

**Clinical trial results:****A Dose-optimization, Exploratory Phase Ib/II Study to Assess Safety and Efficacy of the Second Mitochondrial-derived Activator of Caspases (SMAC) Mimetic Debio 1143, When Given in Combination With the Anti-PD-1 Antibody Nivolumab in Patients With Specific Solid Tumors Who Have Progressed During or Immediately After Anti-PD-1/PD-L1 Treatment****Summary**

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2018-003546-16 |
| Trial protocol           | ES             |
| Global end of trial date | 06 April 2022  |

**Results information**

|                                |   |
|--------------------------------|---|
| Result version number          | v2 (current)  |
| This version publication date  | 19 October 2023   |
| First version publication date | 21 April 2023   |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li></ul> Update to the description of endpoints #1, #5, #13, and title of endpoint #5, #24, #25, #26. Updated the endpoints #4, #6 #7, #8, #15, #17, #27. Updates to the timeframe of endpoints #18 to #26 and adverse event reporting time frame. |

**Trial information****Trial identification**

|                       |                |
|-----------------------|----------------|
| Sponsor protocol code | Debio 1143-106 |
|-----------------------|----------------|

**Additional study identifiers**

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04122625 |
| WHO universal trial number (UTN)   | -           |

Notes:

**Sponsors**

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Debiopharm International S.A.  |
| Sponsor organisation address | Case postale 5911, Chemin Messidor 5-7, Lausanne, Switzerland, 1002                              |
| Public contact               | Clinical department, Debiopharm International SA, +34 91756 78 25, ClinicalTrials@debiopharm.com |
| Scientific contact           | Clinical department, Debiopharm International SA, +34 91756 78 25, ClinicalTrials@debiopharm.com |

Notes:

**Paediatric regulatory details**

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No                                | No |

|                                |
|--------------------------------|
| 1901/2006 apply to this trial? |
|--------------------------------|

Notes:

### Results analysis stage

|  |               |
|--|---------------|
| Analysis stage                                       | Final         |
| Date of interim/final analysis                       | 06 April 2022 |
| Is this the analysis of the primary completion data? | No            |

|                                  |               |
|----------------------------------|---------------|
| Global end of trial reached?     | Yes           |
| Global end of trial date         | 06 April 2022 |
| Was the trial ended prematurely? | No            |

Notes:

### General information about the trial

Main objective of the trial:

Part A (dose optimisation)- To determine the recommended phase 2 dose (RP2D) taking into account dose-limiting toxicity (DLT/s) in Cycle 1, overall safety/tolerability and pharmacokinetic (PK), by optimizing doses of Debio 1143 when combined with the standard dose of nivolumab, as well as treatment compliance in subjects with advanced solid malignancies who failed prior systemic standard treatments.

Part B (basket trial)- To evaluate the preliminary antitumor activity of Debio 1143 at the RP2D in combination with nivolumab, overall and in each cohort.

Protection of trial subjects:

Written approval of the study protocol and the informed consent was obtained from the independent ethics committee (IEC), prior to initiation of the study. The study was conducted in accordance with local regulations, Good Clinical Practice (GCP), International Council for Harmonisation (ICH) notes for GCP (ICH/CPMP/135/95), and ethical principles that have their origin in the Declaration of Helsinki and its amendments.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 26 April 2019 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | Yes           |

Notes:

### Population of trial subjects

#### Subjects enrolled per country

|                                      |                  |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | Spain: 26        |
| Country: Number of subjects enrolled | France: 11       |
| Country: Number of subjects enrolled | United States: 9 |
| Worldwide total number of subjects   | 46               |
| EEA total number of subjects         | 37               |

Notes:

#### Subjects enrolled per age group

|          |   |
|----------|---|
| In utero | 0 |
|----------|---|

|   |    |
|---|----|
| Preterm newborn - gestational age < 37 wk | 0  |
| Newborns (0-27 days)                      | 0  |
| Infants and toddlers (28 days-23 months)  | 0  |
| Children (2-11 years)                     | 0  |
| Adolescents (12-17 years)                 | 0  |
| Adults (18-64 years)                      | 23 |
| From 65 to 84 years                       | 23 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Subjects took part at 24 investigational sites in the United States, Spain, and France from 26 April 2019 to 6 April 2022.

### Pre-assignment

Screening details:

A total of 46 subjects were enrolled in this study, 11 subjects with advanced solid malignancies into Part A of study who failed prior systemic standard treatments and 35 subjects into Part B of the study. Part B of the study was started after the completion of Part A and did not include any subjects from Part A.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Not applicable                 |
| Blinding used                | Not blinded                    |

### Arms

|                              |                                       |
|------------------------------|---------------------------------------|
| Are arms mutually exclusive? | Yes                                   |
| <b>Arm title</b>             | Part A: Debio 1143 150 mg + Nivolumab |

Arm description:

Subjects received Debio 1143, 150 milligrams (mg) capsules, orally once on Days 1 to 10 and Days 15 to 24 of each 28-day treatment cycle along with nivolumab 240 mg, intravenous (IV) infusion over 30 minutes on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Debio 1143   |
| Investigational medicinal product code |              |
| Other name                             | Xevinapant   |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

150 mg administered once on Days 1 to 10 and Days 15 to 24 of each 28-day treatment cycle allowed for a maximum of 26 cycles.

