 (-0.32, 2.15) 0.1449 | 0.18 (-0.06, 0.43) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | | 0.9283 |
| US AND CANADA | 89 | 1.5 (10.8) | 1.35 (0.32, 2.39) | 44 | 0.4 (2.5) | 1.24 (-0.17, 2.65) | 0.11 (-1.64, 1.86) 0.9003 | 0.02 (-0.34, 0.38) | |
| WESTERN EUROPE | 282 | 1.6 (9.7) | 1.46 (0.87, 2.05) | 152 | 0.8 (4.0) | 0.81 (0.02, 1.60) | 0.65 (-0.34, 1.64) 0.1967 | 0.13 (-0.07, 0.33) | |
| EASTERN EUROPE | 51 | 2.9 (6.4) | 1.05 (-0.26, 2.35) | 27 | 1.2 (4.4) | 0.31 (-1.48, 2.09) | 0.74 (-1.47, 2.95) 0.5105 | 0.15 (-0.31, 0.62) | |
| AUSTRALIA | 61 | 1.4 (4.6) | 1.54 (0.29, 2.79) | 30 | 0.6 (3.0) | 0.57 (-1.15, 2.29) | 0.97 (-1.15, 3.10) 0.3684 | 0.20 (-0.24, 0.64) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| PAIN | | | | | | | | | |
| OVERALL | 485 | 9.4 (18.6) | 2.03 (0.91, 3.15) | 253 | 10.0 (18.0) | -0.14 (-1.66, 1.38) | 2.17 (0.28, 4.06) 0.0244 | 0.17 (0.02, 0.33) | |
| AGE CATEGORY I | | | | | | | | | 0.6929 |
| < 65 | 291 | 9.9 (18.8) | 1.70 (0.30, 3.11) | 151 | 10.3 (18.7) | -0.76 (-2.68, 1.16) | 2.46 (0.09, 4.84) 0.0421 | 0.20 (0.01, 0.40) | |
| >= 65 | 194 | 8.8 (18.4) | 2.53 (0.82, 4.24) | 102 | 9.6 (17.0) | 0.79 (-1.53, 3.12) | 1.73 (-1.15, 4.62) 0.2385 | 0.14 (-0.10, 0.38) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | | 0.0937 |
| >= 18 AND < 65 | 291 | 9.9 (18.8) | 1.69 (0.29, 3.09) | 151 | 10.3 (18.7) | -0.80 (-2.71, 1.12) | 2.49 (0.11, 4.86) 0.0404 | 0.21 (0.01, 0.40) | |
| >= 65 AND < 75 | 125 | 9.3 (18.4) | 1.53 (-0.57, 3.62) | 74 | 9.2 (16.8) | 1.88 (-0.83, 4.60) | -0.36 (-3.78, 3.07) 0.8384 | -0.03 (-0.32, 0.26) | |
| >= 75 AND < 85 | 66 | 7.6 (19.0) | 4.45 (1.55, 7.35) | 26 | 11.5 (18.1) | -2.02 (-6.55, 2.51) | 6.47 (1.09, 11.85) 0.0184 | 0.54 (0.08, 1.00) | |
| SEX | | | | | | | | | 0.8960 |
| MALE | 298 | 8.1 (17.2) | 1.18 (-0.20, 2.57) | 156 | 7.1 (15.2) | -1.07 (-2.96, 0.82) | 2.26 (-0.09, 4.60) 0.0590 | 0.19 (-0.01, 0.38) | |
| FEMALE | 187 | 11.5 (20.6) | 3.37 (1.65, 5.10) | 97 | 14.8 (21.1) | 1.36 (-1.01, 3.73) | 2.01 (-0.91, 4.94) 0.1770 | 0.17 (-0.08, 0.41) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | | 0.2310 |
| STAGE IIB | 296 | 9.5 (19.0) | 2.54 (1.14, 3.93) | 160 | 9.2 (17.4) | -0.48 (-2.34, 1.38) | 3.01 (0.69, 5.34) 0.0112 | 0.25 (0.06, 0.44) | |
| STAGE IIC | 189 | 9.3 (18.1) | 1.23 (-0.49, 2.95) | 93 | 11.5 (19.0) | 0.46 (-1.98, 2.90) | 0.77 (-2.22, 3.76) 0.6129 | 0.06 (-0.18, 0.31) | |
| T STAGE | | | | | | | | | 0.0089** |
| T3B | 190 | 9.0 (18.3) | 3.21 (1.50, 4.92) | 103 | 7.4 (16.8) | -2.18 (-4.45, 0.09) | 5.39 (2.55, 8.23) 0.0002 | 0.45 (0.21, 0.70) | |
| T4A | 106 | 10.2 (20.3) | 1.35 (-0.90, 3.61) | 57 | 12.3 (18.2) | 2.70 (-0.35, 5.76) | -1.35 (-5.15, 2.45) 0.4849 | -0.11 (-0.44, 0.21) | |
| T4B | 189 | 9.3 (18.1) | 1.22 (-0.50, 2.94) | 93 | 11.5 (19.0) | 0.45 (-1.99, 2.88) | 0.77 (-2.21, 3.75) 0.6117 | 0.06 (-0.18, 0.31) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain<br>Subgroup | Nivolumab 480 mg Q4W<br>N (1) | Nivolumab 480 mg Q4W<br>Baseline Mean (SD) | Nivolumab 480 mg Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W<br>N (1) | Placebo Q4W<br>Baseline Mean (SD) | Placebo Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | | 0.2452 |
| US AND CANADA | 89 | 9.4 (18.1) | 1.57 (-0.91, 4.05) | 44 | 9.5 (19.2) | -1.55 (-5.00, 1.89) | 3.12 (-1.13, 7.36) 0.1495 | 0.26 (-0.10, 0.63) | |
| WESTERN EUROPE | 283 | 9.3 (19.2) | 2.22 (0.80, 3.64) | 152 | 8.9 (17.3) | -0.58 (-2.50, 1.34) | 2.80 (0.41, 5.19) 0.0215 | 0.23 (0.03, 0.43) | |
| EASTERN EUROPE | 51 | 13.4 (19.2) | -1.09 (-4.28, 2.10) | 27 | 10.5 (18.0) | 1.99 (-2.39, 6.38) | -3.08 (-8.50, 2.34) 0.2645 | -0.26 (-0.73, 0.21) | |
| AUSTRALIA | 62 | 6.7 (16.1) | 4.59 (1.60, 7.58) | 30 | 16.1 (19.8) | 2.29 (-1.91, 6.49) | 2.30 (-2.86, 7.47) 0.3814 | 0.19 (-0.24, 0.63) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| DYSPNEA | | | | | | | | | |
| OVERALL | 483 | 6.6 (17.1) | 1.80 (0.76, 2.84) | 253 | 5.3 (14.8) | 2.31 (0.90, 3.72) | -0.51 (-2.26, 1.25) 0.5714 | -0.04 (-0.20, 0.11) | |
| AGE CATEGORY I | | | | | | | | | 0.5915 |
| < 65 | 291 | 6.1 (16.3) | 1.63 (0.34, 2.92) | 151 | 3.3 (11.4) | 1.78 (0.01, 3.54) | -0.14 (-2.33, 2.05) 0.8989 | -0.01 (-0.21, 0.18) | |
| >= 65 | 192 | 7.5 (18.3) | 2.07 (0.50, 3.64) | 102 | 8.2 (18.4) | 3.11 (0.97, 5.25) | -1.04 (-3.69, 1.61) 0.4396 | -0.09 (-0.33, 0.15) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain<br>Subgroup | Nivolumab 480 mg Q4W<br>N (1) | Nivolumab 480 mg Q4W<br>Baseline Mean (SD) | Nivolumab 480 mg Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W<br>N (1) | Placebo Q4W<br>Baseline Mean (SD) | Placebo Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | | 0.6386 |
| >= 18 AND < 65 | 291 | 6.1 (16.3) | 1.67 (0.37, 2.96) | 151 | 3.3 (11.4) | 1.81 (0.03, 3.58) | -0.14 (-2.33, 2.06) 0.9026 | -0.01 (-0.21, 0.18) | |
| >= 65 AND < 75 | 123 | 6.8 (17.0) | 1.87 (-0.06, 3.80) | 74 | 7.2 (17.7) | 2.30 (-0.19, 4.79) | -0.42 (-3.57, 2.73) 0.7917 | -0.04 (-0.33, 0.25) | |
| >= 75 AND < 85 | 66 | 8.6 (20.5) | 2.49 (-0.16, 5.13) | 26 | 10.3 (20.6) | 5.17 (1.03, 9.30) | -2.68 (-7.58, 2.22) 0.2835 | -0.25 (-0.70, 0.21) | |
| SEX | | | | | | | | | 0.9485 |
| MALE | 296 | 6.4 (17.1) | 1.29 (0.01, 2.57) | 156 | 3.2 (11.2) | 1.84 (0.09, 3.59) | -0.55 (-2.71, 1.62) 0.6204 | -0.05 (-0.24, 0.15) | |
| FEMALE | 187 | 7.0 (17.1) | 2.62 (1.04, 4.20) | 97 | 8.6 (18.8) | 3.06 (0.89, 5.23) | -0.44 (-3.12, 2.25) 0.7491 | -0.04 (-0.29, 0.21) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | | 0.2961 |
| STAGE IIB | 294 | 6.3 (17.1) | 1.82 (0.53, 3.10) | 160 | 5.0 (13.6) | 1.68 (-0.03, 3.39) | 0.13 (-2.01, 2.27) 0.9021 | 0.01 (-0.18, 0.20) | |
| STAGE IIC | 189 | 7.1 (17.1) | 1.78 (0.20, 3.36) | 93 | 5.7 (16.8) | 3.43 (1.19, 5.66) | -1.64 (-4.38, 1.09) 0.2389 | -0.15 (-0.40, 0.10) | |
| T STAGE | | | | | | | | | 0.5275 |
| T3B | 189 | 6.3 (16.3) | 1.70 (0.13, 3.28) | 103 | 2.9 (9.5) | 1.90 (-0.20, 4.00) | -0.20 (-2.82, 2.42) 0.8812 | -0.02 (-0.26, 0.22) | |
| T4A | 105 | 6.3 (18.5) | 2.03 (-0.05, 4.10) | 57 | 8.8 (18.4) | 1.28 (-1.52, 4.09) | 0.74 (-2.75, 4.23) 0.6759 | 0.07 (-0.25, 0.39) | |
| T4B | 189 | 7.1 (17.1) | 1.78 (0.20, 3.36) | 93 | 5.7 (16.8) | 3.42 (1.19, 5.66) | -1.64 (-4.38, 1.10) 0.2392 | -0.15 (-0.40, 0.10) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | | 0.4977 |
| US AND CANADA | 89 | 6.7 (19.6) | -0.12 (-2.39, 2.14) | 44 | 2.3 (8.5) | 2.17 (-0.99, 5.34) | -2.30 (-6.19, 1.60) 0.2471 | -0.21 (-0.57, 0.15) | |
| WESTERN EUROPE | 282 | 7.1 (17.0) | 2.36 (1.05, 3.67) | 152 | 4.8 (15.1) | 2.29 (0.52, 4.06) | 0.07 (-2.14, 2.27) 0.9524 | 0.01 (-0.19, 0.20) | |
| EASTERN EUROPE | 51 | 5.9 (14.5) | 1.19 (-1.72, 4.10) | 27 | 8.6 (14.9) | 3.76 (-0.26, 7.78) | -2.57 (-7.54, 2.39) 0.3089 | -0.24 (-0.71, 0.23) | |
| AUSTRALIA | 61 | 4.9 (15.9) | 2.56 (-0.19, 5.30) | 30 | 8.9 (19.4) | 1.28 (-2.53, 5.09) | 1.28 (-3.42, 5.98) 0.5944 | 0.12 (-0.32, 0.55) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| INSOMNIA | | | | | | | | | |
| OVERALL | 482 | 17.4 (25.0) | -0.20 (-1.54, 1.14) | 253 | 14.5 (23.2) | -0.62 (-2.44, 1.20) | 0.42 (-1.84, 2.68) 0.7159 | 0.03 (-0.12, 0.18) | |
| AGE CATEGORY I | | | | | | | | | 0.9398 |
| < 65 | 290 | 17.4 (26.0) | 0.26 (-1.45, 1.96) | 151 | 13.9 (23.5) | -0.23 (-2.55, 2.10) | 0.48 (-2.40, 3.36) 0.7421 | 0.03 (-0.16, 0.23) | |
| >= 65 | 192 | 17.5 (23.4) | -0.91 (-3.00, 1.19) | 102 | 15.4 (22.8) | -1.22 (-4.06, 1.62) | 0.31 (-3.22, 3.84) 0.8631 | 0.02 (-0.22, 0.26) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | | 0.9401 |
| >= 18 AND < 65 | 290 | 17.4 (26.0) | 0.28 (-1.42, 1.98) | 151 | 13.9 (23.5) | -0.16 (-2.48, 2.16) | 0.44 (-2.44, 3.32) 0.7636 | 0.03 (-0.17, 0.23) | |
| >= 65 AND < 75 | 123 | 18.2 (23.9) | -1.96 (-4.55, 0.63) | 74 | 14.9 (24.1) | -1.52 (-4.84, 1.80) | -0.44 (-4.65, 3.78) 0.8385 | -0.03 (-0.32, 0.26) | |
| >= 75 AND < 85 | 66 | 16.2 (22.8) | 0.67 (-2.90, 4.25) | 26 | 16.7 (19.4) | 0.22 (-5.37, 5.80) | 0.46 (-6.18, 7.09) 0.8929 | 0.03 (-0.42, 0.48) | |
| SEX | | | | | | | | | 0.4213 |
| MALE | 296 | 16.8 (24.4) | -2.02 (-3.68, -0.35) | 156 | 11.1 (19.8) | -3.16 (-5.44, -0.89) | 1.15 (-1.67, 3.97) 0.4245 | 0.08 (-0.12, 0.27) | |
| FEMALE | 186 | 18.5 (25.9) | 2.72 (0.64, 4.80) | 97 | 19.9 (27.1) | 3.39 (0.55, 6.23) | -0.68 (-4.19, 2.84) 0.7062 | -0.05 (-0.29, 0.20) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | | 0.3248 |
| STAGE IIB | 294 | 18.3 (25.0) | 0.03 (-1.67, 1.73) | 160 | 13.3 (22.5) | -1.23 (-3.48, 1.02) | 1.26 (-1.56, 4.08) 0.3813 | 0.09 (-0.11, 0.28) | |
| STAGE IIC | 188 | 16.1 (25.0) | -0.56 (-2.67, 1.55) | 93 | 16.5 (24.4) | 0.47 (-2.52, 3.46) | -1.03 (-4.69, 2.63) 0.5808 | -0.07 (-0.32, 0.18) | |
| T STAGE | | | | | | | | | 0.0547 |
| T3B | 189 | 18.5 (25.3) | 1.01 (-1.09, 3.10) | 103 | 10.4 (18.7) | -2.56 (-5.34, 0.22) | 3.57 (0.08, 7.06) 0.0450 | 0.24 (0.00, 0.49) | |
| T4A | 105 | 17.8 (24.5) | -1.73 (-4.52, 1.07) | 57 | 18.7 (27.5) | 1.22 (-2.53, 4.97) | -2.95 (-7.62, 1.73) 0.2167 | -0.20 (-0.53, 0.12) | |
| T4B | 188 | 16.1 (25.0) | -0.56 (-2.66, 1.55) | 93 | 16.5 (24.4) | 0.47 (-2.52, 3.45) | -1.02 (-4.68, 2.63) 0.5820 | -0.07 (-0.32, 0.18) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | | 0.6524 |
| US AND CANADA | 89 | 15.4 (26.1) | -2.19 (-5.25, 0.88) | 44 | 15.9 (23.3) | 0.31 (-3.94, 4.56) | -2.50 (-7.74, 2.74) 0.3501 | -0.17 (-0.53, 0.19) | |
| WESTERN EUROPE | 282 | 15.8 (24.1) | 0.05 (-1.68, 1.78) | 152 | 13.4 (23.1) | -0.75 (-3.09, 1.59) | 0.80 (-2.11, 3.71) 0.5902 | 0.05 (-0.14, 0.25) | |
| EASTERN EUROPE | 51 | 22.2 (24.6) | 1.37 (-2.57, 5.31) | 27 | 16.0 (23.3) | 0.11 (-5.32, 5.54) | 1.26 (-5.45, 7.97) 0.7126 | 0.09 (-0.38, 0.55) | |
| AUSTRALIA | 60 | 23.9 (26.8) | 0.14 (-3.62, 3.90) | 30 | 16.7 (24.4) | -2.05 (-7.23, 3.12) | 2.19 (-4.20, 8.59) 0.5006 | 0.15 (-0.29, 0.59) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain<br>Subgroup | Nivolumab 480 mg Q4W<br>N (1) | Nivolumab 480 mg Q4W<br>Baseline Mean (SD) | Nivolumab 480 mg Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W<br>N (1) | Placebo Q4W<br>Baseline Mean (SD) | Placebo Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| APPETITE LOSS | | | | | | | | | |
| OVERALL | 483 | 3.7 (13.3) | 2.83 (1.99, 3.67) | 253 | 2.8 (9.7) | 0.72 (-0.41, 1.86) | 2.11 (0.69, 3.52) 0.0036 | 0.23 (0.07, 0.38) | |
| AGE CATEGORY I | | | | | | | | | 0.8001 |
| < 65 | 291 | 3.2 (12.9) | 3.05 (2.00, 4.10) | 151 | 2.9 (9.4) | 0.81 (-0.62, 2.24) | 2.24 (0.47, 4.01) 0.0133 | 0.25 (0.05, 0.45) | |
| >= 65 | 192 | 4.3 (14.0) | 2.49 (1.20, 3.78) | 102 | 2.6 (10.2) | 0.59 (-1.14, 2.33) | 1.89 (-0.27, 4.06) 0.0861 | 0.21 (-0.03, 0.45) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | | 0.4417 |
| >= 18 AND < 65 | 291 | 3.2 (12.9) | 3.11 (2.06, 4.16) | 151 | 2.9 (9.4) | 0.91 (-0.52, 2.34) | 2.20 (0.42, 3.97) 0.0154 | 0.24 (0.05, 0.44) | |
| >= 65 AND < 75 | 123 | 3.3 (10.8) | 2.54 (0.96, 4.11) | 74 | 2.3 (10.1) | -0.19 (-2.21, 1.83) | 2.73 (0.16, 5.30) 0.0371 | 0.31 (0.02, 0.60) | |
| >= 75 AND < 85 | 66 | 4.5 (14.2) | 2.67 (0.49, 4.85) | 26 | 2.6 (9.1) | 2.97 (-0.43, 6.37) | -0.30 (-4.34, 3.74) 0.8846 | -0.03 (-0.49, 0.42) | |
| SEX | | | | | | | | | 0.5449 |
| MALE | 296 | 3.4 (14.1) | 2.04 (1.00, 3.08) | 156 | 1.7 (8.3) | 0.26 (-1.16, 1.67) | 1.78 (0.03, 3.54) 0.0462 | 0.20 (0.00, 0.39) | |
| FEMALE | 187 | 4.1 (12.0) | 4.09 (2.80, 5.37) | 97 | 4.5 (11.4) | 1.47 (-0.28, 3.22) | 2.62 (0.44, 4.79) 0.0185 | 0.29 (0.05, 0.54) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | | 0.6715 |
| STAGE IIB | 294 | 3.9 (13.8) | 3.14 (2.09, 4.19) | 160 | 2.7 (9.1) | 0.80 (-0.59, 2.18) | 2.34 (0.61, 4.08) 0.0082 | 0.26 (0.07, 0.45) | |
| STAGE IIC | 189 | 3.4 (12.7) | 2.35 (1.06, 3.64) | 93 | 2.9 (10.6) | 0.59 (-1.24, 2.42) | 1.75 (-0.49, 3.99) 0.1248 | 0.19 (-0.05, 0.44) | |
| T STAGE | | | | | | | | | 0.2276 |
| T3B | 189 | 3.4 (11.2) | 3.61 (2.33, 4.89) | 103 | 2.6 (9.0) | 0.23 (-1.46, 1.92) | 3.38 (1.26, 5.50) 0.0018 | 0.38 (0.14, 0.62) | |
| T4A | 105 | 4.8 (17.6) | 2.28 (0.58, 3.99) | 57 | 2.9 (9.5) | 1.85 (-0.42, 4.13) | 0.43 (-2.41, 3.27) 0.7667 | 0.05 (-0.27, 0.37) | |
| T4B | 189 | 3.4 (12.7) | 2.35 (1.06, 3.64) | 93 | 2.9 (10.6) | 0.59 (-1.24, 2.42) | 1.76 (-0.48, 4.00) 0.1237 | 0.19 (-0.05, 0.44) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | | 0.7166 |
| US AND CANADA | 89 | 4.9 (19.8) | 3.17 (1.30, 5.04) | 44 | 2.3 (8.5) | 2.17 (-0.41, 4.74) | 1.00 (-2.18, 4.18) 0.5374 | 0.11 (-0.25, 0.47) | |
| WESTERN EUROPE | 282 | 2.7 (10.4) | 2.72 (1.65, 3.79) | 152 | 2.2 (9.1) | 0.57 (-0.87, 2.01) | 2.15 (0.36, 3.94) 0.0186 | 0.24 (0.04, 0.43) | |
| EASTERN EUROPE | 51 | 7.8 (15.8) | 3.23 (0.85, 5.60) | 27 | 7.4 (14.1) | -0.75 (-4.02, 2.51) | 3.98 (-0.05, 8.00) 0.0527 | 0.46 (-0.02, 0.93) | |
| AUSTRALIA | 61 | 2.7 (11.0) | 2.51 (0.25, 4.77) | 30 | 2.2 (8.5) | 0.71 (-2.41, 3.83) | 1.80 (-2.05, 5.65) 0.3599 | 0.20 (-0.24, 0.64) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain<br>Subgroup | Nivolumab 480 mg Q4W<br>N (1) | Nivolumab 480 mg Q4W<br>Baseline Mean (SD) | Nivolumab 480 mg Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W<br>N (1) | Placebo Q4W<br>Baseline Mean (SD) | Placebo Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| CONSTIPATION | | | | | | | | | |
| OVERALL | 483 | 4.9 (14.8) | 1.31<br>(0.42, 2.21) | 253 | 5.3 (15.1) | 0.78<br>(-0.43, 1.98) | 0.53<br>(-0.97, 2.04)<br>0.4859 | 0.05<br>(-0.10, 0.21) | |
| AGE CATEGORY I | | | | | | | | | 0.4224 |
| < 65 | 291 | 4.6 (15.7) | 0.75<br>(-0.36, 1.85) | 151 | 2.9 (12.1) | 0.66<br>(-0.84, 2.16) | 0.09<br>(-1.78, 1.95)<br>0.9281 | 0.01<br>(-0.19, 0.21) | |
| >= 65 | 192 | 5.4 (13.2) | 2.19<br>(0.84, 3.54) | 102 | 8.8 (18.1) | 0.96<br>(-0.87, 2.78) | 1.23<br>(-1.04, 3.50)<br>0.2867 | 0.13<br>(-0.11, 0.37) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | | 0.7042 |
| >= 18 AND < 65 | 291 | 4.6 (15.7) | 0.79 (-0.30, 1.88) | 151 | 2.9 (12.1) | 0.63 (-0.85, 2.11) | 0.16 (-1.68, 2.00) 0.8672 | 0.02 (-0.18, 0.21) | |
| >= 65 AND < 75 | 123 | 3.3 (9.9) | 0.62 (-1.00, 2.23) | 74 | 9.0 (19.3) | 0.44 (-1.64, 2.53) | 0.17 (-2.47, 2.81) 0.8993 | 0.02 (-0.27, 0.31) | |
| >= 75 AND < 85 | 66 | 9.6 (17.3) | 4.81 (2.58, 7.05) | 26 | 7.7 (14.3) | 2.82 (-0.62, 6.27) | 1.99 (-2.11, 6.09) 0.3409 | 0.22 (-0.24, 0.67) | |
| SEX | | | | | | | | | 0.4822 |
| MALE | 296 | 4.2 (13.5) | 0.53 (-0.57, 1.63) | 156 | 3.4 (10.8) | 0.39 (-1.10, 1.87) | 0.14 (-1.70, 1.99) 0.8788 | 0.02 (-0.18, 0.21) | |
| FEMALE | 187 | 6.1 (16.5) | 2.56 (1.20, 3.91) | 97 | 8.2 (19.9) | 1.41 (-0.43, 3.25) | 1.15 (-1.14, 3.43) 0.3240 | 0.12 (-0.12, 0.37) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

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Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | | 0.5352 |
| STAGE IIB | 294 | 5.8 (16.1) | 1.32 (0.22, 2.43) | 160 | 5.8 (15.2) | 0.47 (-0.98, 1.93) | 0.85 (-0.97, 2.68) 0.3604 | 0.09 (-0.10, 0.28) | |
| STAGE IIC | 189 | 3.5 (12.4) | 1.29 (-0.06, 2.65) | 93 | 4.3 (14.9) | 1.34 (-0.57, 3.25) | -0.05 (-2.39, 2.30) 0.9695 | 0.00 (-0.25, 0.24) | |
| T STAGE | | | | | | | | | 0.4328 |
| T3B | 189 | 5.8 (14.4) | 1.06 (-0.29, 2.40) | 103 | 4.5 (13.2) | 0.94 (-0.83, 2.71) | 0.12 (-2.11, 2.34) 0.9187 | 0.01 (-0.23, 0.25) | |
| T4A | 105 | 5.7 (18.8) | 1.80 (0.03, 3.58) | 57 | 8.2 (18.1) | -0.40 (-2.78, 1.98) | 2.21 (-0.76, 5.17) 0.1449 | 0.24 (-0.08, 0.56) | |
| T4B | 189 | 3.5 (12.4) | 1.30 (-0.06, 2.65) | 93 | 4.3 (14.9) | 1.34 (-0.58, 3.25) | -0.04 (-2.39, 2.31) 0.9728 | 0.00 (-0.25, 0.24) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | | 0.8613 |
| US AND CANADA | 89 | 6.4 (18.0) | 1.56 (-0.39, 3.51) | 44 | 5.3 (12.3) | -0.11 (-2.78, 2.56) | 1.67 (-1.63, 4.98) 0.3211 | 0.18 (-0.18, 0.54) | |
| WESTERN EUROPE | 282 | 3.4 (11.6) | 1.53 (0.40, 2.65) | 152 | 5.0 (15.7) | 1.33 (-0.18, 2.84) | 0.20 (-1.68, 2.08) 0.8357 | 0.02 (-0.18, 0.22) | |
| EASTERN EUROPE | 51 | 7.8 (18.4) | 0.71 (-1.76, 3.18) | 27 | 4.9 (15.2) | -0.42 (-3.82, 2.99) | 1.13 (-3.08, 5.33) 0.5997 | 0.12 (-0.34, 0.59) | |
| AUSTRALIA | 61 | 7.1 (18.4) | 0.45 (-1.91, 2.82) | 30 | 6.7 (16.1) | 0.42 (-2.83, 3.68) | 0.03 (-3.99, 4.05) 0.9885 | 0.00 (-0.43, 0.44) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain<br>Subgroup | Nivolumab 480 mg Q4W<br>N (1) | Nivolumab 480 mg Q4W<br>Baseline Mean (SD) | Nivolumab 480 mg Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W<br>N (1) | Placebo Q4W<br>Baseline Mean (SD) | Placebo Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| DIARRHEA | | | | | | | | | |
| OVERALL | 484 | 4.2 (12.6) | 1.75 (0.96, 2.53) | 251 | 4.0 (12.4) | 0.67 (-0.38, 1.73) | 1.07 (-0.24, 2.39) 0.1096 | 0.12 (-0.03, 0.28) | |
| AGE CATEGORY I | | | | | | | | | 0.8440 |
| < 65 | 290 | 4.4 (13.2) | 2.17 (1.20, 3.14) | 149 | 4.3 (11.2) | 1.00 (-0.31, 2.32) | 1.17 (-0.46, 2.80) 0.1606 | 0.14 (-0.06, 0.34) | |
| >= 65 | 194 | 4.0 (11.8) | 1.09 (-0.08, 2.27) | 102 | 3.6 (14.0) | 0.17 (-1.41, 1.76) | 0.92 (-1.05, 2.89) 0.3588 | 0.11 (-0.13, 0.35) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | | 0.9527 |
| >= 18 AND < 65 | 290 | 4.4 (13.2) | 2.16 (1.19, 3.13) | 149 | 4.3 (11.2) | 1.01 (-0.30, 2.33) | 1.15 (-0.49, 2.78) 0.1686 | 0.14 (-0.06, 0.34) | |
| >= 65 AND < 75 | 125 | 3.5 (11.1) | 0.93 (-0.50, 2.36) | 74 | 5.0 (16.3) | 0.04 (-1.80, 1.89) | 0.89 (-1.45, 3.22) 0.4558 | 0.11 (-0.18, 0.40) | |
| >= 75 AND < 85 | 66 | 4.5 (12.9) | 1.33 (-0.66, 3.33) | 26 | 0.0 (0.0) | 0.76 (-2.31, 3.82) | 0.58 (-3.08, 4.23) 0.7567 | 0.07 (-0.38, 0.52) | |
| SEX | | | | | | | | | 0.3705 |
| MALE | 298 | 4.3 (12.7) | 1.53 (0.57, 2.49) | 155 | 2.8 (9.3) | 0.03 (-1.27, 1.33) | 1.50 (-0.11, 3.12) 0.0682 | 0.18 (-0.01, 0.37) | |
| FEMALE | 186 | 4.1 (12.5) | 2.08 (0.90, 3.27) | 96 | 5.9 (16.0) | 1.70 (0.09, 3.31) | 0.39 (-1.61, 2.38) 0.7052 | 0.05 (-0.20, 0.29) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | | 0.6566 |
| STAGE IIB | 296 | 5.0 (14.2) | 1.78 (0.82, 2.74) | 159 | 3.6 (11.0) | 0.51 (-0.77, 1.78) | 1.27 (-0.32, 2.87) 0.1176 | 0.15 (-0.04, 0.35) | |
| STAGE IIC | 188 | 3.0 (9.6) | 1.69 (0.50, 2.88) | 92 | 4.7 (14.5) | 0.98 (-0.70, 2.66) | 0.71 (-1.35, 2.77) 0.4982 | 0.09 (-0.16, 0.34) | |
| T STAGE | | | | | | | | | 0.8752 |
| T3B | 190 | 4.6 (12.9) | 2.03 (0.85, 3.20) | 102 | 2.6 (9.0) | 0.60 (-0.95, 2.15) | 1.42 (-0.52, 3.37) 0.1511 | 0.18 (-0.07, 0.42) | |
| T4A | 106 | 5.7 (16.2) | 1.34 (-0.21, 2.89) | 57 | 5.3 (13.8) | 0.33 (-1.74, 2.40) | 1.01 (-1.57, 3.59) 0.4438 | 0.13 (-0.20, 0.45) | |
| T4B | 188 | 3.0 (9.6) | 1.69 (0.50, 2.88) | 92 | 4.7 (14.5) | 0.98 (-0.71, 2.66) | 0.71 (-1.35, 2.77) 0.4987 | 0.09 (-0.16, 0.34) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