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Nivolumab       |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

Dosage and administration details:

240 mg administered once on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.

|                  |                                       |
|------------------|---------------------------------------|
| <b>Arm title</b> | Part A: Debio 1143 200 mg + Nivolumab |
|------------------|---------------------------------------|

Arm description:

Subjects received Debio 1143, 200 mg capsules, orally once on Days 1 to 10 and Days 15 to 24 of each 28-day treatment cycle along with nivolumab 240 mg, IV infusion over 30 minutes on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Debio 1143   |
| Investigational medicinal product code |              |
| Other name                             | Xevinapant   |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

200 mg administered once on Days 1 to 10 and Days 15 to 24 of each 28-day treatment cycle allowed for a maximum of 26 cycles.

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Nivolumab       |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

Dosage and administration details:

240 mg administered once on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab |
|------------------|--|

Arm description:

Subjects with small-cell lung cancer (SCLC) received Debio 1143, 200 mg capsules, orally once on Days 1 to 28 in each 28-day treatment cycle along with nivolumab 240 mg, IV infusion on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Debio 1143   |
| Investigational medicinal product code |              |
| Other name                             | Xevinapant   |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

200 mg administered once on Days 1 to 28 in each 28-day treatment cycle allowed for a maximum of 26 cycles.

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Nivolumab       |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

Dosage and administration details:

240 mg administered once on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab |
|------------------|---|

Arm description:

Subjects with squamous cell carcinoma of the head and neck (SCCHN) received Debio 1143, 200 mg capsules, orally once on Days 1 to 28 in each 28-day treatment cycle along with nivolumab 240 mg, IV infusion on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Debio 1143   |
| Investigational medicinal product code |              |
| Other name                             | Xevinapant   |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

200 mg administered once on Days 1 to 28 in each 28-day treatment cycle allowed for a maximum of 26 cycles.

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Nivolumab       |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

Dosage and administration details:

240 mg administered once on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of

26 cycles.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab |
|------------------|--|

**Arm description:**

Subjects with gastrointestinal (GI) cancers received Debio 1143, 200 mg capsules orally once on Days 1 to 28 in each 28-day treatment cycle along with nivolumab 240 mg, IV infusion on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Debio 1143   |
| Investigational medicinal product code |              |
| Other name                             | Xevinapant   |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

**Dosage and administration details:**

200 mg administered once on Days 1 to 28 in each 28-day treatment cycle allowed for a maximum of 26 cycles.

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Nivolumab       |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

**Dosage and administration details:**

240 mg administered once on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.

|                  |  |
|------------------|--|
| <b>Arm title</b> | PartB:Cohort4(Gynaecologic Cancers):Debio1143 200 mg+Nivolumab |
|------------------|--|

**Arm description:**

Subjects with gynaecologic cancers received Debio 1143, 200 mg capsules, orally once on Days 1 to 28 in each 28-day treatment cycle along with nivolumab 240 mg, IV infusion on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Debio 1143   |
| Investigational medicinal product code |              |
| Other name                             | Xevinapant   |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

**Dosage and administration details:**

200 mg administered once on Days 1 to 28 in each 28-day treatment cycle allowed for a maximum of 26 cycles.

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Nivolumab       |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

**Dosage and administration details:**

240 mg administered once on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.

| Number of subjects in period 1 | Part A: Debio 1143<br>150 mg +<br>Nivolumab | Part A: Debio 1143<br>200 mg +<br>Nivolumab | Part B: Cohort 1<br>(SCLC): Debio 1143<br>200 mg +<br>Nivolumab |
|--------------------------------|---|---|---|
|                                |   |   |   |
| Started                        | 3   | 8   | 8   |
| Completed                      | 1   | 4   | 2   |
| Not completed                  | 2   | 4   | 6   |
| Death                          | 2   | 4   | 5   |
| Lost to follow-up              | -   | -   | 1   |

| Number of subjects in period 1 | Part B: Cohort 2<br>(SCCHN): Debio<br>1143 200 mg +<br>Nivolumab | Part B: Cohort 3 (GI<br>Cancers): Debio<br>1143 200 mg +<br>Nivolumab | PartB:Cohort4(Gyna<br>ecologic<br>Cancers):Debio1143<br>200 mg+Nivolumab |
|--------------------------------|--|---|--|
|                                |  |   |  |
| Started                        | 8  | 8   | 11   |
| Completed                      | 0  | 0   | 4  |
| Not completed                  | 8  | 8   | 7  |
| Death                          | 7  | 6   | 7  |
| Lost to follow-up              | 1  | 2   | -  |

## Baseline characteristics

### Reporting groups

|   |  |
|---|--|
| Reporting group title   | Part A: Debio 1143 150 mg + Nivolumab                                  |
| Reporting group description:<br>Subjects received Debio 1143, 150 milligrams (mg) capsules, orally once on Days 1 to 10 and Days 15 to 24 of each 28-day treatment cycle along with nivolumab 240 mg, intravenous (IV) infusion over 30 minutes on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles. |  |
| Reporting group title   | Part A: Debio 1143 200 mg + Nivolumab                                  |
| Reporting group description:<br>Subjects received Debio 1143, 200 mg capsules, orally once on Days 1 to 10 and Days 15 to 24 of each 28-day treatment cycle along with nivolumab 240 mg, IV infusion over 30 minutes on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.                            |  |
| Reporting group title   | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab                 |
| Reporting group description:<br>Subjects with small-cell lung cancer (SCLC) received Debio 1143, 200 mg capsules, orally once on Days 1 to 28 in each 28-day treatment cycle along with nivolumab 240 mg, IV infusion on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.                           |  |
| Reporting group title   | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab                |
| Reporting group description:<br>Subjects with squamous cell carcinoma of the head and neck (SCCHN) received Debio 1143, 200 mg capsules, orally once on Days 1 to 28 in each 28-day treatment cycle along with nivolumab 240 mg, IV infusion on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.    |  |
| Reporting group title   | Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab           |
| Reporting group description:<br>Subjects with gastrointestinal (GI) cancers received Debio 1143, 200 mg capsules orally once on Days 1 to 28 in each 28-day treatment cycle along with nivolumab 240 mg, IV infusion on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.                            |  |
| Reporting group title   | Part B: Cohort 4 (Gynaecologic Cancers): Debio 1143 200 mg + Nivolumab |
| Reporting group description:<br>Subjects with gynaecologic cancers received Debio 1143, 200 mg capsules, orally once on Days 1 to 28 in each 28-day treatment cycle along with nivolumab 240 mg, IV infusion on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.                                    |  |