Protocol: CA20976K 

Table 32.20.1
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EORTC QLQ-C30
All Randomized Subjects

| EORTC QLQ-C30 Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | | 0.0747 |
| US AND CANADA | 89 | 4.5 (14.4) | 2.06 (0.36, 3.75) | 44 | 3.0 (9.7) | 3.43 (1.13, 5.74) | -1.38 (-4.24, 1.48) 0.3451 | -0.17 (-0.53, 0.19) | |
| WESTERN EUROPE | 282 | 4.6 (13.1) | 2.04 (1.07, 3.02) | 150 | 4.0 (13.3) | -0.24 (-1.55, 1.08) | 2.28 (0.64, 3.92) 0.0064 | 0.28 (0.08, 0.47) | |
| EASTERN EUROPE | 51 | 3.3 (10.0) | 0.26 (-1.85, 2.38) | 27 | 4.9 (12.1) | -0.76 (-3.66, 2.15) | 1.02 (-2.57, 4.61) 0.5778 | 0.13 (-0.34, 0.60) | |
| AUSTRALIA | 62 | 2.7 (9.2) | 1.24 (-0.79, 3.26) | 30 | 4.4 (11.5) | 2.39 (-0.41, 5.20) | -1.16 (-4.62, 2.31) 0.5117 | -0.14 (-0.58, 0.29) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:21:25:03

**Anhang 4-G 3.1.1.4: Subgruppenanalysen für Endpunkt Gesundheitszustand gemäß EQ-5D-VAS aus CA209-76K**

Subgruppenanalysen für den Endpunkt Gesundheitszustand gemäß EQ-5D-VAS aus CA209-76K – Änderung zu Studienbeginn (MMRM)

Protocol: CA20976K 

Table 32.20.2
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EQ-5D-5L VAS
All Randomized Subjects

| EQ-5D-5L Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| EQ5D02-EQ VAS SCORE | | | | | | | | | |
| OVERALL | 482 | 84.6 (13.8) | -0.32 (-1.11, 0.47) | 255 | 84.8 (12.0) | 1.04 (-0.03, 2.11) | -1.36 (-2.68, -0.03) 0.0444 | -0.16 (-0.31, 0.00) | |
| AGE CATEGORY I | | | | | | | | | 0.7398 |
| < 65 | 289 | 83.9 (15.5) | 0.05 (-0.94, 1.03) | 152 | 85.6 (11.3) | 1.23 (-0.11, 2.58) | -1.19 (-2.86, 0.48) 0.1626 | -0.14 (-0.34, 0.06) | |
| >= 65 | 193 | 85.8 (10.9) | -0.87 (-2.07, 0.32) | 103 | 83.6 (12.9) | 0.75 (-0.88, 2.37) | -1.62 (-3.64, 0.40) 0.1163 | -0.19 (-0.43, 0.05) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:20:34:12

Protocol: CA20976K 

Table 32.20.2
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EQ-5D-5L VAS
All Randomized Subjects

| EQ-5D-5L Domain<br>Subgroup | Nivolumab 480 mg Q4W<br>N (1) | Nivolumab 480 mg Q4W<br>Baseline Mean (SD) | Nivolumab 480 mg Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W<br>N (1) | Placebo Q4W<br>Baseline Mean (SD) | Placebo Q4W<br>Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W<br>SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | | 0.3951 |
| >= 18 AND < 65 | 289 | 83.9 (15.5) | 0.05 (-0.93, 1.03) | 152 | 85.6 (11.3) | 1.21 (-0.13, 2.55) | -1.16 (-2.83, 0.50) 0.1698 | -0.14 (-0.33, 0.06) | |
| >= 65 AND < 75 | 124 | 86.2 (11.0) | -0.83 (-2.30, 0.64) | 75 | 83.8 (12.7) | 1.46 (-0.43, 3.35) | -2.29 (-4.68, 0.11) 0.0609 | -0.27 (-0.56, 0.01) | |
| >= 75 AND < 85 | 66 | 84.7 (10.8) | -0.78 (-2.78, 1.23) | 26 | 84.2 (10.9) | -1.51 (-4.68, 1.66) | 0.73 (-3.02, 4.48) 0.7007 | 0.09 (-0.37, 0.54) | |
| SEX | | | | | | | | | 0.6874 |
| MALE | 295 | 84.4 (13.9) | 0.25 (-0.73, 1.22) | 156 | 86.3 (10.9) | 1.81 (0.48, 3.14) | -1.56 (-3.21, 0.08) 0.0630 | -0.18 (-0.38, 0.01) | |
| FEMALE | 187 | 84.9 (13.8) | -1.21 (-2.42, -0.01) | 99 | 82.4 (13.2) | -0.17 (-1.81, 1.47) | -1.04 (-3.08, 1.00) 0.3155 | -0.12 (-0.37, 0.12) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:20:34:12

Protocol: CA20976K 

Table 32.20.2
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EQ-5D-5L VAS
All Randomized Subjects

| EQ-5D-5L Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | | 0.7952 |
| STAGE IIB | 293 | 85.4 (13.2) | -0.40 (-1.39, 0.58) | 161 | 84.6 (11.5) | 1.08 (-0.22, 2.39) | -1.49 (-3.12, 0.15) 0.0743 | -0.17 (-0.37, 0.02) | |
| STAGE IIC | 189 | 83.5 (14.7) | -0.19 (-1.40, 1.02) | 94 | 85.1 (12.9) | 0.96 (-0.75, 2.66) | -1.15 (-3.24, 0.94) 0.2812 | -0.14 (-0.38, 0.11) | |
| T STAGE | | | | | | | | | 0.9284 |
| T3B | 187 | 85.2 (12.5) | -0.19 (-1.40, 1.02) | 104 | 86.4 (10.7) | 1.46 (-0.14, 3.07) | -1.65 (-3.66, 0.36) 0.1066 | -0.20 (-0.44, 0.04) | |
| T4A | 106 | 85.6 (14.4) | -0.79 (-2.37, 0.80) | 57 | 81.2 (12.2) | 0.38 (-1.77, 2.54) | -1.17 (-3.85, 1.51) 0.3916 | -0.14 (-0.46, 0.18) | |
| T4B | 189 | 83.5 (14.7) | -0.19 (-1.40, 1.02) | 94 | 85.1 (12.9) | 0.96 (-0.75, 2.66) | -1.15 (-3.24, 0.95) 0.2826 | -0.14 (-0.38, 0.11) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:20:34:12

Protocol: CA20976K 

Table 32.20.2
Subgroup Analyses of Mixed Model Repeated Measures Analysis of EQ-5D-5L VAS
All Randomized Subjects

| EQ-5D-5L Domain Subgroup | Nivolumab 480 mg Q4W N (1) | Nivolumab 480 mg Q4W Baseline Mean (SD) | Nivolumab 480 mg Q4W Change from baseline: LS Mean (95% CI)(2) | Placebo Q4W N (1) | Placebo Q4W Baseline Mean (SD) | Placebo Q4W Change from baseline: LS Mean (95% CI)(2) | Nivolumab 480 mg Q4W vs. Placebo Q4W Difference in mean change (95% CI); p-value (2) | Nivolumab 480 mg Q4W vs. Placebo Q4W SMD as Hedge's g (95% CI) (3) | Test for Interaction P-value (4) |
|---|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | | 0.8543 |
| US AND CANADA | 88 | 84.4 (13.4) | 0.13 (-1.62, 1.87) | 45 | 85.6 (11.5) | 1.24 (-1.17, 3.65) | -1.11 (-4.09, 1.86) 0.4623 | -0.13 (-0.49, 0.23) | |
| WESTERN EUROPE | 280 | 84.7 (14.7) | -0.57 (-1.57, 0.44) | 152 | 84.0 (12.8) | 1.22 (-0.14, 2.57) | -1.78 (-3.47, -0.10) 0.0380 | -0.21 (-0.41, -0.01) | |
| EASTERN EUROPE | 53 | 82.6 (12.1) | -0.12 (-2.33, 2.09) | 28 | 86.2 (11.0) | 0.08 (-2.96, 3.13) | -0.21 (-3.98, 3.56) 0.9141 | -0.02 (-0.48, 0.43) | |
| AUSTRALIA | 61 | 86.5 (11.6) | 0.00 (-2.10, 2.11) | 30 | 85.9 (9.1) | 0.72 (-2.23, 3.67) | -0.72 (-4.34, 2.90) 0.6974 | -0.09 (-0.52, 0.35) | |

Apr 2023 DBL. NE = Not estimated. SMD = standardized mean difference.
(1) N is the number of randomized subjects with non-missing baseline and at least one post-baseline on-treatment assessment.
(2) Estimates are based on a MMRM, with chg from baseline as the primary dependent variable, trt and trt*visit week interaction, subgroup and subgroup*trt interaction as fixed effects, baseline PRO score as covariate, and visit week as repeated measure. Models run using an UN covariance matrix, if any model failed to converge, CS and then AR(1) were used, respectively.
(3) Hedges g = (mean chg nivolumab - mean chg Placebo)/pooled-SD, all multiplied by (1-(3/(4*df-1))).
(4) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Only the on-treatment timepoints in the blinded phase with 10 subjects or more in each treatment group are included in the analysis.
Functional scale/GHS/QoL: pos. (neg.) diff. favors nivolumab (Pbo.). Symptom scale/item: pos. (neg.) diff. favors Pbo. (nivolumab).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-sy-mmrmsub-ebr1575-b5.sas 13JUL2023:20:34:12

## Anhang 4-G 3.1.2: Subgruppenanalysen für Endpunkte Verträglichkeit aus CA209-76K

Subgruppenanalysen für die Endpunkte unerwünschte Ereignisse ohne Erfassung des Progresses der Grunderkrankung – Zeit bis zum ersten Auftreten des UE: jegliche UE, schwere UE, schwerwiegende UE und zum Therapieabbruch führende UE.

### Anhang 4-G 3.1.2.1: Subgruppenanalysen für den Endpunkt jegliche UE ohne Erfassung des Progresses der Grunderkrankung – Zeit bis zum ersten Auftreten des UE

Protocol: CA20976K 

Table 21.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
Excluding Progression Terms
All Treated Subjects Censoring at Open-Label Nivolumab

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 508 ( 96.9) | 0.95 ( 0.89, 0.95) | 264 | 233 ( 88.3) | 1.77 ( 1.12, 1.91) | 1.714 ( 1.464, 2.007) <0.0001 | |
| AGE CATEGORY I | | | | | | | | 0.4528 |
| < 65 | 305 | 295 ( 96.7) | 0.95 ( 0.89, 0.95) | 155 | 136 ( 87.7) | 1.68 ( 0.95, 1.87) | 1.592 ( 1.297, 1.956) <0.0001 | |
| >= 65 | 219 | 213 ( 97.3) | 0.95 ( 0.79, 0.95) | 109 | 97 ( 89.0) | 1.87 ( 1.08, 2.79) | 1.939 ( 1.513, 2.485) <0.0001 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard (PH) model. HR is nivolumab over Placebo. (3) Unstratified Log-rank test.
(4) Unstratified Cox PH model with treatment, subgroup and treatment*subgroup interaction.
(5) A p-value of <0.05 needs to be indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-subae-ebr1575.sas 23JUN2023:07:34:02

Protocol: CA20976K 

Table 21.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
Excluding Progression Terms
All Treated Subjects Censoring at Open-Label Nivolumab

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | 0.4427 |
| >= 18 AND < 65 | 305 | 295 ( 96.7) | 0.95 ( 0.89, 0.95) | 155 | 136 ( 87.7) | 1.68 ( 0.95, 1.87) | 1.592 ( 1.297, 1.956) <0.0001 | |
| >= 65 AND < 75 | 139 | 135 ( 97.1) | 0.95 ( 0.76, 0.95) | 77 | 69 ( 89.6) | 1.97 ( 1.45, 3.68) | 2.197 ( 1.619, 2.982) <0.0001 | |
| >= 75 AND < 85 | 77 | 75 ( 97.4) | 0.95 ( 0.69, 1.15) | 30 | 26 ( 86.7) | 1.05 ( 0.66, 2.69) | 1.479 ( 0.943, 2.320) 0.0862 | |
| SEX | | | | | | | | 0.5893 |
| MALE | 320 | 316 ( 98.8) | 0.95 ( 0.82, 0.95) | 161 | 142 ( 88.2) | 1.87 ( 1.38, 2.79) | 1.819 ( 1.486, 2.226) <0.0001 | |
| FEMALE | 204 | 192 ( 94.1) | 0.95 ( 0.85, 0.95) | 103 | 91 ( 88.3) | 1.18 ( 0.95, 1.87) | 1.559 ( 1.210, 2.007) 0.0005 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard (PH) model. HR is nivolumab over Placebo. (3) Unstratified Log-rank test.
(4) Unstratified Cox PH model with treatment, subgroup and treatment*subgroup interaction.
(5) A p-value of <0.05 needs to be indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-subae-ebr1575.sas 23JUN2023:07:34:02

Protocol: CA20976K 

Table 21.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
Excluding Progression Terms
All Treated Subjects Censoring at Open-Label Nivolumab

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.5840 |
| STAGE IIB | 315 | 305 ( 96.8) | 0.92 ( 0.79, 0.95) | 162 | 147 ( 90.7) | 1.72 ( 1.12, 1.97) | 1.655 ( 1.356, 2.021) <0.0001 | |
| STAGE IIC | 209 | 203 ( 97.1) | 0.95 ( 0.89, 0.95) | 102 | 86 ( 84.3) | 1.84 ( 0.95, 2.76) | 1.814 ( 1.400, 2.350) <0.0001 | |
| T STAGE (SOURCE: ECRF) | | | | | | | | 0.5784 |
| T3B | 203 | 196 ( 96.6) | 0.95 ( 0.92, 1.02) | 104 | 91 ( 87.5) | 1.87 ( 1.45, 2.86) | 1.805 ( 1.402, 2.324) <0.0001 | |
| T4A | 112 | 109 ( 97.3) | 0.54 ( 0.26, 0.82) | 58 | 56 ( 96.6) | 0.99 ( 0.82, 1.84) | 1.430 ( 1.034, 1.978) 0.0295 | |
| T4B | 209 | 203 ( 97.1) | 0.95 ( 0.89, 0.95) | 102 | 86 ( 84.3) | 1.84 ( 0.95, 2.76) | 1.814 ( 1.400, 2.350) <0.0001 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard (PH) model. HR is nivolumab over Placebo. (3) Unstratified Log-rank test.
(4) Unstratified Cox PH model with treatment, subgroup and treatment*subgroup interaction.
(5) A p-value of <0.05 needs to be indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-subae-ebr1575.sas 23JUN2023:07:34:02

Protocol: CA20976K 

Table 21.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
Excluding Progression Terms
All Treated Subjects Censoring at Open-Label Nivolumab

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.5043 |
| US AND CANADA | 97 | 96 ( 99.0) | 0.49 ( 0.23, 0.89) | 46 | 44 ( 95.7) | 0.66 ( 0.20, 0.99) | 1.427 ( 0.993, 2.051) 0.0619 | |
| WESTERN EUROPE | 301 | 290 ( 96.3) | 0.95 ( 0.92, 0.99) | 160 | 141 ( 88.1) | 1.91 ( 1.48, 3.38) | 1.705 ( 1.389, 2.091) <0.0001 | |
| EASTERN EUROPE | 58 | 55 ( 94.8) | 1.87 ( 0.95, 2.69) | 28 | 19 ( 67.9) | 6.82 ( 1.84, 9.89) | 2.619 ( 1.532, 4.479) 0.0003 | |
| AUSTRALIA | 68 | 67 ( 98.5) | 0.49 ( 0.23, 0.85) | 30 | 29 ( 96.7) | 1.03 ( 0.43, 2.27) | 1.716 ( 1.096, 2.689) 0.0161 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard (PH) model. HR is nivolumab over Placebo. (3) Unstratified Log-rank test.
(4) Unstratified Cox PH model with treatment, subgroup and treatment*subgroup interaction.
(5) A p-value of <0.05 needs to be indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-subae-ebr1575.sas 23JUN2023:07:34:02

**Anhang 4-G 3.1.2.2: Subgruppenanalysen für den Endpunkt schwere UE ohne Erfassung des Progresses der Grunderkrankung – Zeit bis zum ersten Auftreten des UE**

Protocol: CA20976K 

Table 21.20.3
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
Excluding Progression Terms
All Treated Subjects Censoring at Open-Label Nivolumab

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 146 ( 27.9) | N.A. | 264 | 42 ( 15.9) | N.A. | 1.961 ( 1.391, 2.765) <0.0001 | |
| AGE CATEGORY I | | | | | | | | 0.7942 |
| < 65 | 305 | 76 ( 24.9) | N.A. | 155 | 21 ( 13.5) | N.A. | 2.069 ( 1.276, 3.355) 0.0026 | |
| >= 65 | 219 | 70 ( 32.0) | N.A. | 109 | 21 ( 19.3) | N.A. | 1.854 ( 1.138, 3.019) 0.0118 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard (PH) model. HR is nivolumab over Placebo. (3) Unstratified Log-rank test.
(4) Unstratified Cox PH model with treatment, subgroup and treatment*subgroup interaction.
(5) A p-value of <0.05 needs to be indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-subae-ebr1575.sas 23JUN2023:07:34:19

Protocol: CA20976K 

Table 21.20.3
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
Excluding Progression Terms
All Treated Subjects Censoring at Open-Label Nivolumab

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | 0.9257 |
| >= 18 AND < 65 | 305 | 76 ( 24.9) | N.A. | 155 | 21 ( 13.5) | N.A. | 2.069 ( 1.276, 3.355) 0.0026 | |
| >= 65 AND < 75 | 139 | 37 ( 26.6) | N.A. | 77 | 13 ( 16.9) | N.A. | 1.743 ( 0.926, 3.280) 0.0806 | |
| >= 75 AND < 85 | 77 | 32 ( 41.6) | N.A. (10.87, N.A.) | 30 | 7 ( 23.3) | N.A. (14.52, N.A.) | 2.002 ( 0.883, 4.539) 0.0899 | |
| SEX | | | | | | | | 0.5537 |
| MALE | 320 | 100 ( 31.3) | N.A. | 161 | 27 ( 16.8) | N.A. | 2.101 ( 1.373, 3.215) 0.0005 | |
| FEMALE | 204 | 46 ( 22.5) | N.A. | 103 | 15 ( 14.6) | N.A. | 1.700 ( 0.949, 3.045) 0.0712 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard (PH) model. HR is nivolumab over Placebo. (3) Unstratified Log-rank test.
(4) Unstratified Cox PH model with treatment, subgroup and treatment*subgroup interaction.
(5) A p-value of <0.05 needs to be indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-subae-ebr1575.sas 23JUN2023:07:34:19

Protocol: CA20976K 

Table 21.20.3
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
Excluding Progression Terms
All Treated Subjects Censoring at Open-Label Nivolumab

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.3134 |
| STAGE IIB | 315 | 86 ( 27.3) | N.A. | 162 | 29 ( 17.9) | N.A. | 1.729<br>( 1.135, 2.634)<br>0.0098 | |
| STAGE IIC | 209 | 60 ( 28.7) | N.A. | 102 | 13 ( 12.7) | N.A. | 2.478<br>( 1.360, 4.514)<br>0.0022 | |
| T STAGE (SOURCE: ECRF) | | | | | | | | 0.5955 |
| T3B | 203 | 49 ( 24.1) | N.A. | 104 | 17 ( 16.3) | N.A. | 1.700<br>( 0.979, 2.952)<br>0.0564 | |
| T4A | 112 | 37 ( 33.0) | N.A. | 58 | 12 ( 20.7) | N.A. | 1.767<br>( 0.921, 3.390)<br>0.0826 | |
| T4B | 209 | 60 ( 28.7) | N.A. | 102 | 13 ( 12.7) | N.A. | 2.478<br>( 1.360, 4.514)<br>0.0022 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard (PH) model. HR is nivolumab over Placebo. (3) Unstratified Log-rank test.
(4) Unstratified Cox PH model with treatment, subgroup and treatment*subgroup interaction.
(5) A p-value of <0.05 needs to be indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-subae-ebr1575.sas 23JUN2023:07:34:19

Protocol: CA20976K 

Table 21.20.3
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
Excluding Progression Terms
All Treated Subjects Censoring at Open-Label Nivolumab

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.3957 |
| US AND CANADA | 97 | 34 ( 35.1) | N.A. (14.55, N.A.) | 46 | 12 ( 26.1) | N.A. | 1.738 ( 0.898, 3.362) 0.0958 | |
| WESTERN EUROPE | 301 | 83 ( 27.6) | N.A. | 160 | 21 ( 13.1) | N.A. | 2.285 ( 1.415, 3.688) 0.0005 | |
| EASTERN EUROPE | 58 | 6 ( 10.3) | N.A. | 28 | 4 ( 14.3) | N.A. | 0.758 ( 0.214, 2.686) 0.6667 | |
| AUSTRALIA | 68 | 23 ( 33.8) | N.A. | 30 | 5 ( 16.7) | N.A. | 2.375 ( 0.902, 6.252) 0.0709 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard (PH) model. HR is nivolumab over Placebo. (3) Unstratified Log-rank test.
(4) Unstratified Cox PH model with treatment, subgroup and treatment*subgroup interaction.
(5) A p-value of <0.05 needs to be indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-subae-ebr1575.sas 23JUN2023:07:34:19

**Anhang 4-G 3.1.2.3: Subgruppenanalysen für den Endpunkt schwerwiegende UE ohne Erfassung des Progresses der Grunderkrankung – Zeit bis zum ersten Auftreten des UE**

Protocol: CA20976K 

Table 21.20.5
Serious Adverse Events: Subgroup Time-Adjusted Analyses
Excluding Progression Terms
All Treated Subjects Censoring at Open-Label Nivolumab

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 98 ( 18.7) | N.A. | 264 | 32 ( 12.1) | N.A. | 1.690<br>( 1.134, 2.518)<br>0.0091 | |
| AGE CATEGORY I | | | | | | | | 0.9998 |
| < 65 | 305 | 49 ( 16.1) | N.A. | 155 | 16 ( 10.3) | N.A. | 1.712<br>( 0.974, 3.011)<br>0.0588 | |
| >= 65 | 219 | 49 ( 22.4) | N.A. | 109 | 16 ( 14.7) | N.A. | 1.665<br>( 0.947, 2.929)<br>0.0733 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard (PH) model. HR is nivolumab over Placebo. (3) Unstratified Log-rank test.
(4) Unstratified Cox PH model with treatment, subgroup and treatment*subgroup interaction.
(5) A p-value of <0.05 needs to be indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-subae-ebr1575.sas 23JUN2023:07:34:34

Protocol: CA20976K 

Table 21.20.5
Serious Adverse Events: Subgroup Time-Adjusted Analyses
Excluding Progression Terms
All Treated Subjects Censoring at Open-Label Nivolumab

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | 0.9803 |
| >= 18 AND < 65 | 305 | 49 ( 16.1) | N.A. | 155 | 16 ( 10.3) | N.A. | 1.712 ( 0.974, 3.011) 0.0588 | |
| >= 65 AND < 75 | 139 | 23 ( 16.5) | N.A. | 77 | 8 ( 10.4) | N.A. | 1.724 ( 0.771, 3.855) 0.1792 | |
| >= 75 AND < 85 | 77 | 25 ( 32.5) | N.A. (14.95, N.A.) | 30 | 7 ( 23.3) | N.A. (14.52, N.A.) | 1.526 ( 0.660, 3.530) 0.3198 | |
| SEX | | | | | | | | 0.8622 |
| MALE | 320 | 63 ( 19.7) | N.A. | 161 | 20 ( 12.4) | N.A. | 1.727 ( 1.044, 2.857) 0.0311 | |
| FEMALE | 204 | 35 ( 17.2) | N.A. | 103 | 12 ( 11.7) | N.A. | 1.609 ( 0.835, 3.099) 0.1512 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard (PH) model. HR is nivolumab over Placebo. (3) Unstratified Log-rank test.
(4) Unstratified Cox PH model with treatment, subgroup and treatment*subgroup interaction.
(5) A p-value of <0.05 needs to be indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-subae-ebr1575.sas 23JUN2023:07:34:34

Protocol: CA20976K 

Table 21.20.5
Serious Adverse Events: Subgroup Time-Adjusted Analyses
Excluding Progression Terms
All Treated Subjects Censoring at Open-Label Nivolumab

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.2200 |
| STAGE IIB | 315 | 60 ( 19.0) | N.A. | 162 | 24 ( 14.8) | N.A. | 1.433 ( 0.893, 2.301) 0.1340 | |
| STAGE IIC | 209 | 38 ( 18.2) | N.A. | 102 | 8 ( 7.8) | N.A. | 2.461 ( 1.148, 5.276) 0.0167 | |
| T STAGE (SOURCE: ECRF) | | | | | | | | 0.4618 |
| T3B | 203 | 36 ( 17.7) | N.A. | 104 | 15 ( 14.4) | N.A. | 1.388 ( 0.760, 2.536) 0.2839 | |
| T4A | 112 | 24 ( 21.4) | N.A. | 58 | 9 ( 15.5) | N.A. | 1.501 ( 0.697, 3.231) 0.2955 | |
| T4B | 209 | 38 ( 18.2) | N.A. | 102 | 8 ( 7.8) | N.A. | 2.461 ( 1.148, 5.276) 0.0167 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard (PH) model. HR is nivolumab over Placebo. (3) Unstratified Log-rank test.
(4) Unstratified Cox PH model with treatment, subgroup and treatment*subgroup interaction.
(5) A p-value of <0.05 needs to be indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-subae-ebr1575.sas 23JUN2023:07:34:34

Protocol: CA20976K 

Table 21.20.5
Serious Adverse Events: Subgroup Time-Adjusted Analyses
Excluding Progression Terms
All Treated Subjects Censoring at Open-Label Nivolumab

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.7205 |
| US AND CANADA | 97 | 14 ( 14.4) | N.A. | 46 | 7 ( 15.2) | N.A. | 1.126 ( 0.453, 2.795) 0.7983 | |
| WESTERN EUROPE | 301 | 60 ( 19.9) | N.A. | 160 | 17 ( 10.6) | N.A. | 2.010 ( 1.173, 3.444) 0.0095 | |
| EASTERN EUROPE | 58 | 9 ( 15.5) | N.A. | 28 | 3 ( 10.7) | N.A. | 1.599 ( 0.433, 5.907) 0.4771 | |
| AUSTRALIA | 68 | 15 ( 22.1) | N.A. | 30 | 5 ( 16.7) | N.A. | 1.468 ( 0.533, 4.041) 0.4543 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard (PH) model. HR is nivolumab over Placebo. (3) Unstratified Log-rank test.
(4) Unstratified Cox PH model with treatment, subgroup and treatment*subgroup interaction.
(5) A p-value of <0.05 needs to be indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-subae-ebr1575.sas 23JUN2023:07:34:34

**Anhang 4-G 3.1.2.4: Subgruppenanalysen für den Endpunkt zum Therapieabbruch führende UE ohne Erfassung des Progresses der Grunderkrankung – Zeit bis zum ersten Auftreten des UE**

Protocol: CA20976K 

Table 21.20.7
Adverse Events Leading to Discontinuation of Study Treatment: Subgroup Time-Adjusted Analyses
Excluding Progression Terms
All Treated Subjects Censoring at Open-Label Nivolumab

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 116 ( 22.1) | N.A. | 264 | 9 ( 3.4) | N.A. | 7.216 ( 3.662, 14.219) <0.0001 | |
| AGE CATEGORY I | | | | | | | | 0.2701 |
| < 65 | 305 | 56 ( 18.4) | N.A. | 155 | 6 ( 3.9) | N.A. | 5.194 ( 2.238, 12.055) <0.0001 | |
| >= 65 | 219 | 60 ( 27.4) | N.A. | 109 | 3 ( 2.8) | N.A. | 11.258 ( 3.532, 35.882) <0.0001 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard (PH) model. HR is nivolumab over Placebo. (3) Unstratified Log-rank test.
(4) Unstratified Cox PH model with treatment, subgroup and treatment*subgroup interaction.
(5) A p-value of <0.05 needs to be indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-subae-ebr1575.sas 23JUN2023:07:34:47

Protocol: CA20976K 

Table 21.20.7
Adverse Events Leading to Discontinuation of Study Treatment: Subgroup Time-Adjusted Analyses
Excluding Progression Terms
All Treated Subjects Censoring at Open-Label Nivolumab

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | 0.5529 |
| >= 18 AND < 65 | 305 | 56 ( 18.4) | N.A. | 155 | 6 ( 3.9) | N.A. | 5.194 ( 2.238, 12.055) <0.0001 | |
| >= 65 AND < 75 | 139 | 38 ( 27.3) | N.A. | 77 | 2 ( 2.6) | N.A. | 11.886 ( 2.869, 49.246) <0.0001 | |
| >= 75 AND < 85 | 77 | 22 ( 28.6) | N.A. | 30 | 1 ( 3.3) | N.A. | 9.495 ( 1.281, 70.401) 0.0070 | |
| SEX | | | | | | | | 0.0696 |
| MALE | 320 | 76 ( 23.8) | N.A. | 161 | 3 ( 1.9) | N.A. | 14.169 ( 4.470, 44.919) <0.0001 | |
| FEMALE | 204 | 40 ( 19.6) | N.A. | 103 | 6 ( 5.8) | N.A. | 3.713 ( 1.574, 8.758) 0.0013 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard (PH) model. HR is nivolumab over Placebo. (3) Unstratified Log-rank test.
(4) Unstratified Cox PH model with treatment, subgroup and treatment*subgroup interaction.
(5) A p-value of <0.05 needs to be indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-subae-ebr1575.sas 23JUN2023:07:34:47