| Reporting group values  | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab |
|---|---------------------------------------|---------------------------------------|--|
| Number of subjects  | 3                                     | 8                                     | 8  |
| Age categorical<br>Units: Subjects                                      |                                       |                                       |  |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 71.0<br>± 11.36                       | 55.5<br>± 16.70                       | 65.5<br>± 5.37   |
| Gender categorical<br>Units: Subjects                                   |                                       |                                       |  |
| Female  | 1                                     | 1                                     | 4  |
| Male  | 2                                     | 7                                     | 4  |



|                        |   |   |   |
|------------------------|---|---|---|
| Ethnicity              |   |   |   |
| Units: Subjects        |   |   |   |
| Hispanic or Latino     | 0 | 0 | 1 |
| Not Hispanic or Latino | 3 | 7 | 5 |
| Unknown                | 0 | 1 | 2 |
| Race                   |   |   |   |
| Units: Subjects        |   |   |   |
| White                  | 3 | 7 | 6 |
| Other                  | 0 | 0 | 0 |
| Unknown                | 0 | 1 | 2 |

|                               |   |  |  |
|-------------------------------|---|--|--|
| <b>Reporting group values</b> | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab | Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab | PartB:Cohort4(Gynaecologic Cancers):Debio1143 200 mg+Nivolumab |
| Number of subjects            | 8   | 8  | 11   |
| Age categorical               |   |  |  |
| Units: Subjects               |   |  |  |

|                        |        |         |         |
|------------------------|--------|---------|---------|
| Age continuous         |        |         |         |
| Units: years           |        |         |         |
| arithmetic mean        | 61.6   | 63.9    | 64.8    |
| standard deviation     | ± 7.42 | ± 14.17 | ± 10.02 |
| Gender categorical     |        |         |         |
| Units: Subjects        |        |         |         |
| Female                 | 1      | 3       | 11      |
| Male                   | 7      | 5       | 0       |
| Ethnicity              |        |         |         |
| Units: Subjects        |        |         |         |
| Hispanic or Latino     | 0      | 0       | 0       |
| Not Hispanic or Latino | 6      | 7       | 6       |
| Unknown                | 2      | 1       | 5       |
| Race                   |        |         |         |
| Units: Subjects        |        |         |         |
| White                  | 5      | 7       | 6       |
| Other                  | 1      | 0       | 0       |
| Unknown                | 2      | 1       | 5       |

|                               |       |  |  |
|-------------------------------|-------|--|--|
| <b>Reporting group values</b> | Total |  |  |
| Number of subjects            | 46    |  |  |
| Age categorical               |       |  |  |
| Units: Subjects               |       |  |  |

|                    |    |  |  |
|--------------------|----|--|--|
| Age continuous     |    |  |  |
| Units: years       |    |  |  |
| arithmetic mean    | -  |  |  |
| standard deviation |    |  |  |
| Gender categorical |    |  |  |
| Units: Subjects    |    |  |  |
| Female             | 21 |  |  |
| Male               | 25 |  |  |

|                        |    |  |  |
|------------------------|----|--|--|
| Ethnicity              |    |  |  |
| Units: Subjects        |    |  |  |
| Hispanic or Latino     | 1  |  |  |
| Not Hispanic or Latino | 34 |  |  |
| Unknown                | 11 |  |  |
| Race                   |    |  |  |
| Units: Subjects        |    |  |  |
| White                  | 34 |  |  |
| Other                  | 1  |  |  |
| Unknown                | 11 |  |  |

## End points

### End points reporting groups

|   |  |
|---|--|
| Reporting group title   | Part A: Debio 1143 150 mg + Nivolumab                                  |
| Reporting group description:<br>Subjects received Debio 1143, 150 milligrams (mg) capsules, orally once on Days 1 to 10 and Days 15 to 24 of each 28-day treatment cycle along with nivolumab 240 mg, intravenous (IV) infusion over 30 minutes on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles. |  |
| Reporting group title   | Part A: Debio 1143 200 mg + Nivolumab                                  |
| Reporting group description:<br>Subjects received Debio 1143, 200 mg capsules, orally once on Days 1 to 10 and Days 15 to 24 of each 28-day treatment cycle along with nivolumab 240 mg, IV infusion over 30 minutes on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.                            |  |
| Reporting group title   | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab                 |
| Reporting group description:<br>Subjects with small-cell lung cancer (SCLC) received Debio 1143, 200 mg capsules, orally once on Days 1 to 28 in each 28-day treatment cycle along with nivolumab 240 mg, IV infusion on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.                           |  |
| Reporting group title   | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab                |
| Reporting group description:<br>Subjects with squamous cell carcinoma of the head and neck (SCCHN) received Debio 1143, 200 mg capsules, orally once on Days 1 to 28 in each 28-day treatment cycle along with nivolumab 240 mg, IV infusion on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.    |  |
| Reporting group title   | Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab           |
| Reporting group description:<br>Subjects with gastrointestinal (GI) cancers received Debio 1143, 200 mg capsules orally once on Days 1 to 28 in each 28-day treatment cycle along with nivolumab 240 mg, IV infusion on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.                            |  |
| Reporting group title   | Part B: Cohort 4 (Gynaecologic Cancers): Debio 1143 200 mg + Nivolumab |
| Reporting group description:<br>Subjects with gynaecologic cancers received Debio 1143, 200 mg capsules, orally once on Days 1 to 28 in each 28-day treatment cycle along with nivolumab 240 mg, IV infusion on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.                                    |  |

### Primary: Part A: Number of Subjects With Dose-Limiting Toxicities (DLTs)

|   |   |
|---|---|
| End point title   | Part A: Number of Subjects With Dose-Limiting Toxicities (DLTs) <sup>[1][2]</sup> |
| End point description:<br>DLT: any of following treatment-emergent adverse events (TEAEs) as per NCI CTCAE Grade V5.0 Criteria (Grades 1=mild, 2=moderate, 3=severe and 4 or 5= life-threatening/fatal outcomes) which are related to combination treatment and occurring in Cycle[C]1 (1 Cycle=28 days): Any Grade (Gr) 4/5 hematologic toxicity, clinical/laboratory non-hematologic toxicity; febrile neutropenia any grade, Gr3 thrombocytopenia if associated with bleeding/requiring platelet transfusion; Gr2; Gr3 and any other Gr3 non-hematologic, treatment-related clinical toxicity lasting ≥3 days; delay of >2 weeks due to drug-related toxicity in initiating C2; unable to complete at least 70% of the scheduled treatment, i.e. >6 Debio 1143 skipped doses in C1 due to treatment-related toxicity; required dose reduction in C1 or on C2 Day1/requirement for treatment withdrawal due to treatment-related toxicity (even if not meeting other DLT criteria). RP2D population=subjects who received ≥70% of Debio 1143 and ≥1 nivolumab dose as |   |
| End point type  | Primary   |
| End point timeframe:<br>Part A: Cycle 1 (28 days)   |   |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistical analysis was planned to be reported for this endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was applicable only for Part A arm groups of the study.

|                             |                                       |                                       |  |  |
|-----------------------------|---------------------------------------|---------------------------------------|--|--|
| <b>End point values</b>     | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab |  |  |
| Subject group type          | Reporting group                       | Reporting group                       |  |  |
| Number of subjects analysed | 3                                     | 6                                     |  |  |
| Units: subjects             | 0                                     | 0                                     |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Confirmed Objective Response Rate (ORR)

|                 |   |
|-----------------|---|
| End point title | Part B: Confirmed Objective Response Rate (ORR) <sup>[3][4]</sup> |
|-----------------|---|

End point description:

ORR was determined per response evaluation criteria in solid tumors (RECIST) v1.1 and/or gynaecologic cancer intergroup (GCIG) criteria (for Cohort 4). ORR was calculated as the percentage of subjects with a confirmed objective response. A confirmed objective response was derived as any partial response (PR) or complete response (CR) recorded after the start of study treatment until disease progression/recurrence was documented, a new systemic anti-cancer therapy was started or analysis cut-off, whichever occurred first. CR is defined by the disappearance of all target lesions and reduction of any pathological lymph nodes in short axis to <10 millimetres (mm). PR is defined by at least a 30% decrease in the sum of diameters of target lesions taking as reference the baseline sum diameter. Safety analysis set included all enrolled subjects who received at least one dose of any study drug in Part B.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Part B: From the start of study treatment until disease progression/recurrence was documented, a new systemic anti-cancer therapy was started or analysis cut-off, whichever occurred first (up to approximately 2.05 years)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistical analysis was planned to be reported for this endpoint.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was applicable only for Part B arm groups of the study.

|                                  |  |   |  |  |
|----------------------------------|--|---|--|--|
| <b>End point values</b>          | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab | Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab | PartB:Cohort4( Gynaecologic Cancers):Debio 1143 200 mg+Nivolumab |
| Subject group type               | Reporting group  | Reporting group   | Reporting group  | Reporting group  |
| Number of subjects analysed      | 8  | 8   | 8  | 11   |
| Units: percentage of subjects    |  |   |  |  |
| number (confidence interval 95%) | 0.0 (0 to 37)  | 0.0 (0 to 37)   | 0.0 (0 to 37)  | 9.1 (0 to 41)  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Parts A and B: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) Including Laboratory Abnormalities Reported as TEAEs, and Serious Adverse Events (SAEs)

|                 |  |
|-----------------|--|
| End point title | Parts A and B: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) Including Laboratory Abnormalities Reported as TEAEs, and Serious Adverse Events (SAEs) |
|-----------------|--|

#### End point description:

An adverse event(AE) is any untoward medical occurrence in a clinical trial subject administered a medicinal product that does not necessarily have a causal relationship with this treatment. TEAE is any new,related or non-related,undesirable medical occurrence or change of an existing condition in a subject that occurs during the TE period,starting/ worsening on or after the first study drug administration and up to 5 months after last nivolumab infusion,or the earliest date of new anticancer therapy –1 day,whichever occurs first.An SAE is defined as any untoward medical occurrence that at any dose results in death;is life-threatening(i.e.,puts the subject at immediate risk of death);requires inpatient hospitalization or prolongation of existing hospitalization;results in persistent or significant disability/incapacity;is a congenital anomaly/birth defect,or is otherwise medically significant.Safety analysis set= all enrolled subjects who received at least one dose of any study drug.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