Protocol: CA20976K 

Table 21.20.7
Adverse Events Leading to Discontinuation of Study Treatment: Subgroup Time-Adjusted Analyses
Excluding Progression Terms
All Treated Subjects Censoring at Open-Label Nivolumab

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.8907 |
| STAGE IIB | 315 | 64 ( 20.3) | N.A. | 162 | 5 ( 3.1) | N.A. | 7.491 ( 3.015, 18.615) <0.0001 | |
| STAGE IIC | 209 | 52 ( 24.9) | N.A. | 102 | 4 ( 3.9) | N.A. | 6.766 ( 2.447, 18.706) <0.0001 | |
| T STAGE (SOURCE: ECRF) | | | | | | | | 0.7338 |
| T3B | 203 | 37 ( 18.2) | N.A. | 104 | 2 ( 1.9) | N.A. | 10.904 ( 2.629, 45.228) <0.0001 | |
| T4A | 112 | 27 ( 24.1) | N.A. | 58 | 3 ( 5.2) | N.A. | 5.152 ( 1.562, 16.988) 0.0027 | |
| T4B | 209 | 52 ( 24.9) | N.A. | 102 | 4 ( 3.9) | N.A. | 6.766 ( 2.447, 18.706) <0.0001 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard (PH) model. HR is nivolumab over Placebo. (3) Unstratified Log-rank test.
(4) Unstratified Cox PH model with treatment, subgroup and treatment*subgroup interaction.
(5) A p-value of <0.05 needs to be indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-subae-ebr1575.sas 23JUN2023:07:34:47

Protocol: CA20976K 

Table 21.20.7
Adverse Events Leading to Discontinuation of Study Treatment: Subgroup Time-Adjusted Analyses
Excluding Progression Terms
All Treated Subjects Censoring at Open-Label Nivolumab

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.9080 |
| US AND CANADA | 97 | 19 ( 19.6) | N.A. | 46 | 2 ( 4.3) | N.A. | 5.410<br>( 1.259, 23.242)<br>0.0108 | |
| WESTERN EUROPE | 301 | 66 ( 21.9) | N.A. | 160 | 6 ( 3.8) | N.A. | 6.275<br>( 2.721, 14.475)<br><0.0001 | |
| EASTERN EUROPE | 58 | 7 ( 12.1) | N.A. | 28 | 0 | N.E. | N.E.<br>0.0578 | |
| AUSTRALIA | 68 | 24 ( 35.3) | N.A.<br>(10.48, N.A.) | 30 | 1 ( 3.3) | N.A. | 12.823<br>( 1.734, 94.832)<br>0.0012 | |

Apr 2023 DBL, HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
(1) KME of median time to event. Two-sided 95% CI is computed by Brookmeyer and Crowley method (log log transformation).
(2) Unstratified Cox proportional hazard (PH) model. HR is nivolumab over Placebo. (3) Unstratified Log-rank test.
(4) Unstratified Cox PH model with treatment, subgroup and treatment*subgroup interaction.
(5) A p-value of <0.05 needs to be indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-subae-ebr1575.sas 23JUN2023:07:34:47

## Anhang 4-G 3.2: Subgruppenanalysen zu Endpunkten dieses Anhangs aus CA209-76K

Matrix der durchgeführten Subgruppenanalysen

| **Endpunkte**<br>Studie<br>CA209-76K | **Altersgruppe I** | **Altersgruppe II** | **Geschlecht** | **Ethnie[(1)]** | **Stadium der Erkrankung nach AJCC** | **AJCC-Tumorstadium gemäß eCRF** | **Region** |
|---|---|---|---|---|---|---|---|
| **Endpunkte Verträglichkeit – UE von speziellem Interesse (UESI)** | | | | | | | |
| jegliche spezifische immunvermittelte UE | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| jegliche spezifische UE | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| jegliche weitere UE von speziellem Interesse | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| **Endpunkte Verträglichkeit – häufige UE auf SOC/PT-Ebene[(2)]** | | | | | | | |
| UE: Gesamtzahl Patienten mit Ereignis | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Erkrankungen der Haut und des Unterhautgewebes (SOC) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Pruritus (PT) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Ausschlag mit Juckreiz (PT) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Erkrankungen des Gastrointestinaltrakts (SOC) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Diarrhoe (PT) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Allgemeine Erkrankungen und Beschwerden am Verabreichungsort (SOC) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Grippeähnliche Erkrankung (PT) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Skelettmuskulatur-, Bindegewebs- und Knochenerkrankungen (SOC) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |

| **Endpunkte**<br>Studie<br>CA209-76K | **Altersgruppe I** | **Altersgruppe II** | **Geschlecht** | **Ethnie[1]** | **Stadium der Erkrankung nach AJCC** | **AJCC-Tumorstadium gemäß eCRF** | **Region** |
|---|---|---|---|---|---|---|---|
| UE Arthralgie (PT) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Arthritis (PT) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Aspartataminotransferase erhöht (PT) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Alkalische Phosphatase im Blut erhöht (PT) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Infektionen und parasitäre Erkrankungen (SOC) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Harnwegsinfektion (PT) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Stoffwechsel- und Ernährungsstörungen (SOC) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Appetitvermindert (PT) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Synkope (PT) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Erkrankungen der Atemwege, des Brustraums und Mediastinums (SOC) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Endokrine Erkrankungen (SOC) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Hypothyreose (PT) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Hyperthyroidismus (PT) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Reaktion im Zusammenhang mit einer Infusion (PT) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Eosinophilie (PT) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| UE Augenerkrankungen (SOC) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |

Ergänzende Analysen

| **Endpunkte**<br>Studie<br>CA209-76K | **Altersgruppe I** | **Altersgruppe II** | **Geschlecht** | **Ethnie[1]** | **Stadium der Erkrankung nach AJCC** | **AJCC-Tumorstadium gemäß eCRF** | **Region** |
|---|---|---|---|---|---|---|---|
| UE Trockenes Auge (PT) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| Schwere UE: Gesamtzahl Patienten mit Ereignis | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| Schwere UE Untersuchungen (SOC) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| Schwere UE Alaninaminotransferase erhöht (PT) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| Schwere UE Infektionen und parasitäre Erkrankungen (SOC) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| Schwere UE Stoffwechsel- und Ernährungsstörungen (SOC) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| Schwere UE Gefäßerkrankungen (SOC) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| SUE Infektionen und parasitäre Erkrankungen (SOC) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |
| SUE Gutartige, bösartige und nicht spezifizierte Neubildungen (einschl. Zysten und Polypen) (SOC) | ○ | ○ | ○ | n.d. | ○ | ○ | ○ |

AJCC = American Joint Committee on Cancer; eCRF = elektronisches Datenerhebungsformular (electronic Case Report Form); n.d. = Nicht durchgeführt; PT = Preferred Term; SOC = Systemorganklasse (System Organ Class); SUE = Schwerwiegende(s) unerwünschte(s) Ereignis(se); UE = Unerwünschte(s) Ereignis(se); UESI = Unerwünschte(s) Ereignis(se) von speziellem Interesse

● = Gemäß Studienprotokoll und SAP geplante Subgruppenanalyse; ○ = Für das vorliegende Dossier durchgeführte Subgruppenanalyse;

(1) Für das Subgruppenmerkmal Ethnie wird keine Subgruppenanalyse durchgeführt, da nur eine der Subgruppen ≥ 10 Patienten enthält.

(2) Subgruppenanalysen werden nur für diejenigen UE auf SOC/PT-Ebene dargestellt, für welche die Gesamtanalyse gemäß p-Wert statistisch signifikant war.

Ergebnis des Interaktionsterms der Subgruppenanalysen je Endpunkt für Studie CA209-76K und alle Effektmodifikatoren

| **Endpunkte**[1]<br>Studie<br>CA209-76K | **Altersgruppe I** | **Altersgruppe II** | **Geschlecht** | **Stadium der Erkrankung nach AJCC** | **AJCC-Tumorstadium gemäß eCRF** | **Region** |
|---|---|---|---|---|---|---|
| **Endpunkte Verträglichkeit – UE von speziellem Interesse (UESI)**[2] | | | | | | |
| jegliche spezifische immunvermittelte UE | 0,3465 | 0,4513 | 0,3832 | 0,5977 | 0,7198 | 0,7550 |
| jegliche spezifische UE | **0,0404*** | 0,1081 | 0,3102 | 0,5634 | 0,3549 | 0,9236 |
| jegliche weitere UE von speziellem Interesse | 0,9902 | >0,9999 | 0,9879 | 0,7505 | N.M.E. | 0,5917 |
| **Endpunkte Verträglichkeit – häufige UE auf SOC/PT-Ebene**[2] | | | | | | |
| UE: Gesamtzahl Patienten mit Ereignis | 0,4323 | 0,4349 | 0,5252 | 0,5580 | 0,5947 | 0,5918 |
| UE Erkrankungen der Haut und des Unterhautgewebes (SOC) | 0,1321 | **0,0317*** | 0,1895 | 0,5349 | 0,8109 | 0,7061 |
| UE Pruritus (PT) | 0,3019 | 0,4479 | 0,3001 | 0,2258 | 0,2382 | 0,7846 |
| UE Ausschlag mit Juckreiz (PT) | N.M.E. | N.M.E. | 0,9902 | N.M.E. | N.M.E. | N.M.E. |
| UE Erkrankungen des Gastrointestinaltrakts (SOC) | 0,2746 | 0,3096 | 0,9150 | 0,9287 | 0,7618 | 0,6473 |
| UE Diarrhoe (PT) | 0,2239 | 0,4715 | 0,4633 | 0,2926 | 0,3936 | 0,9255 |
| UE Allgemeine Erkrankungen und Beschwerden am Verabreichungsort (SOC) | 0,2904 | 0,4186 | 0,7000 | 0,9356 | 0,5851 | 0,0557 |
| UE Grippeähnliche Erkrankung (PT) | 0,1986 | 0,2958 | 0,6557 | 0,4621 | 0,7200 | 0,9889 |
| UE Skelettmuskulatur-, Bindegewebs- und Knochenerkrankungen (SOC) | 0,6603 | 0,7050 | 0,4504 | 0,5396 | 0,4387 | 0,2977 |
| UE Arthralgie (PT) | 0,7141 | 0,8871 | 0,3744 | 0,2533 | 0,1433 | 0,2354 |

Ergänzende Analysen

| **Endpunkte**[(1)]<br>Studie<br>CA209-76K | **Altersgruppe I** | **Altersgruppe II** | **Geschlecht** | **Stadium der Erkrankung nach AJCC** | **AJCC-Tumorstadium gemäß eCRF** | **Region** |
|---|---|---|---|---|---|---|
| UE Arthritis (PT) | N.M.E. | N.M.E. | N.M.E. | N.M.E. | N.M.E. | N.M.E. |
| UE Aspartataminotransferase erhöht (PT) | 0,4997 | 0,9367 | 0,4999 | 0,4877 | 0,2119 | 0,8199 |
| UE Alkalische Phosphatase im Blut erhöht (PT) | 0,6748 | 0,9390 | 0,9908 | 0,9906 | N.M.E. | N.M.E. |
| UE Infektionen und parasitäre Erkrankungen (SOC) | 0,6629 | 0,9038 | 0,1624 | **0,0030*** | **0,0120*** | 0,1427 |
| UE Harnwegsinfektion (PT) | 0,9898 | N.M.E. | 0,9872 | N.M.E. | N.M.E. | 0,9743 |
| UE Stoffwechsel- und Ernährungsstörungen (SOC) | 0,9122 | 0,8537 | 0,1572 | 0,1301 | 0,1824 | 0,9604 |
| UE Appetit vermindert (PT) | 0,2939 | 0,4538 | 0,6332 | 0,5122 | 0,5928 | 0,9958 |
| UE Synkope (PT) | N.M.E. | N.M.E. | N.M.E. | N.M.E. | N.M.E. | N.M.E. |
| UE Erkrankungen der Atemwege, des Brustraums und Mediastinums (SOC) | 0,0554 | 0,0560 | 0,1722 | 0,8802 | 0,8003 | 0,0861 |
| UE Endokrine Erkrankungen (SOC) | 0,4191 | 0,6783 | 0,6593 | 0,6777 | 0,3208 | 0,7779 |
| UE Hypothyreose (PT) | 0,9999 | >0,9999 | 0,9997 | 0,9998 | >0,9999 | >0,9999 |
| UE Hyperthyroidismus (PT) | 0,7014 | 0,7887 | 0,9855 | 0,7202 | 0,7197 | 0,3578 |
| UE Reaktion im Zusammenhang mit einer Infusion (PT) | 0,7516 | 0,9316 | 0,9886 | 0,8030 | 0,9899 | >0,9999 |
| UE Eosinophilie (PT) | 0,7171 | 0,8769 | 0,4959 | 0,8929 | 0,9803 | >0,9999 |
| UE Augenerkrankungen (SOC) | 0,5266 | 0,0899 | 0,6849 | 0,0811 | 0,1935 | 0,0717 |
| UE Trockenes Auge (PT) | 0,5927 | 0,9138 | 0,3671 | 0,4519 | N.M.E. | 0,4503 |

Ergänzende Analysen

| **Endpunkte**[1]<br>Studie<br>CA209-76K | **Altersgruppe I** | **Altersgruppe II** | **Geschlecht** | **Stadium der Erkrankung nach AJCC** | **AJCC-Tumorstadium gemäß eCRF** | **Region** |
|---|---|---|---|---|---|---|
| Schwere UE: Gesamtzahl Patienten mit Ereignis | 0,4278 | 0,6976 | 0,5069 | 0,2980 | 0,5616 | 0,2081 |
| Schwere UE Untersuchungen (SOC) | 0,8967 | 0,9129 | 0,5266 | 0,2043 | 0,3768 | 0,9997 |
| Schwere UE Alaninaminotransferase erhöht (PT) | N.M.E. | N.M.E. | N.M.E. | N.M.E. | N.M.E. | N.M.E. |
| Schwere UE Infektionen und parasitäre Erkrankungen (SOC) | 0,7764 | N.M.E. | 0,1364 | 0,9896 | N.M.E. | N.M.E. |
| Schwere UE Stoffwechsel- und Ernährungsstörungen (SOC) | 0,7314 | N.M.E. | 0,8763 | 0,9909 | N.M.E. | 0,8213 |
| Schwere UE Gefäßerkrankungen (SOC) | 0,9915 | N.M.E. | 0,9926 | 0,9925 | 0,9999 | N.M.E. |
| SUE Infektionen und parasitäre Erkrankungen (SOC) | 0,9882 | N.M.E. | 0,6814 | 0,9895 | 0,9999 | 0,9699 |
| SUE Gutartige, bösartige und nicht spezifizierte Neubildungen (einschl. Zysten und Polypen) (SOC) | 0,3750 | 0,6439 | 0,5092 | 0,0563 | 0,3294 | N.M.E. |

AJCC = American Joint Committee on Cancer; eCRF = elektronisches Datenerhebungsformular (electronic Case Report Form); N.M.E. = Nicht sinnvoll schätzbar; SOC = Systemorganklasse (System Organ Class); SUE = Schwerwiegende(s) unerwünschte(s) Ereignis(se); UE = Unerwünschte(s) Ereignis(se); UESI = Unerwünschte(s) Ereignis(se) von speziellem Interesse

(1) Angegebene Werte sind Interaktions-p-Werte. p-Werte < 0,05 werden mit einem Stern und **fett** markiert.

(2) Zeit bis zum ersten Auftreten des UE.

**Anhang 4-G 3.2.1: Subgruppenanalysen für Endpunkte spezifische immunvermittelte UE aus CA209-76K – Zeit bis zum ersten Auftreten des UE**

Protocol: CA20976K 

Table 24.30.1
Immune-mediated Adverse Events: Subgroup Time-Adjusted Analyses
On Hazard Ratio for Any imAEs

Immune-Mediated Adverse Events Category: Any ImAEs

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 186 ( 35.5) | N.A. | 264 | 17 ( 6.4) | N.A. | 6.925 ( 4.213, 11.383) <0.0001 | |
| AGE CATEGORY I | | | | | | | | 0.3465 |
| < 65 | 305 | 101 ( 33.1) | N.A. | 155 | 11 ( 7.1) | N.A. | 5.738 ( 3.078, 10.695) <0.0001 | |
| >= 65 | 219 | 85 ( 38.8) | N.A. | 109 | 6 ( 5.5) | N.A. | 9.117 ( 3.981, 20.879) <0.0001 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubslae-ebr1575b3.sas 19JUL2023:13:23:15

Protocol: CA20976K 

Table 24.30.1
Immune-mediated Adverse Events: Subgroup Time-Adjusted Analyses
On Hazard Ratio for Any imAEs

Immune-Mediated Adverse Events Category: Any ImAEs

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | 0.4513 |
| >= 18 AND < 65 | 305 | 101 ( 33.1) | N.A. | 155 | 11 ( 7.1) | N.A. | 5.738<br>( 3.078, 10.695)<br><0.0001 | |
| >= 65 AND < 75 | 139 | 53 ( 38.1) | N.A. | 77 | 3 ( 3.9) | N.A. | 12.435<br>( 3.884, 39.805)<br><0.0001 | |
| >= 75 AND < 85 | 77 | 31 ( 40.3) | N.A.<br>( 6.41, N.A.) | 30 | 3 ( 10.0) | N.A. | 5.339<br>( 1.629, 17.500)<br>0.0020 | |
| SEX | | | | | | | | 0.3832 |
| MALE | 320 | 111 ( 34.7) | N.A. | 161 | 8 ( 5.0) | N.A. | 8.657<br>( 4.223, 17.747)<br><0.0001 | |
| FEMALE | 204 | 75 ( 36.8) | N.A. | 103 | 9 ( 8.7) | N.A. | 5.390<br>( 2.698, 10.770)<br><0.0001 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubslae-ebr1575b3.sas 19JUL2023:13:23:15

Protocol: CA20976K 

Table 24.30.1
Immune-mediated Adverse Events: Subgroup Time-Adjusted Analyses
On Hazard Ratio for Any imAEs

Immune-Mediated Adverse Events Category: Any ImAEs

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.5977 |
| STAGE IIB | 315 | 105 ( 33.3) | N.A. | 162 | 11 ( 6.8) | N.A. | 6.194 ( 3.326, 11.533) <0.0001 | |
| STAGE IIC | 209 | 81 ( 38.8) | N.A. | 102 | 6 ( 5.9) | N.A. | 8.175 ( 3.566, 18.741) <0.0001 | |
| T STAGE | | | | | | | | 0.7198 |
| T3B | 203 | 65 ( 32.0) | N.A. | 104 | 8 ( 7.7) | N.A. | 5.367 ( 2.573, 11.195) <0.0001 | |
| T4A | 112 | 40 ( 35.7) | N.A. | 58 | 3 ( 5.2) | N.A. | 8.295 ( 2.565, 26.827) <0.0001 | |
| T4B | 209 | 81 ( 38.8) | N.A. | 102 | 6 ( 5.9) | N.A. | 8.175 ( 3.566, 18.741) <0.0001 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubslae-ebr1575b3.sas 19JUL2023:13:23:15

Protocol: CA20976K 

Table 24.30.1
Immune-mediated Adverse Events: Subgroup Time-Adjusted Analyses
On Hazard Ratio for Any imAEs

Immune-Mediated Adverse Events Category: Any ImAEs

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.7550 |
| US AND CANADA | 97 | 59 ( 60.8) | 7.13 ( 4.60, 9.92) | 46 | 4 ( 8.7) | N.A. | 11.264 ( 4.080, 31.096) <0.0001 | |
| WESTERN EUROPE | 301 | 84 ( 27.9) | N.A. | 160 | 8 ( 5.0) | N.A. | 6.487 ( 3.140, 13.401) <0.0001 | |
| EASTERN EUROPE | 58 | 15 ( 25.9) | N.A. | 28 | 2 ( 7.1) | N.A. | 4.512 ( 1.031, 19.749) 0.0283 | |
| AUSTRALIA | 68 | 28 ( 41.2) | N.A. ( 7.06, N.A.) | 30 | 3 ( 10.0) | N.A. | 5.537 ( 1.680, 18.247) 0.0016 | |

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or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubslae-ebr1575b3.sas 19JUL2023:13:23:15

**Anhang 4-G 3.2.2: Subgruppenanalysen für Endpunkte spezifische UE (select UE) aus CA209-76K – Zeit bis zum ersten Auftreten des UE**

Protocol: CA20976K 

Table 26.20.1
Select Adverse Events: Subgroup Time-Adjusted Analyses
On Hazard Ratio for Any Select AEs

Select Adverse Events Category: Any Select AEs

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 399 ( 76.1) | 2.86 ( 2.46, 3.65) | 264 | 131 ( 49.6) | 11.60 ( 8.94, N.A.) | 2.250 ( 1.845, 2.745) <0.0001 | |
| AGE CATEGORY I | | | | | | | | 0.0404* |
| < 65 | 305 | 228 ( 74.8) | 3.35 ( 2.14, 3.94) | 155 | 83 ( 53.5) | 10.18 ( 6.47, N.A.) | 1.884 ( 1.464, 2.424) <0.0001 | |
| >= 65 | 219 | 171 ( 78.1) | 2.79 ( 1.94, 3.55) | 109 | 48 ( 44.0) | N.A. ( 9.99, N.A.) | 2.958 ( 2.140, 4.087) <0.0001 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubslae-ebr1575b3.sas 04JUL2023:20:24:28

Protocol: CA20976K 

Table 26.20.1
Select Adverse Events: Subgroup Time-Adjusted Analyses
On Hazard Ratio for Any Select AEs

Select Adverse Events Category: Any Select AEs

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | 0.1081 |
| >= 18 AND < 65 | 305 | 228 ( 74.8) | 3.35 ( 2.14, 3.94) | 155 | 83 ( 53.5) | 10.18 ( 6.47, N.A.) | 1.884 ( 1.464, 2.424) <0.0001 | |
| >= 65 AND < 75 | 139 | 112 ( 80.6) | 2.79 ( 1.87, 3.61) | 77 | 35 ( 45.5) | N.A. ( 8.94, N.A.) | 3.164 ( 2.154, 4.646) <0.0001 | |
| >= 75 AND < 85 | 77 | 57 ( 74.0) | 2.79 ( 1.45, 4.96) | 30 | 12 ( 40.0) | N.A. ( 6.01, N.A.) | 2.677 ( 1.431, 5.010) 0.0014 | |
| SEX | | | | | | | | 0.3102 |
| MALE | 320 | 254 ( 79.4) | 2.79 ( 1.94, 3.55) | 161 | 78 ( 48.4) | 12.22 ( 8.51, N.A.) | 2.453 ( 1.900, 3.168) <0.0001 | |
| FEMALE | 204 | 145 ( 71.1) | 3.61 ( 2.33, 4.60) | 103 | 53 ( 51.5) | 11.17 ( 7.16, N.A.) | 1.962 ( 1.431, 2.692) <0.0001 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubslae-ebr1575b3.sas 04JUL2023:20:24:28

Protocol: CA20976K 

Table 26.20.1
Select Adverse Events: Subgroup Time-Adjusted Analyses
On Hazard Ratio for Any Select AEs

Select Adverse Events Category: Any Select AEs

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.5634 |
| STAGE IIB | 315 | 243 ( 77.1) | 3.09 ( 2.33, 3.71) | 162 | 84 ( 51.9) | 10.32 ( 7.43, N.A.) | 2.162 ( 1.685, 2.775) <0.0001 | |
| STAGE IIC | 209 | 156 ( 74.6) | 2.79 ( 1.87, 3.71) | 102 | 47 ( 46.1) | N.A. ( 7.82, N.A.) | 2.396 ( 1.725, 3.327) <0.0001 | |
| T STAGE | | | | | | | | 0.3549 |
| T3B | 203 | 159 ( 78.3) | 2.92 ( 1.97, 3.71) | 104 | 50 ( 48.1) | N.A. ( 7.43, N.A.) | 2.455 ( 1.782, 3.383) <0.0001 | |
| T4A | 112 | 84 ( 75.0) | 3.32 ( 2.07, 5.16) | 58 | 34 ( 58.6) | 9.00 ( 5.32, N.A.) | 1.725 ( 1.157, 2.572) 0.0069 | |
| T4B | 209 | 156 ( 74.6) | 2.79 ( 1.87, 3.71) | 102 | 47 ( 46.1) | N.A. ( 7.82, N.A.) | 2.396 ( 1.725, 3.327) <0.0001 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubslae-ebr1575b3.sas 04JUL2023:20:24:28

Protocol: CA20976K 

Table 26.20.1
Select Adverse Events: Subgroup Time-Adjusted Analyses
On Hazard Ratio for Any Select AEs

Select Adverse Events Category: Any Select AEs

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.9236 |
| US AND CANADA | 97 | 86 ( 88.7) | 1.77 ( 0.95, 2.07) | 46 | 33 ( 71.7) | 4.07 ( 1.94, 9.99) | 2.086 ( 1.384, 3.142) 0.0003 | |
| WESTERN EUROPE | 301 | 217 ( 72.1) | 3.75 ( 2.86, 5.06) | 160 | 67 ( 41.9) | N.A. (10.25, N.A.) | 2.412 ( 1.832, 3.176) <0.0001 | |
| EASTERN EUROPE | 58 | 35 ( 60.3) | 4.63 ( 2.83, 9.69) | 28 | 10 ( 35.7) | N.A. (10.15, N.A.) | 2.587 ( 1.276, 5.246) 0.0064 | |
| AUSTRALIA | 68 | 61 ( 89.7) | 1.43 ( 0.89, 1.91) | 30 | 21 ( 70.0) | 3.70 ( 2.76, 8.25) | 2.076 ( 1.256, 3.431) 0.0036 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubslae-ebr1575b3.sas 04JUL2023:20:24:28

**Anhang 4-G 3.2.3: Subgruppenanalysen für Endpunkte weitere UE von speziellem Interesse (OESI) aus CA209-76K – Zeit bis zum ersten Auftreten des UE**

Protocol: CA20976K 

Table 25.30.1
Other Events of Special Interest: Subgroup Time-Adjusted Analyses
On Hazard Ratio for Any OESIs

Other Events of Special Interest Category: Any OESIs

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 17 ( 3.2) | N.A. | 264 | 2 ( 0.8) | N.A. | 4.579 ( 1.058, 19.823) 0.0253 | |
| AGE CATEGORY I | | | | | | | | 0.9902 |
| < 65 | 305 | 8 ( 2.6) | N.A. | 155 | 2 ( 1.3) | N.A. | 2.173 ( 0.461, 10.236) 0.3143 | |
| >= 65 | 219 | 9 ( 4.1) | N.A. | 109 | 0 | N.E. | N.E. 0.0297 | |
| AGE CATEGORY II | | | | | | | | >0.9999 |
| >= 18 AND < 65 | 305 | 8 ( 2.6) | N.A. | 155 | 2 ( 1.3) | N.A. | 2.173 ( 0.461, 10.236) 0.3143 | |
| >= 65 AND < 75 | 139 | 5 ( 3.6) | N.A. | 77 | 0 | N.E. | N.E. 0.0858 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubslae-ebr1575b3.sas 12JUL2023:14:17:21

Protocol: CA20976K 

Table 25.30.1
Other Events of Special Interest: Subgroup Time-Adjusted Analyses
On Hazard Ratio for Any OESIs

Other Events of Special Interest Category: Any OESIs

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| >= 75 AND < 85 | 77 | 4 ( 5.2) | N.A. | 30 | 0 | N.E. | N.E. | 0.2068 |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubslae-ebr1575b3.sas 12JUL2023:14:17:21

Protocol: CA20976K 

Table 25.30.1
Other Events of Special Interest: Subgroup Time-Adjusted Analyses
On Hazard Ratio for Any OESIs

Other Events of Special Interest Category: Any OESIs

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| SEX | | | | | | | | 0.9879 |
| MALE | 320 | 10 ( 3.1) | N.A. | 161 | 0 | N.E. | N.E. | |
| | | | | | | | 0.0220 | |
| FEMALE | 204 | 7 ( 3.4) | N.A. | 103 | 2 ( 1.9) | N.A. | 1.956 | |
| | | | | | | | ( 0.406, 9.419) | |
| | | | | | | | 0.3942 | |
| DISEASE STAGE CATEGORY | | | | | | | | 0.7505 |
| STAGE IIB | 315 | 10 ( 3.2) | N.A. | 162 | 1 ( 0.6) | N.A. | 5.713 | |
| | | | | | | | ( 0.731, 44.647) | |
| | | | | | | | 0.0602 | |
| STAGE IIC | 209 | 7 ( 3.3) | N.A. | 102 | 1 ( 1.0) | N.A. | 3.496 | |
| | | | | | | | ( 0.430, 28.411) | |
| | | | | | | | 0.2116 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubslae-ebr1575b3.sas 12JUL2023:14:17:21

Protocol: CA20976K 

Table 25.30.1
Other Events of Special Interest: Subgroup Time-Adjusted Analyses
On Hazard Ratio for Any OESIs

Other Events of Special Interest Category: Any OESIs

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| T STAGE | | | | | | | | N.M.E. |
| T3B | 203 | 5 ( 2.5) | N.M.E. | 104 | 0 | N.M.E. | N.M.E. | |
| T4A | 112 | 5 ( 4.5) | N.M.E. | 58 | 1 ( 1.7) | N.M.E. | N.M.E. | |
| T4B | 209 | 7 ( 3.3) | N.M.E. | 102 | 1 ( 1.0) | N.M.E. | N.M.E. | |
| REGION | | | | | | | | 0.5917 |
| US AND CANADA | 97 | 1 ( 1.0) | N.A. | 46 | 1 ( 2.2) | N.A. | 0.605<br>( 0.038, 9.668)<br>0.7193 | |
| WESTERN EUROPE | 301 | 11 ( 3.7) | N.A. | 160 | 1 ( 0.6) | N.A. | 6.086<br>( 0.786, 47.140)<br>0.0484 | |
| EASTERN EUROPE | 58 | 1 ( 1.7) | N.A. | 28 | 0 | N.E. | N.E.<br>0.4795 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubslae-ebr1575b3.sas 12JUL2023:14:17:21