#### End point timeframe:

From the first study drug administration and up to 5 months after last nivolumab infusion, or the earliest date of new anticancer therapy –1 day, whichever occurs first (up to approximately 2.08 years in Part A and 2.05 years in Part B)

| End point values            | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab |
|-----------------------------|---------------------------------------|---------------------------------------|--|---|
| Subject group type          | Reporting group                       | Reporting group                       | Reporting group  | Reporting group   |
| Number of subjects analysed | 3                                     | 8                                     | 8  | 8   |
| Units: subjects             |                                       |                                       |  |   |
| TEAEs                       | 3                                     | 8                                     | 8  | 8   |
| SAEs                        | 0                                     | 8                                     | 0  | 6   |

| End point values            | Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab | PartB:Cohort4( Gynaecologic Cancers):Debio 1143 200 mg+Nivolumab |  |  |
|-----------------------------|--|--|--|--|
| Subject group type          | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed | 8  | 11   |  |  |

|                 |   |    |  |  |
|-----------------|---|----|--|--|
| Units: subjects |   |    |  |  |
| TEAEs           | 8 | 11 |  |  |
| SAEs            | 5 | 5  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Parts A and B: Change From Baseline in Weight

|                 |   |
|-----------------|---|
| End point title | Parts A and B: Change From Baseline in Weight |
|-----------------|---|

End point description:

Safety analysis set included all enrolled subjects who received at least one dose of any study drug. Number of subjects analysed indicates the number of subjects with data available for analysis.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Baseline up to end of treatment (up to approximately 1.53 years in Part A and up to 1 year in Part B)

| End point values                     | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab |
|--------------------------------------|---------------------------------------|---------------------------------------|--|---|
| Subject group type                   | Reporting group                       | Reporting group                       | Reporting group  | Reporting group   |
| Number of subjects analysed          | 3                                     | 4                                     | 7  | 3   |
| Units: kilograms (kg)                |                                       |                                       |  |   |
| arithmetic mean (standard deviation) | -5.57 (± 5.705)                       | -10.00 (± 9.416)                      | -4.33 (± 3.888)  | -4.00 (± 6.557)   |

| End point values                     | Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab | PartB:Cohort4(Gynaecologic Cancers):Debio 1143 200 mg+Nivolumab |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group  | Reporting group   |  |  |
| Number of subjects analysed          | 4  | 8   |  |  |
| Units: kilograms (kg)                |  |   |  |  |
| arithmetic mean (standard deviation) | -0.80 (± 5.415)  | -1.11 (± 1.680)   |  |  |

## Statistical analyses

No statistical analyses for this end point

**Secondary: Parts A and B: Number of Subjects With Markedly Abnormal Change From Baseline in Vital Signs**

|                 |  |
|-----------------|--|
| End point title | Parts A and B: Number of Subjects With Markedly Abnormal Change From Baseline in Vital Signs |
|-----------------|--|

End point description:

Vital sign parameters assessed comprise of systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate. Markedly abnormal criteria for vital signs include SBP [millimeters of mercury (mmHg)]:  $\leq 90$  mmHg OR change from baseline  $\leq -20$  mmHg,  $\geq 140$  mmHg OR change from baseline  $\geq 20$  mmHg; DBP (mmHg):  $\leq 60$  mmHg OR change from baseline  $\leq -20$  mmHg,  $\geq 90$  mmHg OR change from baseline  $\geq 20$  mmHg; Heart rate [beats per minute (bpm)]:  $\leq 50$  bpm OR change from baseline  $\leq -20$  bpm,  $\geq 100$  bpm OR change from baseline  $\geq 20$  bpm. Safety analysis set included all enrolled subjects who received at least one dose of any study drug.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Baseline up to end of treatment (up to approximately 1.53 years in Part A and up to 1 year in Part B)

|                             |                                       |                                       |  |   |
|-----------------------------|---------------------------------------|---------------------------------------|--|---|
| <b>End point values</b>     | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab |
| Subject group type          | Reporting group                       | Reporting group                       | Reporting group  | Reporting group   |
| Number of subjects analysed | 3                                     | 8                                     | 8  | 8   |
| Units: subjects             | 0                                     | 0                                     | 0  | 0   |

|                             |  |  |  |  |
|-----------------------------|--|--|--|--|
| <b>End point values</b>     | Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab | Part B: Cohort 4 (Gynaecologic Cancers): Debio 1143 200 mg + Nivolumab |  |  |
| Subject group type          | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed | 8  | 11   |  |  |
| Units: subjects             | 0  | 0  |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Parts A and B: Number of Subjects With Change From Baseline in Temperature Reported as TEAEs**

|                 |  |
|-----------------|--|
| End point title | Parts A and B: Number of Subjects With Change From Baseline in Temperature Reported as TEAEs |
|-----------------|--|

End point description:

Change from baseline in temperature reported as TEAEs included pyrexia. A TEAE is any new, related or non-related, undesirable medical occurrence or change of an existing condition in a subject that occurs during the treatment-emergent period, starting or worsening on or after the first study drug administration and up to 5 months after last nivolumab infusion, or the earliest date of new anticancer therapy - 1 day, whichever occurs first. Safety analysis set included all enrolled subjects who received at

least one dose of any study drug.

|  |           |
|--|-----------|
| End point type   | Secondary |
| End point timeframe:   |           |
| From Baseline up to end of treatment (up to approximately 1.53 years in Part A and up to 1 year in Part B) |           |

|                             |                                       |                                       |  |   |
|-----------------------------|---------------------------------------|---------------------------------------|--|---|
| <b>End point values</b>     | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab |
| Subject group type          | Reporting group                       | Reporting group                       | Reporting group  | Reporting group   |
| Number of subjects analysed | 3                                     | 8                                     | 8  | 8   |
| Units: subjects             | 0                                     | 2                                     | 1  | 1   |

|                             |  |  |  |  |
|-----------------------------|--|--|--|--|
| <b>End point values</b>     | Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab | PartB:Cohort4( Gynaecologic Cancers):Debio 1143 200 mg+Nivolumab |  |  |
| Subject group type          | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed | 8  | 11   |  |  |
| Units: subjects             | 0  | 3  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Parts A and B: Number of Subjects With Markedly Abnormal Change From Baseline in Electrocardiogram (ECG) Readings

|                 |   |
|-----------------|---|
| End point title | Parts A and B: Number of Subjects With Markedly Abnormal Change From Baseline in Electrocardiogram (ECG) Readings |
|-----------------|---|

End point description:

ECG parameters comprised of PR interval(Int) [millisecond(msec)],QRS Int(msec),QT Int(msec),QTcB Int(msec),QTcF Int(msec),heart rate(HR)[bpm],RR Int(msec),derived HR(msec),calculated as 60000/RR Int[for data checking only:should be within 5% of HR].Marked abnormal criteria for ECG parameters=absolute values QRS Int:<50 msec,>110 msec;absolute values for QT Int,QTcB Int:>450 msec,>480 msec,>500 msec,QTcF:>480 msec,>500 msec;change from baseline values for QTcB Int,and QTcF:>30 msec increase from baseline,>60 msec increase from baseline.Data for highest on-treatment change from baseline per markedly abnormal criteria for ECG parameters are reported. On-treatment=time between first and last administration of any study drug.Subjects with ≥1 markedly abnormal change from baseline value in above categories are reported.Safety analysis set=all subjects who were enrolled and received ≥1 dose of any study drug.Number of subjects analysed indicates the number of subjects available for analysis.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Baseline up to end of treatment (up to approximately 1.53 years in Part A and up to 1 year in Part B)



| <b>End point values</b>                           | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab |
|---|---------------------------------------|---------------------------------------|--|---|
| Subject group type                                | Reporting group                       | Reporting group                       | Reporting group  | Reporting group   |
| Number of subjects analysed                       | 2                                     | 8                                     | 8  | 8   |
| Units: subjects                                   |                                       |                                       |  |   |
| QRS duration: >110 msec                           | 0                                     | 3                                     | 1  | 1   |
| QT Interval: >450 msec                            | 0                                     | 1                                     | 2  | 1   |
| QT Interval: >480 msec                            | 0                                     | 1                                     | 0  | 0   |
| QTcB Interval: >450 msec                          | 2                                     | 2                                     | 3  | 5   |
| QTcB Interval: >480 msec                          | 0                                     | 0                                     | 0  | 0   |
| QTcB Interval: >500 msec                          | 0                                     | 1                                     | 0  | 1   |
| QTcB Interval: >30 msec increase from baseline    | 0                                     | 4                                     | 3  | 5   |
| QTcB Interval: >60 msec increase from baseline    | 0                                     | 0                                     | 0  | 1   |
| QTcB Interval: >30/>60msec increase from baseline | 0                                     | 4                                     | 3  | 6   |
| QTcF Interval: >480 msec                          | 0                                     | 1                                     | 0  | 0   |
| QTcF Interval: >500 msec                          | 0                                     | 0                                     | 0  | 1   |
| QTcF Interval: >30 msec increase from baseline    | 0                                     | 1                                     | 2  | 3   |
| QTcF Interval: >60 msec increase from baseline    | 0                                     | 0                                     | 0  | 1   |

| <b>End point values</b>                           | Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab | PartB:Cohort4( Gynaecologic Cancers):Debio 1143 200 mg+Nivolumab |  |  |
|---|--|--|--|--|
| Subject group type                                | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed                       | 8  | 11   |  |  |
| Units: subjects                                   |  |  |  |  |
| QRS duration: >110 msec                           | 2  | 0  |  |  |
| QT Interval: >450 msec                            | 3  | 0  |  |  |
| QT Interval: >480 msec                            | 0  | 0  |  |  |
| QTcB Interval: >450 msec                          | 1  | 5  |  |  |
| QTcB Interval: >480 msec                          | 1  | 1  |  |  |
| QTcB Interval: >500 msec                          | 0  | 0  |  |  |
| QTcB Interval: >30 msec increase from baseline    | 3  | 6  |  |  |
| QTcB Interval: >60 msec increase from baseline    | 0  | 0  |  |  |
| QTcB Interval: >30/>60msec increase from baseline | 3  | 6  |  |  |
| QTcF Interval: >480 msec                          | 0  | 0  |  |  |
| QTcF Interval: >500 msec                          | 0  | 0  |  |  |

|  |   |   |  |  |
|--|---|---|--|--|
| QTcF Interval: >30 msec increase from baseline | 1 | 4 |  |  |
| QTcF Interval: >60 msec increase from baseline | 0 | 0 |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Parts A and B: Number of Subjects With Shift From Baseline to Worst On-Treatment Value in Eastern Cooperative Oncology Group Performance Status (ECOG-PS)

|                 |   |
|-----------------|---|
| End point title | Parts A and B: Number of Subjects With Shift From Baseline to Worst On-Treatment Value in Eastern Cooperative Oncology Group Performance Status (ECOG-PS) |
|-----------------|---|