Protocol: CA20976K 

Table 25.30.1
Other Events of Special Interest: Subgroup Time-Adjusted Analyses
On Hazard Ratio for Any OESIs

Other Events of Special Interest Category: Any OESIs

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AUSTRALIA | 68 | 4 ( 5.9) | N.A. | 30 | 0 | N.E. | N.E. | 0.1613 |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
MedDRA Version: 25.1; CTC Version 5.0
Race Other includes all the races other than White, Asian, Black or African American and Not reported.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubslae-ebr1575b3.sas 12JUL2023:14:17:21

**Anhang 4-G 3.2.4: Subgruppenanalysen für Endpunkte Unerwünschte Ereignisse auf SOC/PT-Ebene aus CA209-76K – Zeit bis zum ersten Auftreten des UE**

**Anhang 4-G 3.2.4.1: Subgruppenanalysen für Endpunkt Jegliche UE auf SOC/PT-Ebene aus CA209-76K**

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

All Subjects with an Event

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 508 ( 96.9) | 0.95 ( 0.89, 0.95) | 264 | 234 ( 88.6) | 1.77 ( 1.12, 1.91) | 1.705 ( 1.457, 1.996) <0.0001 | |
| AGE CATEGORY I | | | | | | | | 0.4323 |
| < 65 | 305 | 295 ( 96.7) | 0.95 ( 0.89, 0.95) | 155 | 137 ( 88.4) | 1.68 ( 0.95, 1.87) | 1.584 ( 1.290, 1.944) <0.0001 | |
| >= 65 | 219 | 213 ( 97.3) | 0.95 ( 0.79, 0.95) | 109 | 97 ( 89.0) | 1.87 ( 1.08, 2.79) | 1.932 ( 1.507, 2.476) <0.0001 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

All Subjects with an Event

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | 0.4349 |
| >= 18 AND < 65 | 305 | 295 ( 96.7) | 0.95 ( 0.89, 0.95) | 155 | 137 ( 88.4) | 1.68 ( 0.95, 1.87) | 1.584 ( 1.290, 1.944) <0.0001 | |
| >= 65 AND < 75 | 139 | 135 ( 97.1) | 0.95 ( 0.76, 0.95) | 77 | 69 ( 89.6) | 1.97 ( 1.45, 3.68) | 2.185 ( 1.610, 2.966) <0.0001 | |
| >= 75 AND < 85 | 77 | 75 ( 97.4) | 0.95 ( 0.69, 1.15) | 30 | 26 ( 86.7) | 1.05 ( 0.66, 2.69) | 1.479 ( 0.943, 2.320) 0.0862 | |
| SEX | | | | | | | | 0.5252 |
| MALE | 320 | 316 ( 98.8) | 0.95 ( 0.82, 0.95) | 161 | 142 ( 88.2) | 1.87 ( 1.38, 2.79) | 1.819 ( 1.486, 2.226) <0.0001 | |
| FEMALE | 204 | 192 ( 94.1) | 0.95 ( 0.85, 0.95) | 103 | 92 ( 89.3) | 1.18 ( 0.95, 1.87) | 1.538 ( 1.195, 1.978) 0.0007 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

All Subjects with an Event

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.5580 |
| STAGE IIB | 315 | 305 ( 96.8) | 0.92 ( 0.79, 0.95) | 162 | 148 ( 91.4) | 1.72 ( 1.12, 1.97) | 1.645 ( 1.348, 2.007) <0.0001 | |
| STAGE IIC | 209 | 203 ( 97.1) | 0.95 ( 0.89, 0.95) | 102 | 86 ( 84.3) | 1.84 ( 0.95, 2.76) | 1.807 ( 1.394, 2.341) <0.0001 | |
| T STAGE | | | | | | | | 0.5947 |
| T3B | 203 | 196 ( 96.6) | 0.95 ( 0.92, 1.02) | 104 | 92 ( 88.5) | 1.87 ( 1.45, 2.86) | 1.788 ( 1.390, 2.301) <0.0001 | |
| T4A | 112 | 109 ( 97.3) | 0.54 ( 0.26, 0.82) | 58 | 56 ( 96.6) | 0.99 ( 0.82, 1.84) | 1.430 ( 1.034, 1.978) 0.0295 | |
| T4B | 209 | 203 ( 97.1) | 0.95 ( 0.89, 0.95) | 102 | 86 ( 84.3) | 1.84 ( 0.95, 2.76) | 1.807 ( 1.394, 2.341) <0.0001 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

All Subjects with an Event

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.5918 |
| US AND CANADA | 97 | 96 ( 99.0) | 0.49 ( 0.23, 0.89) | 46 | 44 ( 95.7) | 0.66 ( 0.20, 0.99) | 1.427 ( 0.993, 2.051) 0.0619 | |
| WESTERN EUROPE | 301 | 290 ( 96.3) | 0.95 ( 0.92, 0.99) | 160 | 141 ( 88.1) | 1.91 ( 1.48, 3.38) | 1.701 ( 1.386, 2.087) <0.0001 | |
| EASTERN EUROPE | 58 | 55 ( 94.8) | 1.87 ( 0.95, 2.69) | 28 | 20 ( 71.4) | 6.82 ( 1.84, 9.63) | 2.519 ( 1.487, 4.267) 0.0004 | |
| AUSTRALIA | 68 | 67 ( 98.5) | 0.49 ( 0.23, 0.85) | 30 | 29 ( 96.7) | 1.03 ( 0.43, 2.27) | 1.716 ( 1.096, 2.689) 0.0161 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Skin and Subcutaneous Tissue Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 271 ( 51.7) | 9.36 ( 6.47, 12.02) | 264 | 90 ( 34.1) | N.A. | 1.900 ( 1.496, 2.413) <0.0001 | |
| AGE CATEGORY I | | | | | | | | 0.1321 |
| < 65 | 305 | 146 ( 47.9) | 14.36 ( 9.23, N.A.) | 155 | 54 ( 34.8) | N.A. | 1.628 ( 1.191, 2.225) 0.0020 | |
| >= 65 | 219 | 125 ( 57.1) | 5.55 ( 4.63, 9.23) | 109 | 36 ( 33.0) | N.A. | 2.355 ( 1.623, 3.416) <0.0001 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Skin and Subcutaneous Tissue Disorders

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| AGE CATEGORY II | | | | | | | | 0.0317* |
| >= 18 AND < 65 | 305 | 146 ( 47.9) | 14.36 ( 9.23, N.A.) | 155 | 54 ( 34.8) | N.A. | 1.628 ( 1.191, 2.225) 0.0020 | |
| >= 65 AND < 75 | 139 | 82 ( 59.0) | 5.65 ( 4.63, 10.58) | 77 | 20 ( 26.0) | N.A. | 3.305 ( 2.023, 5.399) <0.0001 | |
| >= 75 AND < 85 | 77 | 42 ( 54.5) | 5.45 ( 2.53, N.A.) | 30 | 15 ( 50.0) | 8.28 ( 2.76, N.A.) | 1.278 ( 0.708, 2.307) 0.4180 | |
| SEX | | | | | | | | 0.1895 |
| MALE | 320 | 177 ( 55.3) | 7.16 ( 4.90, 10.91) | 161 | 53 ( 32.9) | N.A. | 2.167 ( 1.593, 2.948) <0.0001 | |
| FEMALE | 204 | 94 ( 46.1) | N.A. ( 7.52, N.A.) | 103 | 37 ( 35.9) | N.A. | 1.536 ( 1.049, 2.247) 0.0259 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Skin and Subcutaneous Tissue Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.5349 |
| STAGE IIB | 315 | 171 ( 54.3) | 7.43 ( 4.73, 11.14) | 162 | 57 ( 35.2) | N.A. | 2.006 ( 1.485, 2.709) <0.0001 | |
| STAGE IIC | 209 | 100 ( 47.8) | 11.99 ( 7.20, N.A.) | 102 | 33 ( 32.4) | N.A. | 1.745 ( 1.177, 2.588) 0.0050 | |
| T STAGE | | | | | | | | 0.8109 |
| T3B | 203 | 108 ( 53.2) | 7.16 ( 4.67, N.A.) | 104 | 36 ( 34.6) | N.A. | 1.966 ( 1.347, 2.869) 0.0004 | |
| T4A | 112 | 63 ( 56.3) | 7.43 ( 3.71, N.A.) | 58 | 21 ( 36.2) | N.A. (10.15, N.A.) | 2.071 ( 1.263, 3.398) 0.0032 | |
| T4B | 209 | 100 ( 47.8) | 11.99 ( 7.20, N.A.) | 102 | 33 ( 32.4) | N.A. | 1.745 ( 1.177, 2.588) 0.0050 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Skin and Subcutaneous Tissue Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.7061 |
| US AND CANADA | 97 | 63 ( 64.9) | 3.65 ( 2.07, 4.76) | 46 | 21 ( 45.7) | N.A. ( 5.49, N.A.) | 1.935 ( 1.178, 3.177) 0.0079 | |
| WESTERN EUROPE | 301 | 144 ( 47.8) | 11.99 ( 9.23, N.A.) | 160 | 47 ( 29.4) | N.A. | 2.005 ( 1.442, 2.789) <0.0001 | |
| EASTERN EUROPE | 58 | 18 ( 31.0) | N.A. | 28 | 4 ( 14.3) | N.A. | 2.595 ( 0.878, 7.676) 0.0740 | |
| AUSTRALIA | 68 | 46 ( 67.6) | 3.65 ( 1.74, 5.55) | 30 | 18 ( 60.0) | 5.14 ( 3.42, N.A.) | 1.431 ( 0.828, 2.472) 0.1914 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Skin and Subcutaneous Tissue Disorders. PT: Pruritus

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 107 ( 20.4) | N.A. | 264 | 29 ( 11.0) | N.A. | 2.062 ( 1.368, 3.109) 0.0004 | |
| AGE CATEGORY I | | | | | | | | 0.3019 |
| < 65 | 305 | 59 ( 19.3) | N.A. | 155 | 13 ( 8.4) | N.A. | 2.545 ( 1.396, 4.641) 0.0016 | |
| >= 65 | 219 | 48 ( 21.9) | N.A. | 109 | 16 ( 14.7) | N.A. | 1.664 ( 0.944, 2.931) 0.0748 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Skin and Subcutaneous Tissue Disorders. PT: Pruritus

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| AGE CATEGORY II | | | | | | | | 0.4479 |
| >= 18 AND < 65 | 305 | 59 ( 19.3) | N.A. | 155 | 13 ( 8.4) | N.A. | 2.545 ( 1.396, 4.641) 0.0016 | |
| >= 65 AND < 75 | 139 | 30 ( 21.6) | N.A. | 77 | 10 ( 13.0) | N.A. | 1.849 ( 0.903, 3.784) 0.0876 | |
| >= 75 AND < 85 | 77 | 18 ( 23.4) | N.A. | 30 | 6 ( 20.0) | N.A. | 1.275 ( 0.506, 3.215) 0.6046 | |
| SEX | | | | | | | | 0.3001 |
| MALE | 320 | 67 ( 20.9) | N.A. | 161 | 15 ( 9.3) | N.A. | 2.494 ( 1.424, 4.367) 0.0009 | |
| FEMALE | 204 | 40 ( 19.6) | N.A. | 103 | 14 ( 13.6) | N.A. | 1.598 ( 0.869, 2.937) 0.1282 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Skin and Subcutaneous Tissue Disorders. PT: Pruritus

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.2258 |
| STAGE IIB | 315 | 63 ( 20.0) | N.A. | 162 | 21 ( 13.0) | N.A. | 1.707 ( 1.041, 2.797) 0.0317 | |
| STAGE IIC | 209 | 44 ( 21.1) | N.A. | 102 | 8 ( 7.8) | N.A. | 2.962 ( 1.394, 6.294) 0.0030 | |
| T STAGE | | | | | | | | 0.2382 |
| T3B | 203 | 40 ( 19.7) | N.A. | 104 | 16 ( 15.4) | N.A. | 1.411 ( 0.790, 2.520) 0.2424 | |
| T4A | 112 | 23 ( 20.5) | N.A. | 58 | 5 ( 8.6) | N.A. | 2.631 ( 1.000, 6.923) 0.0416 | |
| T4B | 209 | 44 ( 21.1) | N.A. | 102 | 8 ( 7.8) | N.A. | 2.962 ( 1.394, 6.294) 0.0030 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Skin and Subcutaneous Tissue Disorders. PT: Pruritus

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| REGION | | | | | | | | 0.7846 |
| US AND CANADA | 97 | 27 ( 27.8) | N.A. | 46 | 7 ( 15.2) | N.A. | 2.172 ( 0.945, 4.992) 0.0615 | |
| WESTERN EUROPE | 301 | 48 ( 15.9) | N.A. | 160 | 12 ( 7.5) | N.A. | 2.294 ( 1.218, 4.319) 0.0082 | |
| EASTERN EUROPE | 58 | 6 ( 10.3) | N.A. | 28 | 3 ( 10.7) | N.A. | 1.042 ( 0.261, 4.167) 0.9532 | |
| AUSTRALIA | 68 | 26 ( 38.2) | N.A. ( 9.10, N.A.) | 30 | 7 ( 23.3) | N.A. | 1.877 ( 0.813, 4.334) 0.1324 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Skin and Subcutaneous Tissue Disorders. PT: Rash Pruritic

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 12 ( 2.3) | N.A. | 264 | 1 ( 0.4) | N.A. | 6.231 ( 0.810, 47.925) 0.0441 | |
| AGE CATEGORY I | | | | | | | | N.M.E. |
| < 65 | 305 | 7 ( 2.3) | N.M.E. | 155 | 1 ( 0.6) | N.M.E. | N.M.E. | |
| >= 65 | 219 | 5 ( 2.3) | N.M.E. | 109 | 0 | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Skin and Subcutaneous Tissue Disorders. PT: Rash Pruritic

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| AGE CATEGORY II | | | | | | | | N.M.E. |
| >= 18 AND < 65 | 305 | 7 ( 2.3) | N.M.E. | 155 | 1 ( 0.6) | N.M.E. | N.M.E. | |
| >= 65 AND < 75 | 139 | 5 ( 3.6) | N.M.E. | 77 | 0 | N.M.E. | N.M.E. | |
| >= 75 AND < 85 | 77 | 0 | N.M.E. | 30 | 0 | N.M.E. | N.M.E. | |
| SEX | | | | | | | | 0.9902 |
| MALE | 320 | 10 ( 3.1) | N.A. | 161 | 0 | N.E. | N.E. | |
| FEMALE | 204 | 2 ( 1.0) | N.A. | 103 | 1 ( 1.0) | N.A. | 0.0228<br>1.045<br>( 0.095, 11.529)<br>0.9709 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Skin and Subcutaneous Tissue Disorders. PT: Rash Pruritic

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| DISEASE STAGE CATEGORY | | | | | | | | N.M.E. |
| STAGE IIB | 315 | 8 ( 2.5) | N.M.E. | 162 | 0 | N.M.E. | N.M.E. | |
| STAGE IIC | 209 | 4 ( 1.9) | N.M.E. | 102 | 1 ( 1.0) | N.M.E. | N.M.E. | |
| T STAGE | | | | | | | | N.M.E. |
| T3B | 203 | 7 ( 3.4) | N.M.E. | 104 | 0 | N.M.E. | N.M.E. | |
| T4A | 112 | 1 ( 0.9) | N.M.E. | 58 | 0 | N.M.E. | N.M.E. | |
| T4B | 209 | 4 ( 1.9) | N.M.E. | 102 | 1 ( 1.0) | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Skin and Subcutaneous Tissue Disorders. PT: Rash Pruritic

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| REGION | | | | | | | | N.M.E. |
| US AND CANADA | 97 | 2 ( 2.1) | N.M.E. | 46 | 0 | N.M.E. | N.M.E. | |
| WESTERN EUROPE | 301 | 6 ( 2.0) | N.M.E. | 160 | 1 ( 0.6) | N.M.E. | N.M.E. | |
| EASTERN EUROPE | 58 | 0 | N.M.E. | 28 | 0 | N.M.E. | N.M.E. | |
| AUSTRALIA | 68 | 4 ( 5.9) | N.M.E. | 30 | 0 | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Gastrointestinal Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 269 ( 51.3) | 9.23 ( 7.26, 14.98) | 264 | 112 ( 42.4) | N.A. (12.09, N.A.) | 1.343 ( 1.077, 1.674) 0.0085 | |
| AGE CATEGORY I | | | | | | | | 0.2746 |
| < 65 | 305 | 162 ( 53.1) | 8.57 ( 6.60, 14.98) | 155 | 72 ( 46.5) | N.A. ( 8.51, N.A.) | 1.213 ( 0.919, 1.602) 0.1707 | |
| >= 65 | 219 | 107 ( 48.9) | 9.76 ( 6.87, N.A.) | 109 | 40 ( 36.7) | N.A. (14.13, N.A.) | 1.586 ( 1.102, 2.282) 0.0122 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Gastrointestinal Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | 0.3096 |
| >= 18 AND < 65 | 305 | 162 ( 53.1) | 8.57 ( 6.60, 14.98) | 155 | 72 ( 46.5) | N.A. ( 8.51, N.A.) | 1.213 ( 0.919, 1.602) 0.1707 | |
| >= 65 AND < 75 | 139 | 72 ( 51.8) | 9.00 ( 5.09, N.A.) | 77 | 28 ( 36.4) | N.A. (14.13, N.A.) | 1.830 ( 1.181, 2.836) 0.0060 | |
| >= 75 AND < 85 | 77 | 33 ( 42.9) | N.A. ( 6.97, N.A.) | 30 | 11 ( 36.7) | N.A. ( 3.78, N.A.) | 1.189 ( 0.601, 2.354) 0.6173 | |
| SEX | | | | | | | | 0.9150 |
| MALE | 320 | 156 ( 48.8) | 12.12 ( 8.34, N.A.) | 161 | 64 ( 39.8) | N.A. (14.13, N.A.) | 1.355 ( 1.012, 1.813) 0.0397 | |
| FEMALE | 204 | 113 ( 55.4) | 6.97 ( 5.59, 9.76) | 103 | 48 ( 46.6) | N.A. ( 5.62, N.A.) | 1.321 ( 0.942, 1.852) 0.1055 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Gastrointestinal Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.9287 |
| STAGE IIB | 315 | 166 ( 52.7) | 8.34 ( 5.59, N.A.) | 162 | 72 ( 44.4) | N.A. (10.25, N.A.) | 1.325 ( 1.005, 1.748) 0.0454 | |
| STAGE IIC | 209 | 103 ( 49.3) | 10.64 ( 7.26, N.A.) | 102 | 40 ( 39.2) | N.A. (10.71, N.A.) | 1.375 ( 0.954, 1.982) 0.0857 | |
| T STAGE | | | | | | | | 0.7618 |
| T3B | 203 | 102 ( 50.2) | 9.26 ( 6.47, N.A.) | 104 | 41 ( 39.4) | N.A. (14.13, N.A.) | 1.451 ( 1.010, 2.086) 0.0428 | |
| T4A | 112 | 64 ( 57.1) | 5.09 ( 3.32, N.A.) | 58 | 31 ( 53.4) | 9.99 ( 3.71, N.A.) | 1.159 ( 0.754, 1.780) 0.5000 | |
| T4B | 209 | 103 ( 49.3) | 10.64 ( 7.26, N.A.) | 102 | 40 ( 39.2) | N.A. (10.71, N.A.) | 1.375 ( 0.954, 1.982) 0.0857 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Gastrointestinal Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.6473 |
| US AND CANADA | 97 | 62 ( 63.9) | 4.11 ( 2.63, 6.97) | 46 | 28 ( 60.9) | 5.98 ( 1.38, N.A.) | 1.101 ( 0.703, 1.723) 0.6706 | |
| WESTERN EUROPE | 301 | 142 ( 47.2) | 14.98 ( 8.64, N.A.) | 160 | 58 ( 36.3) | N.A. | 1.427 ( 1.051, 1.937) 0.0216 | |
| EASTERN EUROPE | 58 | 20 ( 34.5) | N.A. (10.02, N.A.) | 28 | 6 ( 21.4) | N.A. | 1.942 ( 0.779, 4.841) 0.1474 | |
| AUSTRALIA | 68 | 45 ( 66.2) | 3.48 ( 2.10, 7.39) | 30 | 20 ( 66.7) | 5.22 ( 3.25, 10.38) | 1.139 ( 0.672, 1.931) 0.6228 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Gastrointestinal Disorders. PT: Diarrhoea

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 128 ( 24.4) | N.A. | 264 | 44 ( 16.7) | N.A. | 1.581 ( 1.122, 2.227) 0.0081 | |
| AGE CATEGORY I | | | | | | | | 0.2239 |
| < 65 | 305 | 85 ( 27.9) | N.A. | 155 | 33 ( 21.3) | N.A. | 1.369 ( 0.916, 2.047) 0.1235 | |
| >= 65 | 219 | 43 ( 19.6) | N.A. | 109 | 11 ( 10.1) | N.A. | 2.177 ( 1.122, 4.225) 0.0184 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Gastrointestinal Disorders. PT: Diarrhoea

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | 0.4715 |
| >= 18 AND < 65 | 305 | 85 ( 27.9) | N.A. | 155 | 33 ( 21.3) | N.A. | 1.369 ( 0.916, 2.047) 0.1235 | |
| >= 65 AND < 75 | 139 | 31 ( 22.3) | N.A. | 77 | 9 ( 11.7) | N.A. | 2.161 ( 1.028, 4.543) 0.0373 | |
| >= 75 AND < 85 | 77 | 11 ( 14.3) | N.A. | 30 | 2 ( 6.7) | N.A. | 2.288 ( 0.507, 10.325) 0.2672 | |
| SEX | | | | | | | | 0.4633 |
| MALE | 320 | 75 ( 23.4) | N.A. | 161 | 23 ( 14.3) | N.A. | 1.771 ( 1.110, 2.826) 0.0151 | |
| FEMALE | 204 | 53 ( 26.0) | N.A. | 103 | 21 ( 20.4) | N.A. | 1.375 ( 0.829, 2.280) 0.2149 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Gastrointestinal Disorders. PT: Diarrhoea

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| DISEASE STAGE CATEGORY | | | | | | | | 0.2926 |
| STAGE IIB | 315 | 77 ( 24.4) | N.A. | 162 | 31 ( 19.1) | N.A. | 1.376 ( 0.906, 2.088) 0.1321 | |
| STAGE IIC | 209 | 51 ( 24.4) | N.A. | 102 | 13 ( 12.7) | N.A. | 2.060 ( 1.120, 3.788) 0.0175 | |
| T STAGE | | | | | | | | 0.3936 |
| T3B | 203 | 46 ( 22.7) | N.A. | 104 | 16 ( 15.4) | N.A. | 1.604 ( 0.908, 2.833) 0.1006 | |
| T4A | 112 | 31 ( 27.7) | N.A. | 58 | 15 ( 25.9) | N.A. | 1.125 ( 0.607, 2.084) 0.7074 | |
| T4B | 209 | 51 ( 24.4) | N.A. | 102 | 13 ( 12.7) | N.A. | 2.060 ( 1.120, 3.788) 0.0175 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Gastrointestinal Disorders. PT: Diarrhoea

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| REGION | | | | | | | | 0.9255 |
| US AND CANADA | 97 | 33 ( 34.0) | N.A. | 46 | 13 ( 28.3) | N.A. | 1.250 ( 0.657, 2.378) 0.4942 | |
| WESTERN EUROPE | 301 | 65 ( 21.6) | N.A. | 160 | 22 ( 13.8) | N.A. | 1.682 ( 1.037, 2.728) 0.0329 | |
| EASTERN EUROPE | 58 | 7 ( 12.1) | N.A. | 28 | 2 ( 7.1) | N.A. | 1.850 ( 0.384, 8.909) 0.4357 | |
| AUSTRALIA | 68 | 23 ( 33.8) | N.A. (10.64, N.A.) | 30 | 7 ( 23.3) | N.A. | 1.625 ( 0.696, 3.790) 0.2553 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: General Disorders and Administration Site Conditions

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 268 ( 51.1) | 8.87 ( 6.67, N.A.) | 264 | 119 ( 45.1) | N.A. (10.15, N.A.) | 1.242 ( 1.000, 1.541) 0.0483 | |
| AGE CATEGORY I | | | | | | | | 0.2904 |
| < 65 | 305 | 173 ( 56.7) | 6.47 ( 5.55, 9.23) | 155 | 71 ( 45.8) | N.A. ( 8.08, N.A.) | 1.355 ( 1.028, 1.786) 0.0296 | |
| >= 65 | 219 | 95 ( 43.4) | N.A. ( 8.67, N.A.) | 109 | 48 ( 44.0) | N.A. ( 9.89, N.A.) | 1.076 ( 0.760, 1.522) 0.6837 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: General Disorders and Administration Site Conditions

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | 0.4186 |
| >= 18 AND < 65 | 305 | 173 ( 56.7) | 6.47 ( 5.55, 9.23) | 155 | 71 ( 45.8) | N.A. ( 8.08, N.A.) | 1.355 ( 1.028, 1.786) 0.0296 | |
| >= 65 AND < 75 | 139 | 60 ( 43.2) | N.A. ( 7.52, N.A.) | 77 | 33 ( 42.9) | N.A. (10.02, N.A.) | 1.165 ( 0.761, 1.782) 0.4832 | |
| >= 75 AND < 85 | 77 | 34 ( 44.2) | N.A. ( 5.91, N.A.) | 30 | 14 ( 46.7) | N.A. ( 2.50, N.A.) | 0.872 ( 0.468, 1.626) 0.6654 | |
| SEX | | | | | | | | 0.7000 |
| MALE | 320 | 157 ( 49.1) | 10.78 ( 6.47, N.A.) | 161 | 69 ( 42.9) | N.A. (10.81, N.A.) | 1.280 ( 0.964, 1.699) 0.0873 | |
| FEMALE | 204 | 111 ( 54.4) | 7.39 ( 5.59, 11.63) | 103 | 50 ( 48.5) | 10.71 ( 5.49, N.A.) | 1.186 ( 0.849, 1.656) 0.3080 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: General Disorders and Administration Site Conditions

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.9356 |
| STAGE IIB | 315 | 167 ( 53.0) | 7.39 ( 5.59, N.A.) | 162 | 76 ( 46.9) | N.A. ( 7.85, N.A.) | 1.248 ( 0.952, 1.637) 0.1068 | |
| STAGE IIC | 209 | 101 ( 48.3) | 10.78 ( 7.06, N.A.) | 102 | 43 ( 42.2) | N.A. ( 9.89, N.A.) | 1.224 ( 0.857, 1.750) 0.2653 | |
| T STAGE | | | | | | | | 0.5851 |
| T3B | 203 | 108 ( 53.2) | 6.97 ( 5.09, N.A.) | 104 | 46 ( 44.2) | N.A. ( 8.31, N.A.) | 1.393 ( 0.986, 1.969) 0.0573 | |
| T4A | 112 | 59 ( 52.7) | 8.84 ( 4.70, N.A.) | 58 | 30 ( 51.7) | 11.96 ( 2.79, N.A.) | 1.041 ( 0.671, 1.616) 0.8606 | |
| T4B | 209 | 101 ( 48.3) | 10.78 ( 7.06, N.A.) | 102 | 43 ( 42.2) | N.A. ( 9.89, N.A.) | 1.224 ( 0.857, 1.750) 0.2653 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: General Disorders and Administration Site Conditions

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.0557 |
| US AND CANADA | 97 | 60 ( 61.9) | 5.55 ( 2.63, 7.69) | 46 | 33 ( 71.7) | 2.79 ( 1.87, 6.70) | 0.846 ( 0.553, 1.295) 0.4411 | |
| WESTERN EUROPE | 301 | 157 ( 52.2) | 8.87 ( 6.70, N.A.) | 160 | 67 ( 41.9) | N.A. (10.02, N.A.) | 1.399 ( 1.051, 1.862) 0.0209 | |
| EASTERN EUROPE | 58 | 16 ( 27.6) | N.A. | 28 | 2 ( 7.1) | N.A. | 4.635 ( 1.065, 20.178) 0.0244 | |
| AUSTRALIA | 68 | 35 ( 51.5) | 6.24 ( 2.66, N.A.) | 30 | 17 ( 56.7) | 4.96 ( 1.87, N.A.) | 0.885 ( 0.495, 1.579) 0.6924 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: General Disorders and Administration Site Conditions. PT: Influenza Like Illness

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 21 ( 4.0) | N.A. | 264 | 4 ( 1.5) | N.A. | 2.822 ( 0.968, 8.223) 0.0469 | |
| AGE CATEGORY I | | | | | | | | 0.1986 |
| < 65 | 305 | 17 ( 5.6) | N.A. | 155 | 2 ( 1.3) | N.A. | 4.638 ( 1.071, 20.078) 0.0239 | |
| >= 65 | 219 | 4 ( 1.8) | N.A. | 109 | 2 ( 1.8) | N.A. | 1.050 ( 0.192, 5.734) 0.9551 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: General Disorders and Administration Site Conditions. PT: Influenza Like Illness

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | 0.2958 |
| >= 18 AND < 65 | 305 | 17 ( 5.6) | N.A. | 155 | 2 ( 1.3) | N.A. | 4.638 ( 1.071, 20.078) 0.0239 | |
| >= 65 AND < 75 | 139 | 3 ( 2.2) | N.A. | 77 | 1 ( 1.3) | N.A. | 1.724 ( 0.179, 16.578) 0.6331 | |
| >= 75 AND < 85 | 77 | 1 ( 1.3) | N.A. | 30 | 1 ( 3.3) | N.A. | 0.410 ( 0.026, 6.561) 0.5145 | |
| SEX | | | | | | | | 0.6557 |
| MALE | 320 | 13 ( 4.1) | N.A. | 161 | 2 ( 1.2) | N.A. | 3.488 ( 0.787, 15.460) 0.0794 | |
| FEMALE | 204 | 8 ( 3.9) | N.A. | 103 | 2 ( 1.9) | N.A. | 2.147 ( 0.456, 10.112) 0.3224 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: General Disorders and Administration Site Conditions. PT: Influenza Like Illness

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| DISEASE STAGE CATEGORY | | | | | | | | 0.4621 |
| STAGE IIB | 315 | 14 ( 4.4) | N.A. | 162 | 2 ( 1.2) | N.A. | 3.988 ( 0.906, 17.551) 0.0477 | |
| STAGE IIC | 209 | 7 ( 3.3) | N.A. | 102 | 2 ( 2.0) | N.A. | 1.705 ( 0.354, 8.208) 0.5008 | |
| T STAGE | | | | | | | | 0.7200 |
| T3B | 203 | 9 ( 4.4) | N.A. | 104 | 1 ( 1.0) | N.A. | 5.141 ( 0.651, 40.597) 0.0833 | |
| T4A | 112 | 5 ( 4.5) | N.A. | 58 | 1 ( 1.7) | N.A. | 2.843 ( 0.332, 24.358) 0.3187 | |
| T4B | 209 | 7 ( 3.3) | N.A. | 102 | 2 ( 2.0) | N.A. | 1.705 ( 0.354, 8.208) 0.5008 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: General Disorders and Administration Site Conditions. PT: Influenza Like Illness

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.9889 |
| US AND CANADA | 97 | 7 ( 7.2) | N.A. | 46 | 1 ( 2.2) | N.A. | 3.806 ( 0.468, 30.960) 0.1787 | |
| WESTERN EUROPE | 301 | 13 ( 4.3) | N.A. | 160 | 3 ( 1.9) | N.A. | 2.389 ( 0.681, 8.385) 0.1607 | |
| EASTERN EUROPE | 58 | 0 | N.E. | 28 | 0 | N.E. | N.E. N.E. | |
| AUSTRALIA | 68 | 1 ( 1.5) | N.A. | 30 | 0 | N.E. | N.E. 0.5034 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Musculoskeletal and Connective Tissue Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 203 ( 38.7) | N.A. | 264 | 85 ( 32.2) | N.A. | 1.338 ( 1.038, 1.724) 0.0236 | |
| AGE CATEGORY I | | | | | | | | 0.6603 |
| < 65 | 305 | 127 ( 41.6) | N.A. | 155 | 56 ( 36.1) | N.A. | 1.289 ( 0.941, 1.766) 0.1115 | |
| >= 65 | 219 | 76 ( 34.7) | N.A. | 109 | 29 ( 26.6) | N.A. | 1.437 ( 0.937, 2.205) 0.0947 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Musculoskeletal and Connective Tissue Disorders

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| AGE CATEGORY II | | | | | | | | 0.7050 |
| >= 18 AND < 65 | 305 | 127 ( 41.6) | N.A. | 155 | 56 ( 36.1) | N.A. | 1.289 ( 0.941, 1.766) 0.1115 | |
| >= 65 AND < 75 | 139 | 49 ( 35.3) | N.A. | 77 | 22 ( 28.6) | N.A. | 1.393 ( 0.842, 2.305) 0.1945 | |
| >= 75 AND < 85 | 77 | 27 ( 35.1) | N.A. (13.04, N.A.) | 30 | 6 ( 20.0) | N.A. | 1.879 ( 0.776, 4.553) 0.1541 | |
| SEX | | | | | | | | 0.4504 |
| MALE | 320 | 114 ( 35.6) | N.A. | 161 | 50 ( 31.1) | N.A. | 1.240 ( 0.889, 1.729) 0.2035 | |
| FEMALE | 204 | 89 ( 43.6) | N.A. ( 9.23, N.A.) | 103 | 35 ( 34.0) | N.A. | 1.492 ( 1.009, 2.206) 0.0437 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Musculoskeletal and Connective Tissue Disorders

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| DISEASE STAGE CATEGORY | | | | | | | | 0.5396 |
| STAGE IIB | 315 | 126 ( 40.0) | N.A. | 162 | 58 ( 35.8) | N.A. | 1.267 ( 0.928, 1.729) 0.1348 | |
| STAGE IIC | 209 | 77 ( 36.8) | N.A. | 102 | 27 ( 26.5) | N.A. | 1.501 ( 0.968, 2.328) 0.0674 | |
| T STAGE | | | | | | | | 0.4387 |
| T3B | 203 | 81 ( 39.9) | N.A. | 104 | 33 ( 31.7) | N.A. | 1.456 ( 0.971, 2.182) 0.0669 | |
| T4A | 112 | 45 ( 40.2) | N.A. ( 9.23, N.A.) | 58 | 25 ( 43.1) | N.A. ( 8.34, N.A.) | 1.018 ( 0.624, 1.660) 0.9447 | |
| T4B | 209 | 77 ( 36.8) | N.A. | 102 | 27 ( 26.5) | N.A. | 1.501 ( 0.968, 2.328) 0.0674 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Musculoskeletal and Connective Tissue Disorders

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| REGION | | | | | | | | 0.2977 |
| US AND CANADA | 97 | 31 ( 32.0) | N.A. ( 9.17, N.A.) | 46 | 20 ( 43.5) | N.A. ( 9.17, N.A.) | 0.810 ( 0.461, 1.421) 0.4609 | |
| WESTERN EUROPE | 301 | 125 ( 41.5) | N.A. (14.16, N.A.) | 160 | 47 ( 29.4) | N.A. | 1.540 ( 1.101, 2.154) 0.0109 | |
| EASTERN EUROPE | 58 | 13 ( 22.4) | N.A. | 28 | 5 ( 17.9) | N.A. | 1.426 ( 0.508, 4.000) 0.4972 | |
| AUSTRALIA | 68 | 34 ( 50.0) | 6.51 ( 4.07, N.A.) | 30 | 13 ( 43.3) | N.A. ( 5.32, N.A.) | 1.397 ( 0.736, 2.651) 0.3031 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Musculoskeletal and Connective Tissue Disorders. PT: Arthralgia

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 89 ( 17.0) | N.A. | 264 | 32 ( 12.1) | N.A. | 1.524 ( 1.017, 2.283) 0.0394 | |
| AGE CATEGORY I | | | | | | | | 0.7141 |
| < 65 | 305 | 58 ( 19.0) | N.A. | 155 | 22 ( 14.2) | N.A. | 1.452 ( 0.889, 2.373) 0.1335 | |
| >= 65 | 219 | 31 ( 14.2) | N.A. | 109 | 10 ( 9.2) | N.A. | 1.673 ( 0.820, 3.412) 0.1517 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Musculoskeletal and Connective Tissue Disorders. PT: Arthralgia

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| AGE CATEGORY II | | | | | | | | 0.8871 |
| >= 18 AND < 65 | 305 | 58 ( 19.0) | N.A. | 155 | 22 ( 14.2) | N.A. | 1.452 ( 0.889, 2.373) 0.1335 | |
| >= 65 AND < 75 | 139 | 21 ( 15.1) | N.A. | 77 | 7 ( 9.1) | N.A. | 1.811 ( 0.769, 4.261) 0.1669 | |
| >= 75 AND < 85 | 77 | 10 ( 13.0) | N.A. | 30 | 3 ( 10.0) | N.A. | 1.386 ( 0.381, 5.037) 0.6177 | |
| SEX | | | | | | | | 0.3744 |
| MALE | 320 | 50 ( 15.6) | N.A. | 161 | 15 ( 9.3) | N.A. | 1.835 ( 1.030, 3.268) 0.0364 | |
| FEMALE | 204 | 39 ( 19.1) | N.A. | 103 | 17 ( 16.5) | N.A. | 1.252 ( 0.708, 2.213) 0.4375 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Musculoskeletal and Connective Tissue Disorders. PT: Arthralgia

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| DISEASE STAGE CATEGORY | | | | | | | | 0.2533 |
| STAGE IIB | 315 | 58 ( 18.4) | N.A. | 162 | 25 ( 15.4) | N.A. | 1.317 ( 0.824, 2.106) 0.2478 | |
| STAGE IIC | 209 | 31 ( 14.8) | N.A. | 102 | 7 ( 6.9) | N.A. | 2.299 ( 1.012, 5.221) 0.0408 | |
| T STAGE | | | | | | | | 0.1433 |
| T3B | 203 | 40 ( 19.7) | N.A. | 104 | 13 ( 12.5) | N.A. | 1.780 ( 0.952, 3.328) 0.0671 | |
| T4A | 112 | 18 ( 16.1) | N.A. | 58 | 12 ( 20.7) | N.A. | 0.827 ( 0.398, 1.718) 0.6107 | |
| T4B | 209 | 31 ( 14.8) | N.A. | 102 | 7 ( 6.9) | N.A. | 2.299 ( 1.012, 5.221) 0.0408 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Musculoskeletal and Connective Tissue Disorders. PT: Arthralgia

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.2354 |
| US AND CANADA | 97 | 17 ( 17.5) | N.A. | 46 | 5 ( 10.9) | N.A. | 1.854 ( 0.683, 5.033) 0.2186 | |
| WESTERN EUROPE | 301 | 48 ( 15.9) | N.A. | 160 | 13 ( 8.1) | N.A. | 2.085 ( 1.129, 3.848) 0.0162 | |
| EASTERN EUROPE | 58 | 6 ( 10.3) | N.A. | 28 | 3 ( 10.7) | N.A. | 1.035 ( 0.259, 4.138) 0.9601 | |
| AUSTRALIA | 68 | 18 ( 26.5) | N.A. ( 8.77, N.A.) | 30 | 11 ( 36.7) | N.A. | 0.789 ( 0.373, 1.672) 0.5383 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Musculoskeletal and Connective Tissue Disorders. PT: Arthritis

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 13 ( 2.5) | N.A. | 264 | 1 ( 0.4) | N.A. | 7.066 ( 0.924, 54.024) 0.0279 | |
| AGE CATEGORY I | | | | | | | | N.M.E. |
| < 65 | 305 | 8 ( 2.6) | N.M.E. | 155 | 0 | N.M.E. | N.M.E. | |
| >= 65 | 219 | 5 ( 2.3) | N.M.E. | 109 | 1 ( 0.9) | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Musculoskeletal and Connective Tissue Disorders. PT: Arthritis

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | N.M.E. |
| >= 18 AND < 65 | 305 | 8 ( 2.6) | N.M.E. | 155 | 0 | N.M.E. | N.M.E. | |
| >= 65 AND < 75 | 139 | 3 ( 2.2) | N.M.E. | 77 | 0 | N.M.E. | N.M.E. | |
| >= 75 AND < 85 | 77 | 2 ( 2.6) | N.M.E. | 30 | 0 | N.M.E. | N.M.E. | |
| SEX | | | | | | | | N.M.E. |
| MALE | 320 | 5 ( 1.6) | N.M.E. | 161 | 1 ( 0.6) | N.M.E. | N.M.E. | |
| FEMALE | 204 | 8 ( 3.9) | N.M.E. | 103 | 0 | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Musculoskeletal and Connective Tissue Disorders. PT: Arthritis

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | N.M.E. |
| STAGE IIB | 315 | 8 ( 2.5) | N.M.E. | 162 | 0 | N.M.E. | N.M.E. | |
| STAGE IIC | 209 | 5 ( 2.4) | N.M.E. | 102 | 1 ( 1.0) | N.M.E. | N.M.E. | |
| T STAGE | | | | | | | | N.M.E. |
| T3B | 203 | 6 ( 3.0) | N.M.E. | 104 | 0 | N.M.E. | N.M.E. | |
| T4A | 112 | 2 ( 1.8) | N.M.E. | 58 | 0 | N.M.E. | N.M.E. | |
| T4B | 209 | 5 ( 2.4) | N.M.E. | 102 | 1 ( 1.0) | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Musculoskeletal and Connective Tissue Disorders. PT: Arthritis

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | N.M.E. |
| US AND CANADA | 97 | 2 ( 2.1) | N.M.E. | 46 | 1 ( 2.2) | N.M.E. | N.M.E. | |
| WESTERN EUROPE | 301 | 7 ( 2.3) | N.M.E. | 160 | 0 | N.M.E. | N.M.E. | |
| EASTERN EUROPE | 58 | 2 ( 3.4) | N.M.E. | 28 | 0 | N.M.E. | N.M.E. | |
| AUSTRALIA | 68 | 2 ( 2.9) | N.M.E. | 30 | 0 | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Investigations. PT: Aspartate Aminotransferase Increased

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 43 ( 8.2) | N.A. | 264 | 8 ( 3.0) | N.A. | 2.917 ( 1.371, 6.204) 0.0036 | |
| AGE CATEGORY I | | | | | | | | 0.4997 |
| < 65 | 305 | 27 ( 8.9) | N.A. | 155 | 6 ( 3.9) | N.A. | 2.448 ( 1.010, 5.930) 0.0404 | |
| >= 65 | 219 | 16 ( 7.3) | N.A. | 109 | 2 ( 1.8) | N.A. | 4.290 ( 0.986, 18.667) 0.0343 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Investigations. PT: Aspartate Aminotransferase Increased

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| AGE CATEGORY II | | | | | | | | 0.9367 |
| >= 18 AND < 65 | 305 | 27 ( 8.9) | N.A. | 155 | 6 ( 3.9) | N.A. | 2.448 ( 1.010, 5.930) 0.0404 | |
| >= 65 AND < 75 | 139 | 11 ( 7.9) | N.A. | 77 | 2 ( 2.6) | N.A. | 3.259 ( 0.722, 14.709) 0.1040 | |
| >= 75 AND < 85 | 77 | 5 ( 6.5) | N.A. | 30 | 0 | N.E. | N.E. 0.1464 | |
| SEX | | | | | | | | 0.4999 |
| MALE | 320 | 27 ( 8.4) | N.A. | 161 | 4 ( 2.5) | N.A. | 3.695 ( 1.293, 10.561) 0.0089 | |
| FEMALE | 204 | 16 ( 7.8) | N.A. | 103 | 4 ( 3.9) | N.A. | 2.148 ( 0.718, 6.427) 0.1610 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Investigations. PT: Aspartate Aminotransferase Increased

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| DISEASE STAGE CATEGORY | | | | | | | | 0.4877 |
| STAGE IIB | 315 | 31 ( 9.8) | N.A. | 162 | 5 ( 3.1) | N.A. | 3.519 ( 1.368, 9.053) 0.0053 | |
| STAGE IIC | 209 | 12 ( 5.7) | N.A. | 102 | 3 ( 2.9) | N.A. | 2.009 ( 0.567, 7.119) 0.2701 | |
| T STAGE | | | | | | | | 0.2119 |
| T3B | 203 | 20 ( 9.9) | N.A. | 104 | 1 ( 1.0) | N.A. | 11.697 ( 1.569, 87.182) 0.0023 | |
| T4A | 112 | 11 ( 9.8) | N.A. | 58 | 4 ( 6.9) | N.A. | 1.496 ( 0.476, 4.701) 0.4876 | |
| T4B | 209 | 12 ( 5.7) | N.A. | 102 | 3 ( 2.9) | N.A. | 2.009 ( 0.567, 7.119) 0.2701 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Investigations. PT: Aspartate Aminotransferase Increased

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.8199 |
| US AND CANADA | 97 | 14 ( 14.4) | N.A. | 46 | 3 ( 6.5) | N.A. | 2.662 ( 0.764, 9.279) 0.1102 | |
| WESTERN EUROPE | 301 | 21 ( 7.0) | N.A. | 160 | 3 ( 1.9) | N.A. | 3.879 ( 1.157, 13.002) 0.0178 | |
| EASTERN EUROPE | 58 | 2 ( 3.4) | N.A. | 28 | 0 | N.E. | N.E. 0.3037 | |
| AUSTRALIA | 68 | 6 ( 8.8) | N.A. | 30 | 2 ( 6.7) | N.A. | 1.401 ( 0.283, 6.942) 0.6785 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Investigations. PT: Blood Alkaline Phosphatase Increased

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 17 ( 3.2) | N.A. | 264 | 2 ( 0.8) | N.A. | 4.589 ( 1.060, 19.865) 0.0251 | |
| AGE CATEGORY I | | | | | | | | 0.6748 |
| < 65 | 305 | 6 ( 2.0) | N.A. | 155 | 1 ( 0.6) | N.A. | 3.203 ( 0.386, 26.605) 0.2545 | |
| >= 65 | 219 | 11 ( 5.0) | N.A. | 109 | 1 ( 0.9) | N.A. | 6.014 ( 0.776, 46.598) 0.0504 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Investigations. PT: Blood Alkaline Phosphatase Increased

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| AGE CATEGORY II | | | | | | | | 0.9390 |
| >= 18 AND < 65 | 305 | 6 ( 2.0) | N.A. | 155 | 1 ( 0.6) | N.A. | 3.203 ( 0.386, 26.605) 0.2545 | |
| >= 65 AND < 75 | 139 | 9 ( 6.5) | N.A. | 77 | 1 ( 1.3) | N.A. | 5.441 ( 0.689, 42.961) 0.0710 | |
| >= 75 AND < 85 | 77 | 2 ( 2.6) | N.A. | 30 | 0 | N.E. | N.E. 0.3597 | |
| SEX | | | | | | | | 0.9908 |
| MALE | 320 | 12 ( 3.8) | N.A. | 161 | 2 ( 1.2) | N.A. | 3.221 ( 0.721, 14.394) 0.1052 | |
| FEMALE | 204 | 5 ( 2.5) | N.A. | 103 | 0 | N.E. | N.E. 0.1015 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Investigations. PT: Blood Alkaline Phosphatase Increased

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| DISEASE STAGE CATEGORY | | | | | | | | 0.9906 |
| STAGE IIB | 315 | 9 ( 2.9) | N.A. | 162 | 2 ( 1.2) | N.A. | 2.531 ( 0.547, 11.720) 0.2185 | |
| STAGE IIC | 209 | 8 ( 3.8) | N.A. | 102 | 0 | N.E. | N.E. 0.0448 | |
| T STAGE | | | | | | | | N.M.E. |
| T3B | 203 | 5 ( 2.5) | N.M.E. | 104 | 2 ( 1.9) | N.M.E. | N.M.E. | |
| T4A | 112 | 4 ( 3.6) | N.M.E. | 58 | 0 | N.M.E. | N.M.E. | |
| T4B | 209 | 8 ( 3.8) | N.M.E. | 102 | 0 | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Investigations. PT: Blood Alkaline Phosphatase Increased

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| REGION | | | | | | | | N.M.E. |
| US AND CANADA | 97 | 5 ( 5.2) | N.M.E. | 46 | 0 | N.M.E. | N.M.E. | |
| WESTERN EUROPE | 301 | 8 ( 2.7) | N.M.E. | 160 | 0 | N.M.E. | N.M.E. | |
| EASTERN EUROPE | 58 | 0 | N.M.E. | 28 | 0 | N.M.E. | N.M.E. | |
| AUSTRALIA | 68 | 4 ( 5.9) | N.M.E. | 30 | 2 ( 6.7) | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Infections and Infestations

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 192 ( 36.6) | N.A. | 264 | 76 ( 28.8) | N.A. | 1.443 ( 1.106, 1.883) 0.0065 | |
| AGE CATEGORY I | | | | | | | | 0.6629 |
| < 65 | 305 | 118 ( 38.7) | N.A. | 155 | 49 ( 31.6) | N.A. | 1.377 ( 0.987, 1.922) 0.0588 | |
| >= 65 | 219 | 74 ( 33.8) | N.A. | 109 | 27 ( 24.8) | N.A. | 1.554 ( 1.000, 2.416) 0.0481 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Infections and Infestations

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | 0.9038 |
| >= 18 AND < 65 | 305 | 118 ( 38.7) | N.A. | 155 | 49 ( 31.6) | N.A. | 1.377 ( 0.987, 1.922) 0.0588 | |
| >= 65 AND < 75 | 139 | 45 ( 32.4) | N.A. | 77 | 18 ( 23.4) | N.A. (15.21, N.A.) | 1.544 ( 0.893, 2.670) 0.1165 | |
| >= 75 AND < 85 | 77 | 28 ( 36.4) | N.A. (12.78, N.A.) | 30 | 8 ( 26.7) | N.A. (10.18, N.A.) | 1.606 ( 0.731, 3.526) 0.2333 | |
| SEX | | | | | | | | 0.1624 |
| MALE | 320 | 104 ( 32.5) | N.A. | 161 | 46 ( 28.6) | N.A. | 1.234 ( 0.872, 1.747) 0.2343 | |
| FEMALE | 204 | 88 ( 43.1) | N.A. (10.81, N.A.) | 103 | 30 ( 29.1) | N.A. | 1.814 ( 1.198, 2.747) 0.0043 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Infections and Infestations

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.0030* |
| STAGE IIB | 315 | 105 ( 33.3) | N.A. | 162 | 57 ( 35.2) | N.A. | 1.058 ( 0.766, 1.461) 0.7302 | |
| STAGE IIC | 209 | 87 ( 41.6) | N.A. (11.73, N.A.) | 102 | 19 ( 18.6) | N.A. | 2.576 ( 1.567, 4.234) 0.0001 | |
| T STAGE | | | | | | | | 0.0120* |
| T3B | 203 | 64 ( 31.5) | N.A. | 104 | 36 ( 34.6) | N.A. | 1.024 ( 0.681, 1.542) 0.9081 | |
| T4A | 112 | 41 ( 36.6) | N.A. (12.81, N.A.) | 58 | 21 ( 36.2) | N.A. (11.40, N.A.) | 1.114 ( 0.658, 1.886) 0.6901 | |
| T4B | 209 | 87 ( 41.6) | N.A. (11.73, N.A.) | 102 | 19 ( 18.6) | N.A. | 2.576 ( 1.567, 4.234) 0.0001 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Infections and Infestations

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.1427 |
| US AND CANADA | 97 | 25 ( 25.8) | N.A. (12.06, N.A.) | 46 | 16 ( 34.8) | N.A. | 0.768 ( 0.410, 1.439) 0.4085 | |
| WESTERN EUROPE | 301 | 120 ( 39.9) | N.A. (13.24, N.A.) | 160 | 43 ( 26.9) | N.A. | 1.706 ( 1.204, 2.418) 0.0024 | |
| EASTERN EUROPE | 58 | 19 ( 32.8) | N.A. (13.11, N.A.) | 28 | 5 ( 17.9) | N.A. | 2.170 ( 0.810, 5.815) 0.1142 | |
| AUSTRALIA | 68 | 28 ( 41.2) | N.A. (10.05, N.A.) | 30 | 12 ( 40.0) | N.A. ( 9.89, N.A.) | 1.179 ( 0.599, 2.319) 0.6338 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Infections and Infestations. PT: Urinary Tract Infection

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 16 ( 3.1) | N.A. | 264 | 2 ( 0.8) | N.A. | 4.457<br>( 1.024, 19.391)<br>0.0291 | |
| AGE CATEGORY I | | | | | | | | 0.9898 |
| < 65 | 305 | 6 ( 2.0) | N.A. | 155 | 0 | N.E. | N.E.<br>0.0722 | |
| >= 65 | 219 | 10 ( 4.6) | N.A. | 109 | 2 ( 1.8) | N.A. | 2.855<br>( 0.625, 13.039)<br>0.1565 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Infections and Infestations. PT: Urinary Tract Infection

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | N.M.E. |
| >= 18 AND < 65 | 305 | 6 ( 2.0) | N.M.E. | 155 | 0 | N.M.E. | N.M.E. | |
| >= 65 AND < 75 | 139 | 7 ( 5.0) | N.M.E. | 77 | 1 ( 1.3) | N.M.E. | N.M.E. | |
| >= 75 AND < 85 | 77 | 3 ( 3.9) | N.M.E. | 30 | 0 | N.M.E. | N.M.E. | |
| SEX | | | | | | | | 0.9872 |
| MALE | 320 | 4 ( 1.3) | N.A. | 161 | 2 ( 1.2) | N.A. | 1.147 ( 0.210, 6.282) 0.8742 | |
| FEMALE | 204 | 12 ( 5.9) | N.A. | 103 | 0 | N.E. | N.E. 0.0094 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Infections and Infestations. PT: Urinary Tract Infection

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | N.M.E. |
| STAGE IIB | 315 | 8 ( 2.5) | N.M.E. | 162 | 1 ( 0.6) | N.M.E. | N.M.E. | |
| STAGE IIC | 209 | 8 ( 3.8) | N.M.E. | 102 | 1 ( 1.0) | N.M.E. | N.M.E. | |
| T STAGE | | | | | | | | N.M.E. |
| T3B | 203 | 8 ( 3.9) | N.M.E. | 104 | 1 ( 1.0) | N.M.E. | N.M.E. | |
| T4A | 112 | 0 | N.M.E. | 58 | 0 | N.M.E. | N.M.E. | |
| T4B | 209 | 8 ( 3.8) | N.M.E. | 102 | 1 ( 1.0) | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Infections and Infestations. PT: Urinary Tract Infection

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.9743 |
| US AND CANADA | 97 | 5 ( 5.2) | N.A. | 46 | 1 ( 2.2) | N.A. | 2.805<br>( 0.328, 24.019)<br>0.3252 | |
| WESTERN EUROPE | 301 | 10 ( 3.3) | N.A. | 160 | 1 ( 0.6) | N.A. | 5.724<br>( 0.732, 44.739)<br>0.0599 | |
| EASTERN EUROPE | 58 | 1 ( 1.7) | N.A. | 28 | 0 | N.E. | N.E.<br>0.4755 | |
| AUSTRALIA | 68 | 0 | N.E. | 30 | 0 | N.E. | N.E.<br>N.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Metabolism and Nutrition Disorders

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| OVERALL | 524 | 139 ( 26.5) | N.A. | 264 | 50 ( 18.9) | N.A. | 1.535 ( 1.111, 2.122) 0.0089 | |
| AGE CATEGORY I | | | | | | | | 0.9122 |
| < 65 | 305 | 79 ( 25.9) | N.A. | 155 | 28 ( 18.1) | N.A. | 1.560 ( 1.014, 2.402) 0.0415 | |
| >= 65 | 219 | 60 ( 27.4) | N.A. | 109 | 22 ( 20.2) | N.A. | 1.503 ( 0.922, 2.451) 0.1004 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Metabolism and Nutrition Disorders

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| AGE CATEGORY II | | | | | | | | 0.8537 |
| >= 18 AND < 65 | 305 | 79 ( 25.9) | N.A. | 155 | 28 ( 18.1) | N.A. | 1.560 ( 1.014, 2.402) 0.0415 | |
| >= 65 AND < 75 | 139 | 40 ( 28.8) | N.A. | 77 | 15 ( 19.5) | N.A. | 1.619 ( 0.894, 2.932) 0.1085 | |
| >= 75 AND < 85 | 77 | 20 ( 26.0) | N.A. | 30 | 7 ( 23.3) | N.A. | 1.239 ( 0.524, 2.931) 0.6263 | |
| SEX | | | | | | | | 0.1572 |
| MALE | 320 | 92 ( 28.8) | N.A. | 161 | 28 ( 17.4) | N.A. | 1.848 ( 1.210, 2.821) 0.0039 | |
| FEMALE | 204 | 47 ( 23.0) | N.A. | 103 | 22 ( 21.4) | N.A. | 1.146 ( 0.691, 1.902) 0.5983 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Metabolism and Nutrition Disorders

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| DISEASE STAGE CATEGORY | | | | | | | | 0.1301 |
| STAGE IIB | 315 | 81 ( 25.7) | N.A. | 162 | 25 ( 15.4) | N.A. | 1.913 ( 1.221, 2.996) 0.0040 | |
| STAGE IIC | 209 | 58 ( 27.8) | N.A. | 102 | 25 ( 24.5) | N.A. | 1.149 ( 0.719, 1.837) 0.5602 | |
| T STAGE | | | | | | | | 0.1824 |
| T3B | 203 | 51 ( 25.1) | N.A. | 104 | 13 ( 12.5) | N.A. | 2.419 ( 1.315, 4.450) 0.0034 | |
| T4A | 112 | 30 ( 26.8) | N.A. | 58 | 12 ( 20.7) | N.A. | 1.387 ( 0.710, 2.710) 0.3373 | |
| T4B | 209 | 58 ( 27.8) | N.A. | 102 | 25 ( 24.5) | N.A. | 1.149 ( 0.719, 1.837) 0.5602 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Metabolism and Nutrition Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.9604 |
| US AND CANADA | 97 | 47 ( 48.5) | 12.16 ( 5.55, N.A.) | 46 | 17 ( 37.0) | N.A. (10.09, N.A.) | 1.578 ( 0.905, 2.751) 0.1063 | |
| WESTERN EUROPE | 301 | 72 ( 23.9) | N.A. | 160 | 26 ( 16.3) | N.A. | 1.581 ( 1.010, 2.476) 0.0433 | |
| EASTERN EUROPE | 58 | 12 ( 20.7) | N.A. | 28 | 5 ( 17.9) | N.A. | 1.250 ( 0.440, 3.549) 0.6780 | |
| AUSTRALIA | 68 | 8 ( 11.8) | N.A. | 30 | 2 ( 6.7) | N.A. | 2.021 ( 0.429, 9.531) 0.3640 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Metabolism and Nutrition Disorders. PT: Decreased Appetite

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| OVERALL | 524 | 42 ( 8.0) | N.A. | 264 | 8 ( 3.0) | N.A. | 2.852 ( 1.339, 6.076) 0.0045 | |
| AGE CATEGORY I | | | | | | | | 0.2939 |
| < 65 | 305 | 23 ( 7.5) | N.A. | 155 | 6 ( 3.9) | N.A. | 2.061 ( 0.839, 5.062) 0.1070 | |
| >= 65 | 219 | 19 ( 8.7) | N.A. | 109 | 2 ( 1.8) | N.A. | 5.251 ( 1.223, 22.555) 0.0126 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Metabolism and Nutrition Disorders. PT: Decreased Appetite

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| AGE CATEGORY II | | | | | | | | 0.4538 |
| >= 18 AND < 65 | 305 | 23 ( 7.5) | N.A. | 155 | 6 ( 3.9) | N.A. | 2.061 ( 0.839, 5.062) 0.1070 | |
| >= 65 AND < 75 | 139 | 14 ( 10.1) | N.A. | 77 | 1 ( 1.3) | N.A. | 8.641 ( 1.136, 65.730) 0.0121 | |
| >= 75 AND < 85 | 77 | 5 ( 6.5) | N.A. | 30 | 1 ( 3.3) | N.A. | 2.108 ( 0.246, 18.054) 0.4863 | |
| SEX | | | | | | | | 0.6332 |
| MALE | 320 | 25 ( 7.8) | N.A. | 161 | 4 ( 2.5) | N.A. | 3.389 ( 1.179, 9.739) 0.0160 | |
| FEMALE | 204 | 17 ( 8.3) | N.A. | 103 | 4 ( 3.9) | N.A. | 2.315 ( 0.779, 6.881) 0.1200 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Metabolism and Nutrition Disorders. PT: Decreased Appetite