End point description:

The ECOG-PS was used to assess the effect of disease progression on subjects' daily activities. ECOG-PS is graded as follows: Grade 0 - fully active, able to carry on all pre-disease performance without restriction; Grade 1 - restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature; Grade 2 - ambulatory and capable of all self-care, but unable to carry out any work activities, up and about more than 50% of waking hours; Grade 3 - capable of only limited self-care, confined to bed or chair for more than 50% of waking hours; Grade 4 - completely disabled, cannot carry on any self-care, totally confined to bed or chair; Grade 5 - dead. Shift values from baseline grade to worst on-treatment grade and missing values were reported. Safety analysis set included all enrolled subjects who received at least one dose of any study drug.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Baseline up to end of treatment (up to approximately 1.53 years in Part A and up to 1 year in Part B)

| End point values              | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab |
|-------------------------------|---------------------------------------|---------------------------------------|--|---|
| Subject group type            | Reporting group                       | Reporting group                       | Reporting group  | Reporting group   |
| Number of subjects analysed   | 3                                     | 8                                     | 8  | 8   |
| Units: subjects               |                                       |                                       |  |   |
| Shift From Grade 0 to Grade 0 | 1                                     | 3                                     | 0  | 2   |
| Shift From Grade 0 to Grade 1 | 0                                     | 2                                     | 3  | 0   |
| Shift From Grade 0 to Grade 2 | 0                                     | 1                                     | 2  | 0   |
| Shift From Grade 0 to Grade 3 | 0                                     | 0                                     | 0  | 0   |
| Shift From Grade 1 to Grade 1 | 2                                     | 1                                     | 2  | 3   |
| Shift From Grade 1 to Grade 2 | 0                                     | 1                                     | 1  | 1   |
| Shift From Grade 1 to Grade 3 | 0                                     | 0                                     | 0  | 2   |
| Missing                       | 0                                     | 0                                     | 0  | 0   |

|                  |                                |                                       |  |  |
|------------------|--------------------------------|---------------------------------------|--|--|
| End point values | Part B: Cohort 3 (GI Cancers): | PartB:Cohort4( Gynaecologic Cancers): |  |  |
|------------------|--------------------------------|---------------------------------------|--|--|

|                               | Debio 1143<br>200 mg +<br>Nivolumab | Debio1143 200<br>mg+Nivolumab |  |  |
|-------------------------------|-------------------------------------|-------------------------------|--|--|
| Subject group type            | Reporting group                     | Reporting group               |  |  |
| Number of subjects analysed   | 8                                   | 11                            |  |  |
| Units: subjects               |                                     |                               |  |  |
| Shift From Grade 0 to Grade 0 | 1                                   | 1                             |  |  |
| Shift From Grade 0 to Grade 1 | 2                                   | 4                             |  |  |
| Shift From Grade 0 to Grade 2 | 1                                   | 0                             |  |  |
| Shift From Grade 0 to Grade 3 | 1                                   | 0                             |  |  |
| Shift From Grade 1 to Grade 1 | 2                                   | 5                             |  |  |
| Shift From Grade 1 to Grade 2 | 1                                   | 0                             |  |  |
| Shift From Grade 1 to Grade 3 | 0                                   | 0                             |  |  |
| Missing                       | 0                                   | 1                             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Parts A and B: Number of Subjects With TEAEs Including Laboratory Abnormalities Leading to Treatment Discontinuations and Dose Modifications

|                 |  |
|-----------------|--|
| End point title | Parts A and B: Number of Subjects With TEAEs Including Laboratory Abnormalities Leading to Treatment Discontinuations and Dose Modifications |
|-----------------|--|

End point description:

Safety analysis set included all enrolled subjects who received at least one dose of any study drug.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the first study drug administration and up to 5 months after last nivolumab infusion, or the earliest date of new anticancer therapy -1 day, whichever occurs first (up to approximately 2.08 years in Part A and 2.05 years in Part B)

| End point values                                    | Part A: Debio<br>1143 150 mg<br>+ Nivolumab | Part A: Debio<br>1143 200 mg<br>+ Nivolumab | Part B: Cohort<br>1 (SCLC):<br>Debio 1143<br>200 mg +<br>Nivolumab | Part B: Cohort<br>2 (SCCHN):<br>Debio 1143<br>200 mg +<br>Nivolumab |
|---|---|---|--|---|
| Subject group type                                  | Reporting group                             | Reporting group                             | Reporting group  | Reporting group   |
| Number of subjects analysed                         | 3   | 8   | 8  | 8   |
| Units: subjects                                     |   |   |  |   |
| TEAEs Leading to Discontinuation of<br>Debio 1143   | 1   | 1   | 0  | 3   |
| TEAEs Leading to Discontinuation of<br>Nivolumab    | 1   | 1   | 0  | 3   |
| TEAEs Leading to Dose Modification of<br>Debio 1143 | 2   | 5   | 5  | 5   |
| TEAEs Leading to Dose Modification of<br>Nivolumab  | 2   | 6   | 4  | 5   |

|   |   |  |  |  |
|---|---|--|--|--|
| <b>End point values</b>                             | Part B: Cohort 3 (GI Cancers):<br>Debio 1143<br>200 mg +<br>Nivolumab | PartB:Cohort4(<br>Gynaecologic<br>Cancers):Debio<br>1143 200<br>mg+Nivolumab |  |  |
| Subject group type                                  | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed                         | 8   | 11   |  |  |
| Units: subjects                                     |   |  |  |  |
| TEAEs Leading to Discontinuation of<br>Debio 1143   | 1   | 2  |  |  |
| TEAEs Leading to Discontinuation of<br>Nivolumab    | 1   | 2  |  |  |
| TEAEs Leading to Dose Modification of<br>Debio 1143 | 3   | 4  |  |  |
| TEAEs Leading to Dose Modification of<br>Nivolumab  | 1   | 4  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Confirmed Objective Response Rate (ORR)

|                 |  |
|-----------------|--|
| End point title | Part A: Confirmed Objective Response Rate (ORR) <sup>[5]</sup> |
|-----------------|--|