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| DISEASE STAGE CATEGORY | | | | | | | | 0.5122 |
| STAGE IIB | 315 | 30 ( 9.5) | N.A. | 162 | 5 ( 3.1) | N.A. | 3.399 ( 1.318, 8.762) 0.0071 | |
| STAGE IIC | 209 | 12 ( 5.7) | N.A. | 102 | 3 ( 2.9) | N.A. | 2.010 ( 0.567, 7.124) 0.2695 | |
| T STAGE | | | | | | | | 0.5928 |
| T3B | 203 | 18 ( 8.9) | N.A. | 104 | 2 ( 1.9) | N.A. | 5.197 ( 1.205, 22.408) 0.0136 | |
| T4A | 112 | 12 ( 10.7) | N.A. | 58 | 3 ( 5.2) | N.A. | 2.243 ( 0.633, 7.954) 0.1987 | |
| T4B | 209 | 12 ( 5.7) | N.A. | 102 | 3 ( 2.9) | N.A. | 2.010 ( 0.567, 7.124) 0.2695 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Metabolism and Nutrition Disorders. PT: Decreased Appetite

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.9958 |
| US AND CANADA | 97 | 9 ( 9.3) | N.A. | 46 | 2 ( 4.3) | N.A. | 2.469 ( 0.532, 11.450) 0.2319 | |
| WESTERN EUROPE | 301 | 20 ( 6.6) | N.A. | 160 | 5 ( 3.1) | N.A. | 2.229 ( 0.836, 5.940) 0.0999 | |
| EASTERN EUROPE | 58 | 7 ( 12.1) | N.A. | 28 | 0 | N.E. | N.E. 0.0538 | |
| AUSTRALIA | 68 | 6 ( 8.8) | N.A. | 30 | 1 ( 3.3) | N.A. | 3.025 ( 0.364, 25.161) 0.2814 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Nervous System Disorders. PT: Syncope

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 10 ( 1.9) | N.A. | 264 | 0 | N.E. | N.E.<br>0.0190 | |
| AGE CATEGORY I | | | | | | | | N.M.E. |
| < 65 | 305 | 4 ( 1.3) | N.M.E. | 155 | 0 | N.M.E. | N.M.E. | |
| >= 65 | 219 | 6 ( 2.7) | N.M.E. | 109 | 0 | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Nervous System Disorders. PT: Syncope

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| AGE CATEGORY II | | | | | | | | N.M.E. |
| >= 18 AND < 65 | 305 | 4 ( 1.3) | N.M.E. | 155 | 0 | N.M.E. | N.M.E. | |
| >= 65 AND < 75 | 139 | 3 ( 2.2) | N.M.E. | 77 | 0 | N.M.E. | N.M.E. | |
| >= 75 AND < 85 | 77 | 3 ( 3.9) | N.M.E. | 30 | 0 | N.M.E. | N.M.E. | |
| SEX | | | | | | | | N.M.E. |
| MALE | 320 | 5 ( 1.6) | N.M.E. | 161 | 0 | N.M.E. | N.M.E. | |
| FEMALE | 204 | 5 ( 2.5) | N.M.E. | 103 | 0 | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Nervous System Disorders. PT: Syncope

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | N.M.E. |
| STAGE IIB | 315 | 7 ( 2.2) | N.M.E. | 162 | 0 | N.M.E. | N.M.E. | |
| STAGE IIC | 209 | 3 ( 1.4) | N.M.E. | 102 | 0 | N.M.E. | N.M.E. | |
| T STAGE | | | | | | | | N.M.E. |
| T3B | 203 | 2 ( 1.0) | N.M.E. | 104 | 0 | N.M.E. | N.M.E. | |
| T4A | 112 | 5 ( 4.5) | N.M.E. | 58 | 0 | N.M.E. | N.M.E. | |
| T4B | 209 | 3 ( 1.4) | N.M.E. | 102 | 0 | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Nervous System Disorders. PT: Syncope

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | N.M.E. |
| US AND CANADA | 97 | 1 ( 1.0) | N.M.E. | 46 | 0 | N.M.E. | N.M.E. | |
| WESTERN EUROPE | 301 | 8 ( 2.7) | N.M.E. | 160 | 0 | N.M.E. | N.M.E. | |
| EASTERN EUROPE | 58 | 1 ( 1.7) | N.M.E. | 28 | 0 | N.M.E. | N.M.E. | |
| AUSTRALIA | 68 | 0 | N.M.E. | 30 | 0 | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Respiratory, Thoracic and Mediastinal Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 117 ( 22.3) | N.A. | 264 | 41 ( 15.5) | N.A. | 1.578<br>( 1.106, 2.253)<br>0.0112 | |
| AGE CATEGORY I | | | | | | | | 0.0554 |
| < 65 | 305 | 70 ( 23.0) | N.A. | 155 | 18 ( 11.6) | N.A. | 2.179<br>( 1.298, 3.658)<br>0.0025 | |
| >= 65 | 219 | 47 ( 21.5) | N.A. | 109 | 23 ( 21.1) | N.A. | 1.105<br>( 0.671, 1.820)<br>0.6952 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Respiratory, Thoracic and Mediastinal Disorders

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| AGE CATEGORY II | | | | | | | | 0.0560 |
| >= 18 AND < 65 | 305 | 70 ( 23.0) | N.A. | 155 | 18 ( 11.6) | N.A. | 2.179 ( 1.298, 3.658) 0.0025 | |
| >= 65 AND < 75 | 139 | 28 ( 20.1) | N.A. | 77 | 13 ( 16.9) | N.A. | 1.301 ( 0.674, 2.513) 0.4315 | |
| >= 75 AND < 85 | 77 | 18 ( 23.4) | N.A. | 30 | 10 ( 33.3) | N.A. ( 7.46, N.A.) | 0.730 ( 0.337, 1.582) 0.4231 | |
| SEX | | | | | | | | 0.1722 |
| MALE | 320 | 68 ( 21.3) | N.A. | 161 | 19 ( 11.8) | N.A. | 1.983 ( 1.192, 3.298) 0.0072 | |
| FEMALE | 204 | 49 ( 24.0) | N.A. | 103 | 22 ( 21.4) | N.A. | 1.212 ( 0.733, 2.004) 0.4533 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Respiratory, Thoracic and Mediastinal Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.8802 |
| STAGE IIB | 315 | 76 ( 24.1) | N.A. | 162 | 28 ( 17.3) | N.A. | 1.558 ( 1.010, 2.403) 0.0434 | |
| STAGE IIC | 209 | 41 ( 19.6) | N.A. | 102 | 13 ( 12.7) | N.A. | 1.644 ( 0.881, 3.068) 0.1141 | |
| T STAGE | | | | | | | | 0.8003 |
| T3B | 203 | 46 ( 22.7) | N.A. | 104 | 19 ( 18.3) | N.A. | 1.413 ( 0.828, 2.413) 0.2028 | |
| T4A | 112 | 30 ( 26.8) | N.A. | 58 | 9 ( 15.5) | N.A. | 1.873 ( 0.889, 3.947) 0.0934 | |
| T4B | 209 | 41 ( 19.6) | N.A. | 102 | 13 ( 12.7) | N.A. | 1.644 ( 0.881, 3.068) 0.1141 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Respiratory, Thoracic and Mediastinal Disorders

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| REGION | | | | | | | | 0.0861 |
| US AND CANADA | 97 | 25 ( 25.8) | N.A. (12.48, N.A.) | 46 | 16 ( 34.8) | N.A. (12.48, N.A.) | 0.802 ( 0.428, 1.502) 0.4880 | |
| WESTERN EUROPE | 301 | 64 ( 21.3) | N.A. | 160 | 20 ( 12.5) | N.A. | 1.849 ( 1.119, 3.056) 0.0148 | |
| EASTERN EUROPE | 58 | 4 ( 6.9) | N.A. | 28 | 1 ( 3.6) | N.A. | 2.054 ( 0.230, 18.376) 0.5108 | |
| AUSTRALIA | 68 | 24 ( 35.3) | N.A. ( 9.23, N.A.) | 30 | 4 ( 13.3) | N.A. | 3.179 ( 1.102, 9.171) 0.0239 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Endocrine Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 114 ( 21.8) | N.A. | 264 | 10 ( 3.8) | N.A. | 6.771 ( 3.546, 12.928) <0.0001 | |
| AGE CATEGORY I | | | | | | | | 0.4191 |
| < 65 | 305 | 65 ( 21.3) | N.A. | 155 | 7 ( 4.5) | N.A. | 5.515 ( 2.528, 12.032) <0.0001 | |
| >= 65 | 219 | 49 ( 22.4) | N.A. | 109 | 3 ( 2.8) | N.A. | 9.658 ( 3.009, 30.996) <0.0001 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Endocrine Disorders

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| AGE CATEGORY II | | | | | | | | 0.6783 |
| >= 18 AND < 65 | 305 | 65 ( 21.3) | N.A. | 155 | 7 ( 4.5) | N.A. | 5.515 ( 2.528, 12.032) <0.0001 | |
| >= 65 AND < 75 | 139 | 34 ( 24.5) | N.A. | 77 | 2 ( 2.6) | N.A. | 11.193 ( 2.688, 46.598) <0.0001 | |
| >= 75 AND < 85 | 77 | 15 ( 19.5) | N.A. | 30 | 1 ( 3.3) | N.A. | 6.929 ( 0.914, 52.528) 0.0294 | |
| SEX | | | | | | | | 0.6593 |
| MALE | 320 | 57 ( 17.8) | N.A. | 161 | 4 ( 2.5) | N.A. | 8.275 ( 3.001, 22.813) <0.0001 | |
| FEMALE | 204 | 57 ( 27.9) | N.A. | 103 | 6 ( 5.8) | N.A. | 5.881 ( 2.534, 13.647) <0.0001 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Endocrine Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.6777 |
| STAGE IIB | 315 | 59 ( 18.7) | N.A. | 162 | 6 ( 3.7) | N.A. | 5.935 ( 2.561, 13.752) <0.0001 | |
| STAGE IIC | 209 | 55 ( 26.3) | N.A. | 102 | 4 ( 3.9) | N.A. | 7.924 ( 2.871, 21.873) <0.0001 | |
| T STAGE | | | | | | | | 0.3208 |
| T3B | 203 | 44 ( 21.7) | N.A. | 104 | 3 ( 2.9) | N.A. | 9.172 ( 2.846, 29.556) <0.0001 | |
| T4A | 112 | 15 ( 13.4) | N.A. | 58 | 3 ( 5.2) | N.A. | 2.819 ( 0.816, 9.741) 0.0870 | |
| T4B | 209 | 55 ( 26.3) | N.A. | 102 | 4 ( 3.9) | N.A. | 7.924 ( 2.871, 21.873) <0.0001 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Endocrine Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.7779 |
| US AND CANADA | 97 | 25 ( 25.8) | N.A. | 46 | 2 ( 4.3) | N.A. | 7.735 ( 1.828, 32.724) 0.0010 | |
| WESTERN EUROPE | 301 | 66 ( 21.9) | N.A. | 160 | 5 ( 3.1) | N.A. | 8.017 ( 3.229, 19.904) <0.0001 | |
| EASTERN EUROPE | 58 | 11 ( 19.0) | N.A. | 28 | 2 ( 7.1) | N.A. | 3.190 ( 0.707, 14.406) 0.1112 | |
| AUSTRALIA | 68 | 12 ( 17.6) | N.A. | 30 | 1 ( 3.3) | N.A. | 6.293 ( 0.817, 48.451) 0.0429 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Endocrine Disorders. PT: Hypothyroidism

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| OVERALL | 524 | 67 ( 12.8) | N.A. | 264 | 0 | N.E. | N.E. <0.0001 | |
| AGE CATEGORY I | | | | | | | | 0.9999 |
| < 65 | 305 | 37 ( 12.1) | N.A. | 155 | 0 | N.E. | N.E. <0.0001 | |
| >= 65 | 219 | 30 ( 13.7) | N.A. | 109 | 0 | N.E. | N.E. <0.0001 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Endocrine Disorders. PT: Hypothyroidism

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| AGE CATEGORY II | | | | | | | | >0.9999 |
| >= 18 AND < 65 | 305 | 37 ( 12.1) | N.A. | 155 | 0 | N.E. | N.E. <0.0001 | |
| >= 65 AND < 75 | 139 | 19 ( 13.7) | N.A. | 77 | 0 | N.E. | N.E. 0.0006 | |
| >= 75 AND < 85 | 77 | 11 ( 14.3) | N.A. | 30 | 0 | N.E. | N.E. 0.0278 | |
| SEX | | | | | | | | 0.9997 |
| MALE | 320 | 33 ( 10.3) | N.A. | 161 | 0 | N.E. | N.E. <0.0001 | |
| FEMALE | 204 | 34 ( 16.7) | N.A. | 103 | 0 | N.E. | N.E. <0.0001 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Endocrine Disorders. PT: Hypothyroidism

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.9998 |
| STAGE IIB | 315 | 36 ( 11.4) | N.A. | 162 | 0 | N.E. | N.E.<br><0.0001 | |
| STAGE IIC | 209 | 31 ( 14.8) | N.A. | 102 | 0 | N.E. | N.E.<br><0.0001 | |
| T STAGE | | | | | | | | >0.9999 |
| T3B | 203 | 27 ( 13.3) | N.A. | 104 | 0 | N.E. | N.E.<br><0.0001 | |
| T4A | 112 | 9 ( 8.0) | N.A. | 58 | 0 | N.E. | N.E.<br>0.0216 | |
| T4B | 209 | 31 ( 14.8) | N.A. | 102 | 0 | N.E. | N.E.<br><0.0001 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Endocrine Disorders. PT: Hypothyroidism

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| REGION | | | | | | | | >0.9999 |
| US AND CANADA | 97 | 18 ( 18.6) | N.A. | 46 | 0 | N.E. | N.E. 0.0014 | |
| WESTERN EUROPE | 301 | 34 ( 11.3) | N.A. | 160 | 0 | N.E. | N.E. <0.0001 | |
| EASTERN EUROPE | 58 | 8 ( 13.8) | N.A. | 28 | 0 | N.E. | N.E. 0.0364 | |
| AUSTRALIA | 68 | 7 ( 10.3) | N.A. | 30 | 0 | N.E. | N.E. 0.0580 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Endocrine Disorders. PT: Hyperthyroidism

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 42 ( 8.0) | N.A. | 264 | 4 ( 1.5) | N.A. | 5.670 ( 2.033, 15.815) 0.0002 | |
| AGE CATEGORY I | | | | | | | | 0.7014 |
| < 65 | 305 | 25 ( 8.2) | N.A. | 155 | 2 ( 1.3) | N.A. | 6.813 ( 1.613, 28.766) 0.0024 | |
| >= 65 | 219 | 17 ( 7.8) | N.A. | 109 | 2 ( 1.8) | N.A. | 4.510 ( 1.042, 19.529) 0.0271 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Endocrine Disorders. PT: Hyperthyroidism

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| AGE CATEGORY II | | | | | | | | 0.7887 |
| >= 18 AND < 65 | 305 | 25 ( 8.2) | N.A. | 155 | 2 ( 1.3) | N.A. | 6.813 ( 1.613, 28.766) 0.0024 | |
| >= 65 AND < 75 | 139 | 11 ( 7.9) | N.A. | 77 | 2 ( 2.6) | N.A. | 3.224 ( 0.714, 14.547) 0.1074 | |
| >= 75 AND < 85 | 77 | 6 ( 7.8) | N.A. | 30 | 0 | N.E. | N.E. 0.1133 | |
| SEX | | | | | | | | 0.9855 |
| MALE | 320 | 19 ( 5.9) | N.A. | 161 | 4 ( 2.5) | N.A. | 2.535 ( 0.862, 7.453) 0.0799 | |
| FEMALE | 204 | 23 ( 11.3) | N.A. | 103 | 0 | N.E. | N.E. 0.0004 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Endocrine Disorders. PT: Hyperthyroidism

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| DISEASE STAGE CATEGORY | | | | | | | | 0.7202 |
| STAGE IIB | 315 | 24 ( 7.6) | N.A. | 162 | 2 ( 1.2) | N.A. | 6.649 ( 1.571, 28.140) 0.0029 | |
| STAGE IIC | 209 | 18 ( 8.6) | N.A. | 102 | 2 ( 2.0) | N.A. | 4.621 ( 1.072, 19.921) 0.0239 | |
| T STAGE | | | | | | | | 0.7197 |
| T3B | 203 | 18 ( 8.9) | N.A. | 104 | 1 ( 1.0) | N.A. | 10.153 ( 1.356, 76.040) 0.0052 | |
| T4A | 112 | 6 ( 5.4) | N.A. | 58 | 1 ( 1.7) | N.A. | 3.218 ( 0.387, 26.726) 0.2526 | |
| T4B | 209 | 18 ( 8.6) | N.A. | 102 | 2 ( 2.0) | N.A. | 4.621 ( 1.072, 19.921) 0.0239 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Endocrine Disorders. PT: Hyperthyroidism

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.3578 |
| US AND CANADA | 97 | 5 ( 5.2) | N.A. | 46 | 1 ( 2.2) | N.A. | 2.489 ( 0.291, 21.307) 0.3890 | |
| WESTERN EUROPE | 301 | 25 ( 8.3) | N.A. | 160 | 1 ( 0.6) | N.A. | 13.969 ( 1.893,>99.999) 0.0007 | |
| EASTERN EUROPE | 58 | 5 ( 8.6) | N.A. | 28 | 2 ( 7.1) | N.A. | 1.358 ( 0.263, 7.002) 0.7137 | |
| AUSTRALIA | 68 | 7 ( 10.3) | N.A. | 30 | 0 | N.E. | N.E. 0.0630 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Injury, Poisoning and Procedural Complications. PT: Infusion Related Reaction

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| OVERALL | 524 | 28 ( 5.3) | N.A. | 264 | 2 ( 0.8) | N.A. | 7.257 ( 1.729, 30.461) 0.0015 | |
| AGE CATEGORY I | | | | | | | | 0.7516 |
| < 65 | 305 | 17 ( 5.6) | N.A. | 155 | 1 ( 0.6) | N.A. | 8.914 ( 1.187, 66.961) 0.0099 | |
| >= 65 | 219 | 11 ( 5.0) | N.A. | 109 | 1 ( 0.9) | N.A. | 5.589 ( 0.722, 43.287) 0.0630 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Injury, Poisoning and Procedural Complications. PT: Infusion Related Reaction

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| AGE CATEGORY II | | | | | | | | 0.9316 |
| >= 18 AND < 65 | 305 | 17 ( 5.6) | N.A. | 155 | 1 ( 0.6) | N.A. | 8.914 ( 1.187, 66.961) 0.0099 | |
| >= 65 AND < 75 | 139 | 9 ( 6.5) | N.A. | 77 | 1 ( 1.3) | N.A. | 5.115 ( 0.648, 40.373) 0.0841 | |
| >= 75 AND < 85 | 77 | 1 ( 1.3) | N.A. | 30 | 0 | N.E. | N.E. 0.5325 | |
| SEX | | | | | | | | 0.9886 |
| MALE | 320 | 17 ( 5.3) | N.A. | 161 | 2 ( 1.2) | N.A. | 4.372 ( 1.010, 18.925) 0.0309 | |
| FEMALE | 204 | 11 ( 5.4) | N.A. | 103 | 0 | N.E. | N.E. 0.0161 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Injury, Poisoning and Procedural Complications. PT: Infusion Related Reaction

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| DISEASE STAGE CATEGORY | | | | | | | | 0.8030 |
| STAGE IIB | 315 | 16 ( 5.1) | N.A. | 162 | 1 ( 0.6) | N.A. | 8.545 ( 1.133, 64.422) 0.0122 | |
| STAGE IIC | 209 | 12 ( 5.7) | N.A. | 102 | 1 ( 1.0) | N.A. | 5.915 ( 0.769, 45.486) 0.0519 | |
| T STAGE | | | | | | | | 0.9899 |
| T3B | 203 | 9 ( 4.4) | N.A. | 104 | 1 ( 1.0) | N.A. | 4.816 ( 0.610, 38.018) 0.0993 | |
| T4A | 112 | 7 ( 6.3) | N.A. | 58 | 0 | N.E. | N.E. 0.0540 | |
| T4B | 209 | 12 ( 5.7) | N.A. | 102 | 1 ( 1.0) | N.A. | 5.915 ( 0.769, 45.486) 0.0519 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Injury, Poisoning and Procedural Complications. PT: Infusion Related Reaction

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| REGION | | | | | | | | >0.9999 |
| US AND CANADA | 97 | 10 ( 10.3) | N.A. | 46 | 1 ( 2.2) | N.A. | 5.031 ( 0.644, 39.304) 0.0861 | |
| WESTERN EUROPE | 301 | 10 ( 3.3) | N.A. | 160 | 1 ( 0.6) | N.A. | 5.343 ( 0.684, 41.742) 0.0730 | |
| EASTERN EUROPE | 58 | 1 ( 1.7) | N.A. | 28 | 0 | N.E. | N.E. 0.4617 | |
| AUSTRALIA | 68 | 7 ( 10.3) | N.A. | 30 | 0 | N.E. | N.E. 0.0708 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Blood and Lymphatic System Disorders. PT: Eosinophilia

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| OVERALL | 524 | 19 ( 3.6) | N.A. | 264 | 2 ( 0.8) | N.A. | 5.115 ( 1.191, 21.965) 0.0144 | |
| AGE CATEGORY I | | | | | | | | 0.7171 |
| < 65 | 305 | 12 ( 3.9) | N.A. | 155 | 1 ( 0.6) | N.A. | 6.563 ( 0.853, 50.487) 0.0370 | |
| >= 65 | 219 | 7 ( 3.2) | N.A. | 109 | 1 ( 0.9) | N.A. | 3.634 ( 0.447, 29.537) 0.1962 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Blood and Lymphatic System Disorders. PT: Eosinophilia

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| AGE CATEGORY II | | | | | | | | 0.8769 |
| >= 18 AND < 65 | 305 | 12 ( 3.9) | N.A. | 155 | 1 ( 0.6) | N.A. | 6.563 ( 0.853, 50.487) 0.0370 | |
| >= 65 AND < 75 | 139 | 5 ( 3.6) | N.A. | 77 | 1 ( 1.3) | N.A. | 2.843 ( 0.332, 24.339) 0.3184 | |
| >= 75 AND < 85 | 77 | 2 ( 2.6) | N.A. | 30 | 0 | N.E. | N.E. 0.3590 | |
| SEX | | | | | | | | 0.4959 |
| MALE | 320 | 14 ( 4.4) | N.A. | 161 | 1 ( 0.6) | N.A. | 7.546 ( 0.992, 57.400) 0.0214 | |
| FEMALE | 204 | 5 ( 2.5) | N.A. | 103 | 1 ( 1.0) | N.A. | 2.680 ( 0.313, 22.942) 0.3489 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Blood and Lymphatic System Disorders. PT: Eosinophilia

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| DISEASE STAGE CATEGORY | | | | | | | | 0.8929 |
| STAGE IIB | 315 | 10 ( 3.2) | N.A. | 162 | 1 ( 0.6) | N.A. | 5.481 ( 0.702, 42.829) 0.0681 | |
| STAGE IIC | 209 | 9 ( 4.3) | N.A. | 102 | 1 ( 1.0) | N.A. | 4.656 ( 0.590, 36.765) 0.1081 | |
| T STAGE | | | | | | | | 0.9803 |
| T3B | 203 | 6 ( 3.0) | N.A. | 104 | 1 ( 1.0) | N.A. | 3.324 ( 0.400, 27.620) 0.2380 | |
| T4A | 112 | 4 ( 3.6) | N.A. | 58 | 0 | N.E. | N.E. 0.1422 | |
| T4B | 209 | 9 ( 4.3) | N.A. | 102 | 1 ( 1.0) | N.A. | 4.656 ( 0.590, 36.765) 0.1081 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Blood and Lymphatic System Disorders. PT: Eosinophilia

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | >0.9999 |
| US AND CANADA | 97 | 6 ( 6.2) | N.A. | 46 | 0 | N.E. | N.E.<br>0.0689 | |
| WESTERN EUROPE | 301 | 13 ( 4.3) | N.A. | 160 | 2 ( 1.3) | N.A. | 3.544<br>( 0.800, 15.702)<br>0.0752 | |
| EASTERN EUROPE | 58 | 0 | N.E. | 28 | 0 | N.E. | N.E.<br>N.E. | |
| AUSTRALIA | 68 | 0 | N.E. | 30 | 0 | N.E. | N.E.<br>N.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Eye Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 48 ( 9.2) | N.A. | 264 | 13 ( 4.9) | N.A. | 2.009 ( 1.088, 3.708) 0.0229 | |
| AGE CATEGORY I | | | | | | | | 0.5266 |
| < 65 | 305 | 25 ( 8.2) | N.A. | 155 | 8 ( 5.2) | N.A. | 1.694 ( 0.764, 3.756) 0.1894 | |
| >= 65 | 219 | 23 ( 10.5) | N.A. | 109 | 5 ( 4.6) | N.A. | 2.520 ( 0.958, 6.633) 0.0525 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Eye Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | 0.0899 |
| >= 18 AND < 65 | 305 | 25 ( 8.2) | N.A. | 155 | 8 ( 5.2) | N.A. | 1.694 ( 0.764, 3.756) 0.1894 | |
| >= 65 AND < 75 | 139 | 17 ( 12.2) | N.A. | 77 | 1 ( 1.3) | N.A. | 10.539 ( 1.403, 79.194) 0.0043 | |
| >= 75 AND < 85 | 77 | 5 ( 6.5) | N.A. | 30 | 3 ( 10.0) | N.A. | 0.681 ( 0.163, 2.854) 0.5973 | |
| SEX | | | | | | | | 0.6849 |
| MALE | 320 | 27 ( 8.4) | N.A. | 161 | 8 ( 5.0) | N.A. | 1.803 ( 0.819, 3.968) 0.1376 | |
| FEMALE | 204 | 21 ( 10.3) | N.A. | 103 | 5 ( 4.9) | N.A. | 2.366 ( 0.892, 6.277) 0.0746 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Eye Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.0811 |
| STAGE IIB | 315 | 30 ( 9.5) | N.A. | 162 | 5 ( 3.1) | N.A. | 3.499 ( 1.357, 9.022) 0.0057 | |
| STAGE IIC | 209 | 18 ( 8.6) | N.A. | 102 | 8 ( 7.8) | N.A. | 1.116 ( 0.485, 2.567) 0.7957 | |
| T STAGE | | | | | | | | 0.1935 |
| T3B | 203 | 17 ( 8.4) | N.A. | 104 | 2 ( 1.9) | N.A. | 5.024 ( 1.160, 21.756) 0.0164 | |
| T4A | 112 | 13 ( 11.6) | N.A. | 58 | 3 ( 5.2) | N.A. | 2.457 ( 0.700, 8.625) 0.1469 | |
| T4B | 209 | 18 ( 8.6) | N.A. | 102 | 8 ( 7.8) | N.A. | 1.116 ( 0.485, 2.567) 0.7957 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Eye Disorders

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| REGION | | | | | | | | 0.0717 |
| US AND CANADA | 97 | 8 ( 8.2) | N.A. | 46 | 7 ( 15.2) | N.A. | 0.579 ( 0.210, 1.599) 0.2850 | |
| WESTERN EUROPE | 301 | 29 ( 9.6) | N.A. | 160 | 5 ( 3.1) | N.A. | 3.296 ( 1.276, 8.515) 0.0090 | |
| EASTERN EUROPE | 58 | 2 ( 3.4) | N.A. | 28 | 0 | N.E. | N.E. 0.3129 | |
| AUSTRALIA | 68 | 9 ( 13.2) | N.A. | 30 | 1 ( 3.3) | N.A. | 4.596 ( 0.582, 36.319) 0.1119 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Eye Disorders. PT: Dry Eye

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| OVERALL | 524 | 18 ( 3.4) | N.A. | 264 | 3 ( 1.1) | N.A. | 3.201 ( 0.943, 10.870) 0.0485 | |
| AGE CATEGORY I | | | | | | | | 0.5927 |
| < 65 | 305 | 9 ( 3.0) | N.A. | 155 | 2 ( 1.3) | N.A. | 2.393 ( 0.517, 11.077) 0.2494 | |
| >= 65 | 219 | 9 ( 4.1) | N.A. | 109 | 1 ( 0.9) | N.A. | 4.836 ( 0.612, 38.196) 0.0981 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Eye Disorders. PT: Dry Eye

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| AGE CATEGORY II | | | | | | | | 0.9138 |
| >= 18 AND < 65 | 305 | 9 ( 3.0) | N.A. | 155 | 2 ( 1.3) | N.A. | 2.393 ( 0.517, 11.077) 0.2494 | |
| >= 65 AND < 75 | 139 | 7 ( 5.0) | N.A. | 77 | 1 ( 1.3) | N.A. | 4.117 ( 0.507, 33.464) 0.1507 | |
| >= 75 AND < 85 | 77 | 2 ( 2.6) | N.A. | 30 | 0 | N.E. | N.E. 0.3433 | |
| SEX | | | | | | | | 0.3671 |
| MALE | 320 | 7 ( 2.2) | N.A. | 161 | 2 ( 1.2) | N.A. | 1.834 ( 0.381, 8.833) 0.4424 | |
| FEMALE | 204 | 11 ( 5.4) | N.A. | 103 | 1 ( 1.0) | N.A. | 6.084 ( 0.785, 47.143) 0.0485 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Eye Disorders. PT: Dry Eye

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| DISEASE STAGE CATEGORY | | | | | | | | 0.4519 |
| STAGE IIB | 315 | 15 ( 4.8) | N.A. | 162 | 2 ( 1.2) | N.A. | 4.256 ( 0.973, 18.618) 0.0361 | |
| STAGE IIC | 209 | 3 ( 1.4) | N.A. | 102 | 1 ( 1.0) | N.A. | 1.456 ( 0.151, 13.998) 0.7433 | |
| T STAGE | | | | | | | | N.M.E. |
| T3B | 203 | 8 ( 3.9) | N.M.E. | 104 | 1 ( 1.0) | N.M.E. | N.M.E. | |
| T4A | 112 | 7 ( 6.3) | N.M.E. | 58 | 1 ( 1.7) | N.M.E. | N.M.E. | |
| T4B | 209 | 3 ( 1.4) | N.M.E. | 102 | 1 ( 1.0) | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

Protocol: CA20976K 

Table 22.20.1
Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Eye Disorders. PT: Dry Eye

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| REGION | | | | | | | | 0.4503 |
| US AND CANADA | 97 | 2 ( 2.1) | N.A. | 46 | 2 ( 4.3) | N.A. | 0.524 ( 0.074, 3.725) 0.5113 | |
| WESTERN EUROPE | 301 | 10 ( 3.3) | N.A. | 160 | 1 ( 0.6) | N.A. | 5.522 ( 0.707, 43.144) 0.0666 | |
| EASTERN EUROPE | 58 | 1 ( 1.7) | N.A. | 28 | 0 | N.E. | N.E. 0.4755 | |
| AUSTRALIA | 68 | 5 ( 7.4) | N.A. | 30 | 0 | N.E. | N.E. 0.1209 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:15:44

**Anhang 4-G 3.2.4.2: Subgruppenanalysen für Endpunkt schwere UE auf SOC/PT-Ebene aus CA209-76K**

Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

All Subjects with an Event

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 148 ( 28.2) | N.A. | 264 | 48 ( 18.2) | N.A. | 1.737 ( 1.254, 2.405) 0.0008 | |
| AGE CATEGORY I | | | | | | | | 0.4278 |
| < 65 | 305 | 77 ( 25.2) | N.A. | 155 | 22 ( 14.2) | N.A. | 2.004 ( 1.247, 3.219) 0.0034 | |
| >= 65 | 219 | 71 ( 32.4) | N.A. | 109 | 26 ( 23.9) | N.A. | 1.510 ( 0.963, 2.367) 0.0702 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:04

Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

All Subjects with an Event

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | 0.6976 |
| >= 18 AND < 65 | 305 | 77 ( 25.2) | N.A. | 155 | 22 ( 14.2) | N.A. | 2.004 ( 1.247, 3.219) 0.0034 | |
| >= 65 AND < 75 | 139 | 38 ( 27.3) | N.A. | 77 | 16 ( 20.8) | N.A. | 1.448 ( 0.807, 2.597) 0.2121 | |
| >= 75 AND < 85 | 77 | 32 ( 41.6) | N.A. (10.87, N.A.) | 30 | 9 ( 30.0) | N.A. (14.52, N.A.) | 1.553 ( 0.741, 3.254) 0.2396 | |
| SEX | | | | | | | | 0.5069 |
| MALE | 320 | 102 ( 31.9) | N.A. | 161 | 31 ( 19.3) | N.A. | 1.872 ( 1.252, 2.799) 0.0019 | |
| FEMALE | 204 | 46 ( 22.5) | N.A. | 103 | 17 ( 16.5) | N.A. | 1.487 ( 0.852, 2.593) 0.1598 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:04

Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

All Subjects with an Event

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| DISEASE STAGE CATEGORY | | | | | | | | 0.2980 |
| STAGE IIB | 315 | 87 ( 27.6) | N.A. | 162 | 33 ( 20.4) | N.A. | 1.536 ( 1.029, 2.293) 0.0343 | |
| STAGE IIC | 209 | 61 ( 29.2) | N.A. | 102 | 15 ( 14.7) | N.A. | 2.172 ( 1.235, 3.823) 0.0058 | |
| T STAGE | | | | | | | | 0.5616 |
| T3B | 203 | 50 ( 24.6) | N.A. | 104 | 20 ( 19.2) | N.A. | 1.475 ( 0.878, 2.478) 0.1396 | |
| T4A | 112 | 37 ( 33.0) | N.A. | 58 | 13 ( 22.4) | N.A. | 1.628 ( 0.865, 3.064) 0.1265 | |
| T4B | 209 | 61 ( 29.2) | N.A. | 102 | 15 ( 14.7) | N.A. | 2.172 ( 1.235, 3.823) 0.0058 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:04

Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

All Subjects with an Event

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.2081 |
| US AND CANADA | 97 | 34 ( 35.1) | N.A. (14.52, N.A.) | 46 | 14 ( 30.4) | N.A. | 1.487 ( 0.796, 2.774) 0.2092 | |
| WESTERN EUROPE | 301 | 85 ( 28.2) | N.A. | 160 | 22 ( 13.8) | N.A. | 2.231 ( 1.396, 3.566) 0.0006 | |
| EASTERN EUROPE | 58 | 6 ( 10.3) | N.A. | 28 | 5 ( 17.9) | N.A. | 0.601 ( 0.183, 1.970) 0.3955 | |
| AUSTRALIA | 68 | 23 ( 33.8) | N.A. | 30 | 7 ( 23.3) | N.A. | 1.695 ( 0.727, 3.954) 0.2167 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:04

Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Investigations

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 43 ( 8.2) | N.A. | 264 | 9 ( 3.4) | N.A. | 2.581<br>( 1.258, 5.295)<br>0.0073 | |
| AGE CATEGORY I | | | | | | | | 0.8967 |
| < 65 | 305 | 23 ( 7.5) | N.A. | 155 | 5 ( 3.2) | N.A. | 2.489<br>( 0.946, 6.547)<br>0.0559 | |
| >= 65 | 219 | 20 ( 9.1) | N.A. | 109 | 4 ( 3.7) | N.A. | 2.686<br>( 0.918, 7.862)<br>0.0603 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:04

Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Investigations

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | 0.9129 |
| >= 18 AND < 65 | 305 | 23 ( 7.5) | N.A. | 155 | 5 ( 3.2) | N.A. | 2.489 ( 0.946, 6.547) 0.0559 | |
| >= 65 AND < 75 | 139 | 12 ( 8.6) | N.A. | 77 | 4 ( 5.2) | N.A. | 1.782 ( 0.575, 5.528) 0.3102 | |
| >= 75 AND < 85 | 77 | 8 ( 10.4) | N.A. | 30 | 0 | N.E. | N.E. 0.0678 | |
| SEX | | | | | | | | 0.5266 |
| MALE | 320 | 29 ( 9.1) | N.A. | 161 | 7 ( 4.3) | N.A. | 2.203 ( 0.965, 5.029) 0.0544 | |
| FEMALE | 204 | 14 ( 6.9) | N.A. | 103 | 2 ( 1.9) | N.A. | 3.871 ( 0.880, 17.031) 0.0535 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:04

Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Investigations

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.2043 |
| STAGE IIB | 315 | 28 ( 8.9) | N.A. | 162 | 4 ( 2.5) | N.A. | 3.963 ( 1.390, 11.298) 0.0054 | |
| STAGE IIC | 209 | 15 ( 7.2) | N.A. | 102 | 5 ( 4.9) | N.A. | 1.509 ( 0.549, 4.153) 0.4218 | |
| T STAGE | | | | | | | | 0.3768 |
| T3B | 203 | 15 ( 7.4) | N.A. | 104 | 3 ( 2.9) | N.A. | 2.881 ( 0.834, 9.956) 0.0798 | |
| T4A | 112 | 13 ( 11.6) | N.A. | 58 | 1 ( 1.7) | N.A. | 7.231 ( 0.946, 55.285) 0.0256 | |
| T4B | 209 | 15 ( 7.2) | N.A. | 102 | 5 ( 4.9) | N.A. | 1.509 ( 0.549, 4.153) 0.4218 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:04

Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Investigations

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.9997 |
| US AND CANADA | 97 | 8 ( 8.2) | N.A. | 46 | 2 ( 4.3) | N.A. | 2.154<br>( 0.457, 10.158)<br>0.3206 | |
| WESTERN EUROPE | 301 | 25 ( 8.3) | N.A. | 160 | 7 ( 4.4) | N.A. | 1.966<br>( 0.850, 4.545)<br>0.1074 | |
| EASTERN EUROPE | 58 | 1 ( 1.7) | N.A. | 28 | 0 | N.E. | N.E.<br>0.4617 | |
| AUSTRALIA | 68 | 9 ( 13.2) | N.A. | 30 | 0 | N.E. | N.E.<br>0.0345 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Investigations. PT: Alanine Aminotransferase Increased

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| OVERALL | 524 | 12 ( 2.3) | N.A. | 264 | 1 ( 0.4) | N.A. | 6.389 ( 0.831, 49.143) 0.0406 | |
| AGE CATEGORY I | | | | | | | | N.M.E. |
| < 65 | 305 | 6 ( 2.0) | N.M.E. | 155 | 1 ( 0.6) | N.M.E. | N.M.E. | |
| >= 65 | 219 | 6 ( 2.7) | N.M.E. | 109 | 0 | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Investigations. PT: Alanine Aminotransferase Increased

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | N.M.E. |
| >= 18 AND < 65 | 305 | 6 ( 2.0) | N.M.E. | 155 | 1 ( 0.6) | N.M.E. | N.M.E. | |
| >= 65 AND < 75 | 139 | 3 ( 2.2) | N.M.E. | 77 | 0 | N.M.E. | N.M.E. | |
| >= 75 AND < 85 | 77 | 3 ( 3.9) | N.M.E. | 30 | 0 | N.M.E. | N.M.E. | |
| SEX | | | | | | | | N.M.E. |
| MALE | 320 | 7 ( 2.2) | N.M.E. | 161 | 1 ( 0.6) | N.M.E. | N.M.E. | |
| FEMALE | 204 | 5 ( 2.5) | N.M.E. | 103 | 0 | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Investigations. PT: Alanine Aminotransferase Increased

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | N.M.E. |
| STAGE IIB | 315 | 8 ( 2.5) | N.M.E. | 162 | 1 ( 0.6) | N.M.E. | N.M.E. | |
| STAGE IIC | 209 | 4 ( 1.9) | N.M.E. | 102 | 0 | N.M.E. | N.M.E. | |
| T STAGE | | | | | | | | N.M.E. |
| T3B | 203 | 3 ( 1.5) | N.M.E. | 104 | 1 ( 1.0) | N.M.E. | N.M.E. | |
| T4A | 112 | 5 ( 4.5) | N.M.E. | 58 | 0 | N.M.E. | N.M.E. | |
| T4B | 209 | 4 ( 1.9) | N.M.E. | 102 | 0 | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:04

Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Investigations. PT: Alanine Aminotransferase Increased

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | N.M.E. |
| US AND CANADA | 97 | 4 ( 4.1) | N.M.E. | 46 | 0 | N.M.E. | N.M.E. | |
| WESTERN EUROPE | 301 | 4 ( 1.3) | N.M.E. | 160 | 1 ( 0.6) | N.M.E. | N.M.E. | |
| EASTERN EUROPE | 58 | 1 ( 1.7) | N.M.E. | 28 | 0 | N.M.E. | N.M.E. | |
| AUSTRALIA | 68 | 3 ( 4.4) | N.M.E. | 30 | 0 | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Infections and Infestations

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 19 ( 3.6) | N.A. | 264 | 3 ( 1.1) | N.A. | 3.361 ( 0.995, 11.358) 0.0382 | |
| AGE CATEGORY I | | | | | | | | 0.7764 |
| < 65 | 305 | 8 ( 2.6) | N.A. | 155 | 1 ( 0.6) | N.A. | 4.253 ( 0.532, 34.011) 0.1370 | |
| >= 65 | 219 | 11 ( 5.0) | N.A. | 109 | 2 ( 1.8) | N.A. | 2.910 ( 0.645, 13.131) 0.1454 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
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Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Infections and Infestations

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | N.M.E. |
| >= 18 AND < 65 | 305 | 8 ( 2.6) | N.M.E. | 155 | 1 ( 0.6) | N.M.E. | N.M.E. | |
| >= 65 AND < 75 | 139 | 5 ( 3.6) | N.M.E. | 77 | 1 ( 1.3) | N.M.E. | N.M.E. | |
| >= 75 AND < 85 | 77 | 6 ( 7.8) | N.M.E. | 30 | 1 ( 3.3) | N.M.E. | N.M.E. | |
| SEX | | | | | | | | 0.1364 |
| MALE | 320 | 15 ( 4.7) | N.A. | 161 | 1 ( 0.6) | N.A. | 7.946 ( 1.050, 60.153) 0.0171 | |
| FEMALE | 204 | 4 ( 2.0) | N.A. | 103 | 2 ( 1.9) | N.A. | 1.068 ( 0.196, 5.835) 0.9393 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:04

Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Infections and Infestations

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.9896 |
| STAGE IIB | 315 | 10 ( 3.2) | N.A. | 162 | 3 ( 1.9) | N.A. | 1.852 ( 0.509, 6.733) 0.3417 | |
| STAGE IIC | 209 | 9 ( 4.3) | N.A. | 102 | 0 | N.E. | N.E. 0.0344 | |
| T STAGE | | | | | | | | N.M.E. |
| T3B | 203 | 6 ( 3.0) | N.M.E. | 104 | 2 ( 1.9) | N.M.E. | N.M.E. | |
| T4A | 112 | 4 ( 3.6) | N.M.E. | 58 | 1 ( 1.7) | N.M.E. | N.M.E. | |
| T4B | 209 | 9 ( 4.3) | N.M.E. | 102 | 0 | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:04

Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Infections and Infestations

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | N.M.E. |
| US AND CANADA | 97 | 2 ( 2.1) | N.M.E. | 46 | 0 | N.M.E. | N.M.E. | |
| WESTERN EUROPE | 301 | 8 ( 2.7) | N.M.E. | 160 | 0 | N.M.E. | N.M.E. | |
| EASTERN EUROPE | 58 | 2 ( 3.4) | N.M.E. | 28 | 1 ( 3.6) | N.M.E. | N.M.E. | |
| AUSTRALIA | 68 | 7 ( 10.3) | N.M.E. | 30 | 2 ( 6.7) | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:04

Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Metabolism and Nutrition Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 16 ( 3.1) | N.A. | 264 | 2 ( 0.8) | N.A. | 4.378 ( 1.006, 19.046) 0.0314 | |
| AGE CATEGORY I | | | | | | | | 0.7314 |
| < 65 | 305 | 6 ( 2.0) | N.A. | 155 | 1 ( 0.6) | N.A. | 3.361 ( 0.404, 27.930) 0.2332 | |
| >= 65 | 219 | 10 ( 4.6) | N.A. | 109 | 1 ( 0.9) | N.A. | 5.385 ( 0.689, 42.088) 0.0717 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:04

Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Metabolism and Nutrition Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | N.M.E. |
| >= 18 AND < 65 | 305 | 6 ( 2.0) | N.M.E. | 155 | 1 ( 0.6) | N.M.E. | N.M.E. | |
| >= 65 AND < 75 | 139 | 6 ( 4.3) | N.M.E. | 77 | 0 | N.M.E. | N.M.E. | |
| >= 75 AND < 85 | 77 | 4 ( 5.2) | N.M.E. | 30 | 1 ( 3.3) | N.M.E. | N.M.E. | |
| SEX | | | | | | | | 0.8763 |
| MALE | 320 | 9 ( 2.8) | N.A. | 161 | 1 ( 0.6) | N.A. | 4.836<br>( 0.613, 38.185)<br>0.0980 | |
| FEMALE | 204 | 7 ( 3.4) | N.A. | 103 | 1 ( 1.0) | N.A. | 3.921<br>( 0.482, 31.866)<br>0.1676 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:04

Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Metabolism and Nutrition Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.9909 |
| STAGE IIB | 315 | 9 ( 2.9) | N.A. | 162 | 2 ( 1.2) | N.A. | 2.623<br>( 0.566, 12.143)<br>0.2001 | |
| STAGE IIC | 209 | 7 ( 3.3) | N.A. | 102 | 0 | N.E. | N.E.<br>0.0586 | |
| T STAGE | | | | | | | | N.M.E. |
| T3B | 203 | 5 ( 2.5) | N.M.E. | 104 | 2 ( 1.9) | N.M.E. | N.M.E. | |
| T4A | 112 | 4 ( 3.6) | N.M.E. | 58 | 0 | N.M.E. | N.M.E. | |
| T4B | 209 | 7 ( 3.3) | N.M.E. | 102 | 0 | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:04

Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Metabolism and Nutrition Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.8213 |
| US AND CANADA | 97 | 5 ( 5.2) | N.A. | 46 | 1 ( 2.2) | N.A. | 2.812<br>( 0.328, 24.114)<br>0.3244 | |
| WESTERN EUROPE | 301 | 10 ( 3.3) | N.A. | 160 | 0 | N.E. | N.E.<br>0.0180 | |
| EASTERN EUROPE | 58 | 0 | N.E. | 28 | 0 | N.E. | N.E.<br>N.E. | |
| AUSTRALIA | 68 | 1 ( 1.5) | N.A. | 30 | 1 ( 3.3) | N.A. | 0.500<br>( 0.031, 8.026)<br>0.6176 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:04

Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Vascular Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 15 ( 2.9) | N.A. | 264 | 1 ( 0.4) | N.A. | 8.131<br>( 1.074, 61.556)<br>0.0155 | |
| AGE CATEGORY I | | | | | | | | 0.9915 |
| < 65 | 305 | 5 ( 1.6) | N.A. | 155 | 0 | N.E. | N.E.<br>0.1034 | |
| >= 65 | 219 | 10 ( 4.6) | N.A. | 109 | 1 ( 0.9) | N.A. | 5.528<br>( 0.707, 43.205)<br>0.0664 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:04

Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Vascular Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | N.M.E. |
| >= 18 AND < 65 | 305 | 5 ( 1.6) | N.M.E. | 155 | 0 | N.M.E. | N.M.E. | |
| >= 65 AND < 75 | 139 | 6 ( 4.3) | N.M.E. | 77 | 1 ( 1.3) | N.M.E. | N.M.E. | |
| >= 75 AND < 85 | 77 | 4 ( 5.2) | N.M.E. | 30 | 0 | N.M.E. | N.M.E. | |
| SEX | | | | | | | | 0.9926 |
| MALE | 320 | 12 ( 3.8) | N.A. | 161 | 1 ( 0.6) | N.A. | 6.420<br>( 0.835, 49.385)<br>0.0399 | |
| FEMALE | 204 | 3 ( 1.5) | N.A. | 103 | 0 | N.E. | N.E.<br>0.1912 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:04

Protocol: CA20976K 

Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Vascular Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.9925 |
| STAGE IIB | 315 | 5 ( 1.6) | N.A. | 162 | 1 ( 0.6) | N.A. | 2.767 ( 0.323, 23.700) 0.3324 | |
| STAGE IIC | 209 | 10 ( 4.8) | N.A. | 102 | 0 | N.E. | N.E. 0.0241 | |
| T STAGE | | | | | | | | 0.9999 |
| T3B | 203 | 4 ( 2.0) | N.A. | 104 | 0 | N.E. | N.E. 0.1389 | |
| T4A | 112 | 1 ( 0.9) | N.A. | 58 | 1 ( 1.7) | N.A. | 0.550 ( 0.034, 8.797) 0.6679 | |
| T4B | 209 | 10 ( 4.8) | N.A. | 102 | 0 | N.E. | N.E. 0.0241 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:04

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Table 22.20.2
Adverse Events with CTCAE Grade 3-4-5: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Vascular Disorders

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | N.M.E. |
| US AND CANADA | 97 | 6 ( 6.2) | N.M.E. | 46 | 1 ( 2.2) | N.M.E. | N.M.E. | |
| WESTERN EUROPE | 301 | 8 ( 2.7) | N.M.E. | 160 | 0 | N.M.E. | N.M.E. | |
| EASTERN EUROPE | 58 | 1 ( 1.7) | N.M.E. | 28 | 0 | N.M.E. | N.M.E. | |
| AUSTRALIA | 68 | 0 | N.M.E. | 30 | 0 | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:04

**Anhang 4-G 3.2.4.3: Subgruppenanalysen für Endpunkt schwerwiegende UE auf SOC/PT-Ebene aus CA209-76K**

Protocol: CA20976K 

Table 22.20.3
Serious Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Infections and Infestations

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 23 ( 4.4) | N.A. | 264 | 2 ( 0.8) | N.A. | 6.067 ( 1.430, 25.733) 0.0053 | |
| AGE CATEGORY I | | | | | | | | 0.9882 |
| < 65 | 305 | 9 ( 3.0) | N.A. | 155 | 0 | N.E. | N.E. 0.0293 | |
| >= 65 | 219 | 14 ( 6.4) | N.A. | 109 | 2 ( 1.8) | N.A. | 3.677 ( 0.836, 16.179) 0.0647 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:14

Protocol: CA20976K 

Table 22.20.3
Serious Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Infections and Infestations

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | N.M.E. |
| >= 18 AND < 65 | 305 | 9 ( 3.0) | N.M.E. | 155 | 0 | N.M.E. | N.M.E. | |
| >= 65 AND < 75 | 139 | 6 ( 4.3) | N.M.E. | 77 | 1 ( 1.3) | N.M.E. | N.M.E. | |
| >= 75 AND < 85 | 77 | 8 ( 10.4) | N.M.E. | 30 | 1 ( 3.3) | N.M.E. | N.M.E. | |
| SEX | | | | | | | | 0.6814 |
| MALE | 320 | 15 ( 4.7) | N.A. | 161 | 1 ( 0.6) | N.A. | 7.795<br>( 1.030, 59.010)<br>0.0184 | |
| FEMALE | 204 | 8 ( 3.9) | N.A. | 103 | 1 ( 1.0) | N.A. | 4.310<br>( 0.539, 34.467)<br>0.1329 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:14

Protocol: CA20976K 

Table 22.20.3
Serious Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Infections and Infestations

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.9895 |
| STAGE IIB | 315 | 11 ( 3.5) | N.A. | 162 | 2 ( 1.2) | N.A. | 3.001 ( 0.665, 13.543) 0.1330 | |
| STAGE IIC | 209 | 12 ( 5.7) | N.A. | 102 | 0 | N.E. | N.E. 0.0145 | |
| T STAGE | | | | | | | | 0.9999 |
| T3B | 203 | 5 ( 2.5) | N.A. | 104 | 2 ( 1.9) | N.A. | 1.378 ( 0.267, 7.103) 0.7005 | |
| T4A | 112 | 6 ( 5.4) | N.A. | 58 | 0 | N.E. | N.E. 0.0714 | |
| T4B | 209 | 12 ( 5.7) | N.A. | 102 | 0 | N.E. | N.E. 0.0145 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:14

Protocol: CA20976K 

Table 22.20.3
Serious Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Infections and Infestations

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| REGION | | | | | | | | 0.9699 |
| US AND CANADA | 97 | 2 ( 2.1) | N.A. | 46 | 0 | N.E. | N.E.<br>0.3211 | |
| WESTERN EUROPE | 301 | 11 ( 3.7) | N.A. | 160 | 0 | N.E. | N.E.<br>0.0143 | |
| EASTERN EUROPE | 58 | 3 ( 5.2) | N.A. | 28 | 1 ( 3.6) | N.A. | 1.571<br>( 0.163, 15.104)<br>0.6929 | |
| AUSTRALIA | 68 | 7 ( 10.3) | N.A. | 30 | 1 ( 3.3) | N.A. | 3.401<br>( 0.418, 27.656)<br>0.2234 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:14

Protocol: CA20976K 

Table 22.20.3
Serious Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps)

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| OVERALL | 524 | 7 ( 1.3) | N.A. | 264 | 12 ( 4.5) | N.A. | 0.318<br>( 0.125, 0.807)<br>0.0109 | |
| AGE CATEGORY I | | | | | | | | 0.3750 |
| < 65 | 305 | 5 ( 1.6) | N.A. | 155 | 6 ( 3.9) | N.A. | 0.456<br>( 0.139, 1.494)<br>0.1833 | |
| >= 65 | 219 | 2 ( 0.9) | N.A. | 109 | 6 ( 5.5) | N.A. | 0.179<br>( 0.036, 0.890)<br>0.0178 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:14

Protocol: CA20976K 

Table 22.20.3
Serious Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps)

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| AGE CATEGORY II | | | | | | | | 0.6439 |
| >= 18 AND < 65 | 305 | 5 ( 1.6) | N.A. | 155 | 6 ( 3.9) | N.A. | 0.456 ( 0.139, 1.494) 0.1833 | |
| >= 65 AND < 75 | 139 | 1 ( 0.7) | N.A. | 77 | 4 ( 5.2) | N.A. | 0.146 ( 0.016, 1.312) 0.0464 | |
| >= 75 AND < 85 | 77 | 1 ( 1.3) | N.A. | 30 | 2 ( 6.7) | N.A. | 0.211 ( 0.019, 2.331) 0.1613 | |
| SEX | | | | | | | | 0.5092 |
| MALE | 320 | 4 ( 1.3) | N.A. | 161 | 5 ( 3.1) | N.A. | 0.444 ( 0.119, 1.654) 0.2137 | |
| FEMALE | 204 | 3 ( 1.5) | N.A. | 103 | 7 ( 6.8) | N.A. | 0.230 ( 0.059, 0.890) 0.0201 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:14

Protocol: CA20976K 

Table 22.20.3
Serious Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps)

| Subgroup | Nivolumab N | Nivolumab Subjects with Event n (%) | Nivolumab KME (95%CI)(mon) (1) | Placebo N | Placebo Subjects with Event n (%) | Placebo KME (95%CI)(mon) (1) | Nivolumab vs. Placebo HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
|---|---|---|---|---|---|---|---|---|
| DISEASE STAGE CATEGORY | | | | | | | | 0.0563 |
| STAGE IIB | 315 | 1 ( 0.3) | N.A. | 162 | 8 ( 4.9) | N.A. | 0.073 ( 0.009, 0.585) 0.0012 | |
| STAGE IIC | 209 | 6 ( 2.9) | N.A. | 102 | 4 ( 3.9) | N.A. | 0.744 ( 0.210, 2.637) 0.6458 | |
| T STAGE | | | | | | | | 0.3294 |
| T3B | 203 | 1 ( 0.5) | N.A. | 104 | 5 ( 4.8) | N.A. | 0.118 ( 0.014, 1.011) 0.0192 | |
| T4A | 112 | 0 | N.E. | 58 | 3 ( 5.2) | N.A. | N.E. 0.0244 | |
| T4B | 209 | 6 ( 2.9) | N.A. | 102 | 4 ( 3.9) | N.A. | 0.744 ( 0.210, 2.637) 0.6458 | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:14

Protocol: CA20976K 

Table 22.20.3
Serious Adverse Events: Subgroup Time-Adjusted Analyses
by Significant SOC/PT on Hazard Ratio
All Treated Subjects Censoring at Open-Label Nivolumab

SOC: Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps)

| | Nivolumab | | | Placebo | | | Nivolumab vs. Placebo | |
|---|---|---|---|---|---|---|---|---|
| Subgroup | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | N | Subjects with Event n (%) | KME (95%CI)(mon) (1) | HR (95%CI) P-value (2)(3) | Test for Interaction P-value (4)(5) |
| REGION | | | | | | | | N.M.E. |
| US AND CANADA | 97 | 0 | N.M.E. | 46 | 2 ( 4.3) | N.M.E. | N.M.E. | |
| WESTERN EUROPE | 301 | 5 ( 1.7) | N.M.E. | 160 | 4 ( 2.5) | N.M.E. | N.M.E. | |
| EASTERN EUROPE | 58 | 1 ( 1.7) | N.M.E. | 28 | 4 ( 14.3) | N.M.E. | N.M.E. | |
| AUSTRALIA | 68 | 1 ( 1.5) | N.M.E. | 30 | 2 ( 6.7) | N.M.E. | N.M.E. | |

Apr 2023 DBL. Includes events reported from the first dose of study therapy in the blinded phase.
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase,
or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
HR = hazard ratio; KME = Kaplan-Meier estimate; N.M.E. = Not meaningful estimate; N.E. = Not estimable.
(1) KME of median time to first AE. (2) Unstratified Cox proportional hazard model. HR is nivolumab over Placebo.
(3) Unstratified log-rank test. (4) Unstratified Cox proportional hazard model with treatment,
subgroup and treatment*subgroup interaction to assess the significance of the interaction between the treatment and the subgroup.
(5) P-values <0.05 are indicated by 1 asterisk (indicates potential effect modification).
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/tables/rt-ae-tsubsoc-ebr1575.sas 11AUG2023:13:16:14

## Anhang 4-G 4: Kaplan-Meier-Kurven aus CA209-76K

### Anhang 4-G 4.1: Kaplan-Meier-Kurven für Endpunkte aus CA209-76K

#### Anhang 4-G 4.1.1: Kaplan-Meier-Kurven für Endpunkte Verträglichkeit aus CA209-76K

Für die Endpunkte unerwünschte Ereignisse ohne Erfassung des Progresses der Grunderkrankung – Zeit bis zum ersten Auftreten des UE: jegliche UE, schwere UE, schwerwiegende UE und zum Therapieabbruch führende UE.

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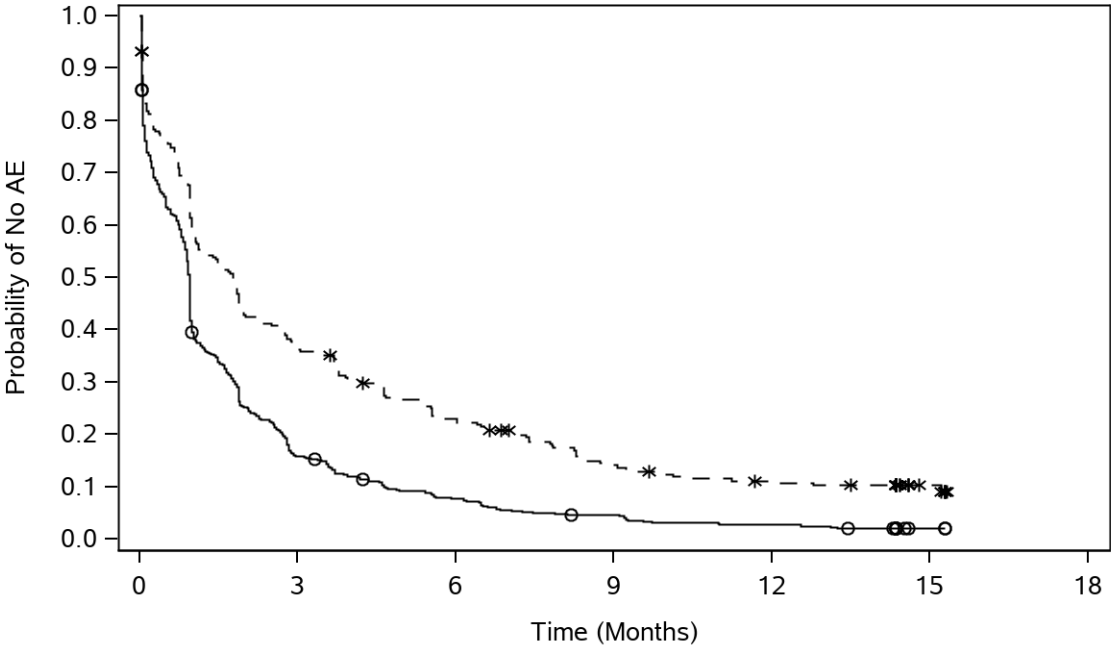
Figure 9.1:
Kaplan-Meier Plot of Time to any Adverse Events - Excluding Progression Terms - All Treated Subjects Censoring at Open-Label Nivolumab




Number of Subjects at Risk

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Nivolumab | 524 | 82 | 39 | 22 | 13 | 2 | 0 |
| Placebo | 264 | 95 | 59 | 34 | 24 | 8 | 0 |

Nivolumab (events: 508/524), median and 95% CI: 0.95 (0.89, 0.95)
Placebo (events: 233/264), median and 95% CI: 1.77 (1.12, 1.91)
Hazard Ratio (Nivolumab vs. Placebo) and 95% CI: 1.709 (1.459, 2.002)

Apr 2023 DBL Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase, or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
Stratified Cox proportional hazard model.
Symbols represent censored observations.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/figures
Program Name: rg-ae-ae-ebr1575-b1.sas 19JUN2023:11:54:21

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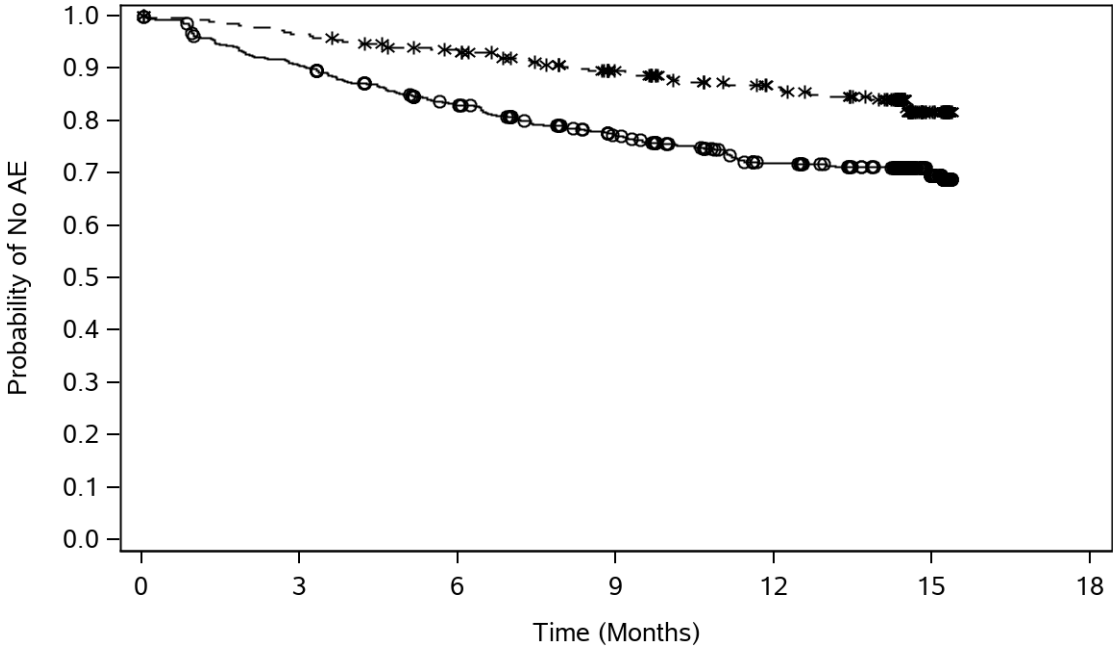
Figure 9.3:
Kaplan-Meier Plot of Time to any Adverse Events with CTCAE Grade 3-4-5 - Excluding Progression Terms - All Treated Subjects Censoring at Open-Label Nivolumab




Number of Subjects at Risk

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Nivolumab | 524 | 469 | 411 | 358 | 306 | 100 | 0 |
| Placebo | 264 | 253 | 239 | 210 | 187 | 67 | 0 |

—o— Nivolumab (events: 146/524), median and 95% CI: N.A.
—*— Placebo (events: 42/264), median and 95% CI: N.A.
Hazard Ratio (Nivolumab vs. Placebo) and 95% CI: 1.963 (1.393, 2.768)

Apr 2023 DBL Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase, or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
Stratified Cox proportional hazard model.
Symbols represent censored observations.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/figures
Program Name: rg-ae-ae-ebr1575-b1.sas 19JUN2023:11:55:20

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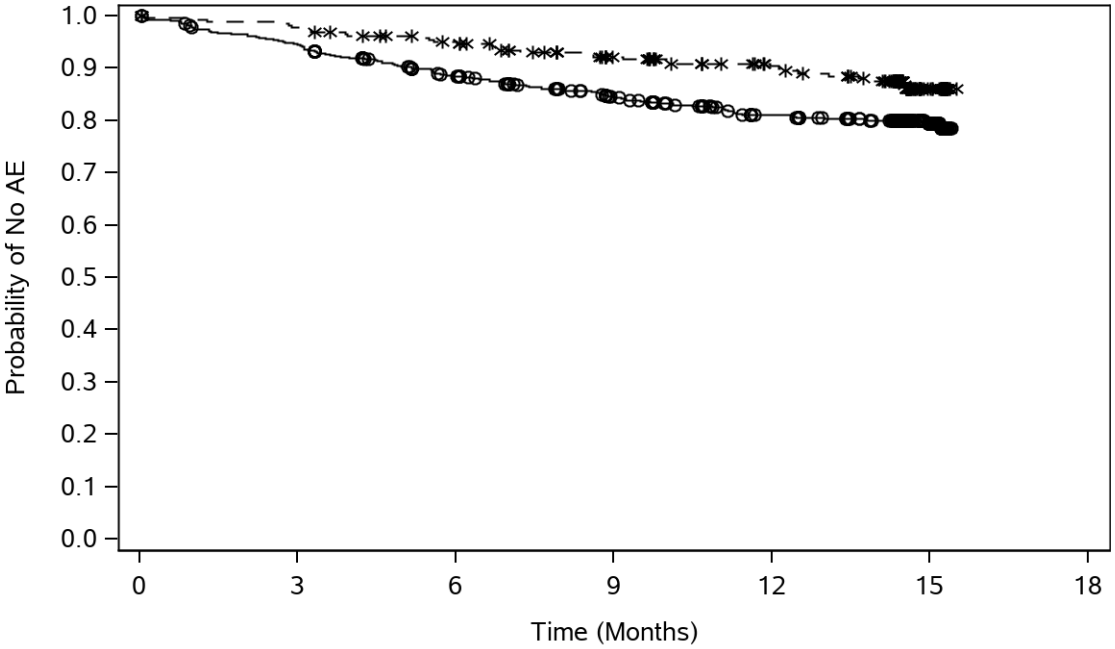
Figure 9.5:
Kaplan-Meier Plot of Time to any Serious Adverse Events - Excluding Progression Terms - All Treated Subjects Censoring at Open-Label Nivolumab




Number of Subjects at Risk

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Nivolumab | 524 | 490 | 428 | 376 | 327 | 113 | 0 |
| Placebo | 264 | 256 | 242 | 215 | 193 | 71 | 0 |

Nivolumab (events: 98/524), median and 95% CI: N.A.
Placebo (events: 32/264), median and 95% CI: N.A.
Hazard Ratio (Nivolumab vs. Placebo) and 95% CI: 1.690 (1.134, 2.519)

Apr 2023 DBL Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase, or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
Stratified Cox proportional hazard model.
Symbols represent censored observations.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/figures
Program Name: rg-ae-ae-ebr1575-b1.sas 19JUN2023:11:56:07

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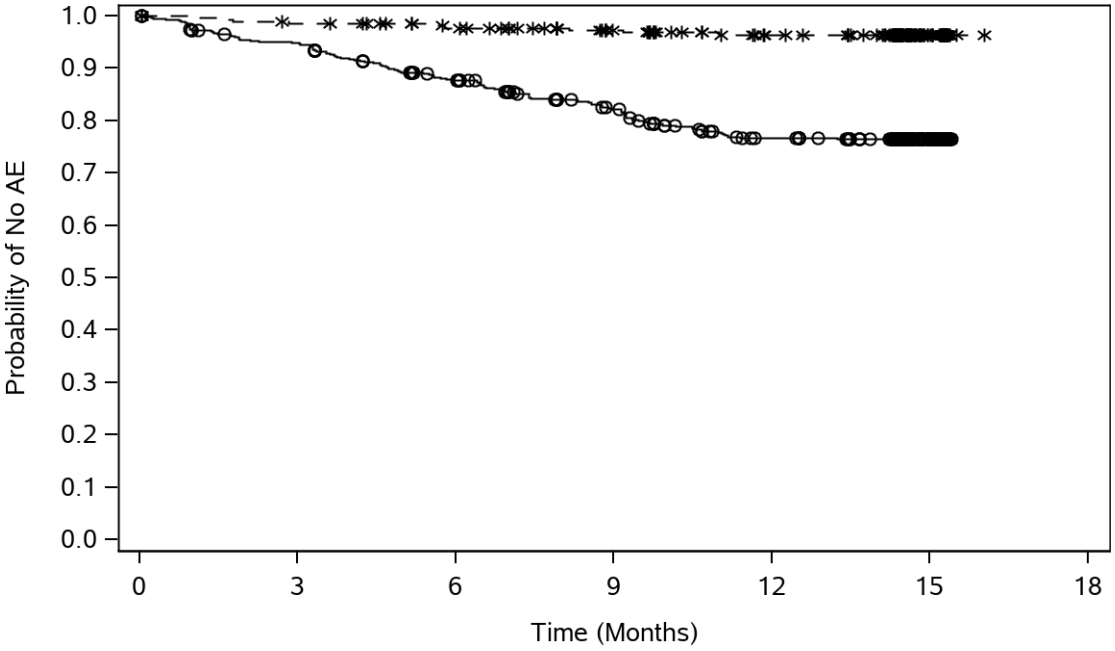
Figure 9.7:
Kaplan-Meier Plot of Time to any Adverse Events Leading to Discontinuation of Study Treatment - Excluding Progression Terms - All Treated Subjects Censoring at Open-Label Nivolumab




Number of Subjects at Risk

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Nivolumab | 524 | 490 | 435 | 386 | 341 | 125 | 0 |
| Placebo | 264 | 257 | 247 | 227 | 207 | 81 | 0 |

—o— Nivolumab (events: 116/524), median and 95% CI: N.A.
—*· Placebo (events: 9/264), median and 95% CI: N.A.
Hazard Ratio (Nivolumab vs. Placebo) and 95% CI: 7.169 (3.638, 14.126)

Apr 2023 DBL Includes events reported from the first dose of study therapy in the blinded phase
Subjects without events are censored 100 days after last dose of study therapy in the blinded phase, or at the day before start of Nivolumab treatment in the open-label phase, whichever occurs earlier.
Stratified Cox proportional hazard model.
Symbols represent censored observations.
Program Source: /opt/zfs001/prd/bms214671/stats/market/prog/figures
Program Name: rg-ae-ae-ebr1575-b1.sas 19JUN2023:11:56:53

## Anhang 4-G 5: Details zur Operationalisierung der Unerwünschten Ereignisse von besonderem Interesse (UESI)

### Anhang 4-G 5.1: Definition von spezifischen immunvermittelten UE (imUE)

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Immune-Mediated Adverse Events Definition

| Category | Preferred Terms |
|---|---|
| ADRENAL INSUFFICIENCY | Adrenal insufficiency |
| | Adrenocortical insufficiency acute |
| | Hypothalamic pituitary adrenal axis suppression |
| | Immune-mediated adrenal insufficiency |
| | Primary adrenal insufficiency |
| | Secondary adrenocortical insufficiency |
| DIABETES MELLITUS | Diabetes mellitus |
| | Diabetic ketoacidosis |
| | Diabetic ketosis |
| | Fulminant type 1 diabetes mellitus |
| | Latent autoimmune diabetes in adults |
| | Type 1 diabetes mellitus |
| DIARRHEA/COLITIS | Autoimmune colitis |
| | Autoimmune enteropathy |
| | Colitis |
| | Colitis ulcerative |
| | Diarrhoea |
| | Enteritis |
| | Enterocolitis |
| | Enterocolitis haemorrhagic |
| | Immune-mediated enterocolitis |
| | Immune-mediated gastritis |
| HEPATITIS | Acute hepatic failure |
| | Acute on chronic liver failure |
| | Alanine aminotransferase increased |
| | Aspartate aminotransferase increased |
| | Autoimmune cholangitis |
| | Autoimmune hepatitis |
| | Biliary cirrhosis |
| | Blood bilirubin increased |
| | Cholangitis |
| | Drug-induced liver injury |
| | Hepatic failure |

MedDRA Version: 25.0
Program Source: /opt/zfs001/prd/bms247316/stats/primary/prog/listings/rl-ae-slaedef-sas.sas 07NOV2022:15:46:54

Protocol: CA20976K 

Immune-Mediated Adverse Events Definition

| Category | Preferred Terms |
|---|---|
| HEPATITIS | Hepatitis<br>Hepatitis acute<br>Hepatotoxicity<br>Hyperbilirubinaemia<br>Hypertransaminasaemia<br>Immune-mediated cholangitis<br>Immune-mediated cholestasis<br>Immune-mediated hepatic disorder<br>Immune-mediated hepatitis<br>Transaminases increased |
| HYPERSENSITIVITY | Anaphylactic reaction<br>Anaphylactic shock<br>Hypersensitivity<br>Infusion related hypersensitivity reaction<br>Infusion related reaction |
| HYPERTHYROIDISM | Basedow's disease<br>Hyperthyroidism<br>Immune-mediated hyperthyroidism<br>Primary hyperthyroidism |
| HYPOPHYSITIS | Hypophysitis<br>Hypopituitarism<br>Immune-mediated hypophysitis<br>Lymphocytic hypophysitis |
| HYPOTHYROIDISM | Autoimmune hypothyroidism<br>Hypothyroidism<br>Immune-mediated hypothyroidism<br>Primary hypothyroidism |
| HYPOTHYROIDISM/THYROIDITIS | Atrophic thyroiditis<br>Autoimmune hypothyroidism<br>Autoimmune thyroiditis<br>Hypothyroidism |

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Immune-Mediated Adverse Events Definition

| Category | Preferred Terms |
|---|---|
| HYPOTHYROIDISM/THYROIDITIS | Immune-mediated hypothyroidism |
| | Immune-mediated thyroiditis |
| | Primary hypothyroidism |
| | Silent thyroiditis |
| | Thyroiditis |
| | Thyroiditis acute |
| NEPHRITIS AND RENAL DYSFUNCTION | Acute kidney injury |
| | Autoimmune nephritis |
| | Blood creatinine increased |
| | Creatinine renal clearance decreased |
| | End stage renal disease |
| | Glomerulonephritis rapidly progressive |
| | Hypercreatininaemia |
| | Immune-mediated nephritis |
| | Immune-mediated renal disorder |
| | Nephritis |
| | Nephritis allergic |
| | Paraneoplastic glomerulonephritis |
| | Renal failure |
| | Renal tubular necrosis |
| | Subacute kidney injury |
| | Tubulointerstitial nephritis |
| PNEUMONITIS | Hypersensitivity pneumonitis |
| | Idiopathic interstitial pneumonia |
| | Immune-mediated lung disease |
| | Interstitial lung disease |
| | Pneumonitis |
| RASH | Autoimmune blistering disease |
| | Autoimmune dermatitis |
| | Bullous haemorrhagic dermatosis |
| | Dermatitis |
| | Dermatitis acneiform |
| | Dermatitis allergic |

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Immune-Mediated Adverse Events Definition

| Category | Preferred Terms |
|---|---|
| RASH | Dermatitis atopic |
| | Dermatitis exfoliative |
| | Drug eruption |
| | Erythema multiforme |
| | Erythrodermic atopic dermatitis |
| | Exfoliative rash |
| | Fixed eruption |
| | Immune-mediated dermatitis |
| | Mucocutaneous disorder |
| | Mucosa vesicle |
| | Mucous membrane pemphigoid |
| | Nodular rash |
| | Paradoxical psoriasis |
| | Pemphigoid |
| | Pemphigus |
| | Pustule |
| | Rash |
| | Rash erythematous |
| | Rash macular |
| | Rash maculo-papular |
| | Rash morbilliform |
| | Rash papular |
| | Rash pruritic |
| | Rash pustular |
| | Rash vesicular |
| | Scrotal dermatitis |
| | Severe cutaneous adverse reaction |
| | Stevens-Johnson syndrome |
| | Toxic epidermal necrolysis |
| | Toxic skin eruption |
| | Urticarial dermatitis |
| THYROIDITIS | Atrophic thyroiditis |
| | Autoimmune thyroiditis |
| | Immune-mediated thyroiditis |
| | Silent thyroiditis |

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Immune-Mediated Adverse Events Definition

| Category | Preferred Terms |
|---|---|
| THYROIDITIS | Thyroiditis<br>Thyroiditis acute |

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## Anhang 4-G 5.2: Definition von spezifischen UE (select UE)

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Select Adverse Events Definition

| Category | Subcategory | Preferred Terms |
|---|---|---|
| ENDOCRINE ADVERSE EVENT | ADRENAL DISORDER | Adrenal insufficiency |
| | | Adrenal suppression |
| | | Adrenocortical insufficiency acute |
| | | Blood corticotrophin decreased |
| | | Blood corticotrophin increased |
| | | Hypothalamic pituitary adrenal axis suppression |
| | | Immune-mediated adrenal insufficiency |
| | | Primary adrenal insufficiency |
| | | Secondary adrenocortical insufficiency |
| | DIABETES | Diabetes mellitus |
| | | Diabetic ketoacidosis |
| | | Diabetic ketosis |
| | | Fulminant type 1 diabetes mellitus |
| | | Latent autoimmune diabetes in adults |
| | | Type 1 diabetes mellitus |
| | PITUITARY DISORDER | Hypogonadism |
| | | Hypophysitis |
| | | Hypopituitarism |
| | | Immune-mediated hypophysitis |
| | | Lymphocytic hypophysitis |
| | THYROID DISORDER | Atrophic thyroiditis |
| | | Autoimmune hypothyroidism |
| | | Autoimmune thyroid disorder |
| | | Autoimmune thyroiditis |
| | | Basedow's disease |
| | | Blood thyroid stimulating hormone decreased |
| | | Blood thyroid stimulating hormone increased |
| | | Hyperthyroidism |
| | | Hypoparathyroidism |
| | | Hypothyroidism |
| | | Immune-mediated hyperthyroidism |
| | | Immune-mediated hypothyroidism |
| | | Immune-mediated thyroiditis |

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Select Adverse Events Definition

| Category | Subcategory | Preferred Terms |
|---|---|---|
| ENDOCRINE ADVERSE EVENT | THYROID DISORDER | Primary hyperthyroidism |
| | | Primary hypothyroidism |
| | | Silent thyroiditis |
| | | Thyroid function test abnormal |
| | | Thyroid hormones decreased |
| | | Thyroid hormones increased |
| | | Thyroiditis |
| | | Thyroiditis acute |
| | | Thyroxine decreased |
| | | Thyroxine free decreased |
| | | Thyroxine free increased |
| | | Thyroxine increased |
| | | Tri-iodothyronine uptake increased |
| GASTROINTESTINAL ADVERSE EVENT | | Autoimmune colitis |
| | | Autoimmune enteropathy |
| | | Colitis |
| | | Colitis ulcerative |
| | | Diarrhoea |
| | | Duodenal perforation |
| | | Enteritis |
| | | Enterocolitis |
| | | Enterocolitis haemorrhagic |
| | | Frequent bowel movements |
| | | Gastrointestinal perforation |
| | | Immune-mediated enterocolitis |
| | | Immune-mediated gastritis |
| | | Lower gastrointestinal perforation |
| | | Ulcerative duodenitis |
| | | Upper gastrointestinal perforation |
| HEPATIC ADVERSE EVENT | | Acute hepatic failure |
| | | Acute on chronic liver failure |
| | | Alanine aminotransferase increased |
| | | Aspartate aminotransferase increased |
| | | Autoimmune cholangitis |

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Select Adverse Events Definition

| Category | Subcategory | Preferred Terms |
|---|---|---|
| HEPATIC ADVERSE EVENT | | Autoimmune hepatitis |
| | | Biliary cirrhosis |
| | | Bilirubin conjugated decreased |
| | | Bilirubin conjugated increased |
| | | Blood alkaline phosphatase increased |
| | | Blood bilirubin increased |
| | | Cholangitis |
| | | Drug-induced liver injury |
| | | Gamma-glutamyltransferase increased |
| | | Hepatic cytolysis |
| | | Hepatic enzyme increased |
| | | Hepatic failure |
| | | Hepatitis |
| | | Hepatitis acute |
| | | Hepatotoxicity |
| | | Hyperbilirubinaemia |
| | | Hypertransaminasaemia |
| | | Immune-mediated cholangitis |
| | | Immune-mediated cholestasis |
| | | Immune-mediated hepatic disorder |
| | | Immune-mediated hepatitis |
| | | Liver disorder |
| | | Liver function test abnormal |
| | | Liver function test increased |
| | | Liver injury |
| | | Transaminases increased |
| HYPERSENSITIVITY/INFUSION REACTION | | Anaphylactic reaction |
| | | Anaphylactic shock |
| | | Bronchospasm |
| | | Hypersensitivity |
| | | Infusion related hypersensitivity reaction |
| | | Infusion related reaction |
| PULMONARY ADVERSE EVENT | | Acute respiratory distress syndrome |
| | | Acute respiratory failure |

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Select Adverse Events Definition

| Category | Subcategory | Preferred Terms |
|---|---|---|
| PULMONARY ADVERSE EVENT | | Autoimmune lung disease |
| | | Hypersensitivity pneumonitis |
| | | Idiopathic interstitial pneumonia |
| | | Immune-mediated lung disease |
| | | Interstitial lung disease |
| | | Lung infiltration |
| | | Pneumonitis |
| RENAL ADVERSE EVENT | | Acute kidney injury |
| | | Autoimmune nephritis |
| | | Blood creatinine increased |
| | | Blood urea increased |
| | | Creatinine renal clearance decreased |
| | | End stage renal disease |
| | | Glomerulonephritis rapidly progressive |
| | | Hypercreatininaemia |
| | | Immune-mediated nephritis |
| | | Immune-mediated renal disorder |
| | | Nephritis |
| | | Nephritis allergic |
| | | Paraneoplastic glomerulonephritis |
| | | Renal failure |
| | | Renal tubular necrosis |
| | | Subacute kidney injury |
| | | Tubulointerstitial nephritis |
| | | Urine output decreased |
| SKIN ADVERSE EVENT | | Anal eczema |
| | | Anal rash |
| | | Autoimmune blistering disease |
| | | Autoimmune dermatitis |
| | | Blister |
| | | Bullous haemorrhagic dermatosis |
| | | Dermatitis |
| | | Dermatitis acneiform |
| | | Dermatitis allergic |

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Select Adverse Events Definition

| Category | Subcategory | Preferred Terms |
|---|---|---|
| SKIN ADVERSE EVENT | | Dermatitis atopic |
| | | Dermatitis exfoliative |
| | | Drug eruption |
| | | Eczema |
| | | Enanthema |
| | | Erythema |
| | | Erythema multiforme |
| | | Erythrodermic atopic dermatitis |
| | | Exfoliative rash |
| | | Fixed eruption |
| | | Generalised bullous fixed drug eruption |
| | | Guttate psoriasis |
| | | Immune-mediated dermatitis |
| | | Mucocutaneous disorder |
| | | Mucosa vesicle |
| | | Mucous membrane pemphigoid |
| | | Nodular rash |
| | | Palmar-plantar erythrodysaesthesia syndrome |
| | | Paradoxical psoriasis |
| | | Pemphigoid |
| | | Pemphigus |
| | | Photosensitivity reaction |
| | | Pruritus |
| | | Pruritus allergic |
| | | Psoriasis |
| | | Pustular psoriasis |
| | | Pustule |
| | | Rash |
| | | Rash erythematous |
| | | Rash macular |
| | | Rash maculo-papular |
| | | Rash morbilliform |
| | | Rash papular |
| | | Rash pruritic |
| | | Rash pustular |
| | | Rash vesicular |

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Select Adverse Events Definition

| Category | Subcategory | Preferred Terms |
|---|---|---|
| SKIN ADVERSE EVENT | | SJS-TEN overlap |
| | | Scrotal dermatitis |
| | | Severe cutaneous adverse reaction |
| | | Skin exfoliation |
| | | Skin hypopigmentation |
| | | Skin irritation |
| | | Stevens-Johnson syndrome |
| | | Toxic epidermal necrolysis |
| | | Toxic skin eruption |
| | | Urticaria |
| | | Urticarial dermatitis |
| | | Vitiligo |
| | | Vulval eczema |

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## Anhang 4-G 5.3: Definition von weiteren UE von speziellem Interesse (OESI)

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Other Events of Special Interest Definition

| Category | Preferred Terms |
|---|---|
| AUTOIMMUNE CYTOPENIA | Antiphospholipid syndrome<br>Autoimmune anaemia<br>Autoimmune aplastic anaemia<br>Autoimmune haemolytic anaemia<br>Autoimmune heparin-induced thrombocytopenia<br>Autoimmune neutropenia<br>Autoimmune pancytopenia<br>Cold type haemolytic anaemia<br>Coombs positive haemolytic anaemia<br>Evans syndrome<br>Idiopathic CD4 lymphocytopenia<br>Immune thrombocytopenia<br>Immune-mediated cytopenia<br>Pernicious anaemia<br>Warm autoimmune haemolytic anaemia |
| AUTOIMMUNE EYE DISORDER | Autoimmune eye disorder<br>Autoimmune retinopathy |
| DEMYELINATION EVENT | Anti-myelin-associated glycoprotein associated polyneuropathy<br>Demyelinating polyneuropathy<br>Demyelination |
| ENCEPHALITIS EVENT | Acute disseminated encephalomyelitis<br>Acute encephalitis with refractory, repetitive partial seizures<br>Autoimmune encephalopathy<br>Bickerstaff's encephalitis<br>Encephalitis<br>Encephalitis allergic<br>Encephalitis autoimmune<br>Encephalitis brain stem<br>Encephalitis haemorrhagic<br>Encephalitis lethargica<br>Encephalitis toxic<br>Immune effector cell-associated neurotoxicity syndrome<br>Immune-mediated encephalitis |

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Other Events of Special Interest Definition

| Category | Preferred Terms |
|---|---|
| ENCEPHALITIS EVENT | Immune-mediated encephalopathy |
| | Limbic encephalitis |
| | Lupus encephalitis |
| | Noninfective encephalitis |
| | Panencephalitis |
| | Rasmussen encephalitis |
| | Subacute sclerosing panencephalitis |
| GRAFT VERSUS HOST DISEASE | Acute graft versus host disease |
| | Acute graft versus host disease in eye |
| | Acute graft versus host disease in intestine |
| | Acute graft versus host disease in liver |
| | Acute graft versus host disease in skin |
| | Acute graft versus host disease oral |
| | Chronic graft versus host disease |
| | Chronic graft versus host disease in eye |
| | Chronic graft versus host disease in intestine |
| | Chronic graft versus host disease in liver |
| | Chronic graft versus host disease in lung |
| | Chronic graft versus host disease in skin |
| | Chronic graft versus host disease oral |
| | Graft versus host disease |
| | Graft versus host disease in eye |
| | Graft versus host disease in gastrointestinal tract |
| | Graft versus host disease in liver |
| | Graft versus host disease in lung |
| | Graft versus host disease in skin |
| | Graft versus host disease oral |
| GUILLAIN-BARRE SYNDROME | Guillain-Barre syndrome |
| | Miller Fisher syndrome |
| IMMUNE MEDIATED ARTHRITIS | Acute aseptic arthritis |
| | Autoimmune arthritis |
| | Immune-mediated arthritis |

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Other Events of Special Interest Definition

| Category | Preferred Terms |
|---|---|
| MYASTHENIC SYNDROME | Myasthenia gravis<br>Myasthenia gravis crisis<br>Myasthenic syndrome<br>Ocular myasthenia |
| MYOCARDITIS EVENT | Autoimmune myocarditis<br>Eosinophilic myocarditis<br>Giant cell myocarditis<br>Hypersensitivity myocarditis<br>Immune-mediated myocarditis<br>Myocarditis<br>Myopericarditis |
| MYOSITIS/RHABDOMYOLYSIS EVENT | Autoimmune myositis<br>Dermatomyositis<br>Immune-mediated myositis<br>Inclusion body myositis<br>Myositis<br>Necrotising myositis<br>Paraneoplastic dermatomyositis<br>Polymyositis<br>Rhabdomyolysis |
| PANCREATITIS EVENT | Autoimmune pancreatitis<br>Haemorrhagic necrotic pancreatitis<br>Immune-mediated pancreatitis<br>Pancreatitis<br>Pancreatitis acute<br>Pancreatitis necrotising<br>Subacute pancreatitis |
| UVEITIS EVENT | Autoimmune uveitis<br>Chorioretinitis<br>Cyclitis<br>Immune recovery uveitis<br>Immune-mediated uveitis |

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Other Events of Special Interest Definition

| Category | Preferred Terms |
|---|---|
| UVEITIS EVENT | Iridocyclitis<br>Iritis<br>Keratouveitis<br>Uveitis<br>Vogt-Koyanagi-Harada disease |

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