End point description:

ORR was determined per RECIST v1.1. ORR was calculated as the percentage of subjects with a confirmed objective response. A confirmed objective response is a confirmed best overall response of PR or CR recorded after the start of study treatment until disease progression/recurrence was documented, a new systemic anti-cancer therapy was started or analysis cut-off, whichever occurred first. CR is defined by the disappearance of all target lesions and reduction of any pathological lymph nodes in short axis to <10 mm. PR is defined by at least a 30% decrease in the sum of diameters of target lesions taking as reference the baseline sum diameter. Safety analysis set included all enrolled subjects who received at least one dose of any study drug in Part A.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Part A: From the start of study treatment until disease progression/recurrence was documented, a new systemic anti-cancer therapy was started or analysis cut-off, whichever occurred first (up to approximately 2.08 years)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only descriptive statistical analysis was planned to be reported for this endpoint.

|                               |   |   |  |  |
|-------------------------------|---|---|--|--|
| <b>End point values</b>       | Part A: Debio<br>1143 150 mg<br>+ Nivolumab | Part A: Debio<br>1143 200 mg<br>+ Nivolumab |  |  |
| Subject group type            | Reporting group                             | Reporting group                             |  |  |
| Number of subjects analysed   | 3   | 8   |  |  |
| Units: percentage of subjects |   |   |  |  |
| number (not applicable)       | 0.0   | 12.5  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Parts A and B: Unconfirmed Objective Response Rate (uORR)

|                 |   |
|-----------------|---|
| End point title | Parts A and B: Unconfirmed Objective Response Rate (uORR) |
|-----------------|---|

End point description:

uORR was calculated as the percentage of subjects with unconfirmed objective response per RECIST v1.1. Unconfirmed objective response is an unconfirmed best overall response of PR or CR. Objective response was derived as any PR or CR recorded after the start of study treatment until disease progression/recurrence was documented, a new systemic anti-cancer therapy was started or analysis cut-off, whichever occurred first. CR is defined by the disappearance of all target lesions and reduction of any pathological lymph nodes in short axis to <10 mm. PR is defined by at least a 30% decrease in the sum of diameters of target lesions taking as reference the baseline sum diameter. Safety analysis set included all enrolled subjects who received at least one dose of any study drug.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the start of study treatment until disease progression/recurrence was documented, a new systemic anti-cancer therapy was started or analysis cut-off, whichever occurred first (up to approximately 2.08 years in Part A and 2.05 years in Part B)

| End point values              | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab |
|-------------------------------|---------------------------------------|---------------------------------------|--|---|
| Subject group type            | Reporting group                       | Reporting group                       | Reporting group  | Reporting group   |
| Number of subjects analysed   | 3                                     | 8                                     | 8  | 8   |
| Units: percentage of subjects |                                       |                                       |  |   |
| number (not applicable)       | 0.0                                   | 25.0                                  | 0.0  | 0.0   |

| End point values              | Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab | PartB:Cohort4(Gynaecologic Cancers):Debio 1143 200 mg+Nivolumab |  |  |
|-------------------------------|--|---|--|--|
| Subject group type            | Reporting group  | Reporting group   |  |  |
| Number of subjects analysed   | 8  | 11  |  |  |
| Units: percentage of subjects |  |   |  |  |
| number (not applicable)       | 0.0  | 9.1   |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Parts A and B: Disease Control Rate (DCR)

|                 |   |
|-----------------|---|
| End point title | Parts A and B: Disease Control Rate (DCR) |
|-----------------|---|

End point description:

DCR was calculated as the percentage of subjects with disease control. Disease control was derived as any CR, PR, or stable disease reported during the study. CR is defined by the disappearance of all target lesions and reduction of any pathological lymph nodes in short axis to <10 mm. PR is defined by at least a 30% decrease in the sum of diameters of target lesions taking as reference the baseline sum diameter. Safety analysis set included all enrolled subjects who received at least one dose of any study drug.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the start of study treatment until disease progression/recurrence was documented, a new systemic anti-cancer therapy was started or analysis cut-off, whichever occurred first (up to approximately 2.08 years in Part A and 2.05 years in Part B)

| End point values              | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab |
|-------------------------------|---------------------------------------|---------------------------------------|--|---|
| Subject group type            | Reporting group                       | Reporting group                       | Reporting group  | Reporting group   |
| Number of subjects analysed   | 3                                     | 8                                     | 8  | 8   |
| Units: percentage of subjects |                                       |                                       |  |   |
| number (not applicable)       | 66.7                                  | 50.0                                  | 25.0   | 75.0  |

| End point values              | Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab | PartB:Cohort4( Gynaecologic Cancers):Debio 1143 200 mg+Nivolumab |  |  |
|-------------------------------|--|--|--|--|
| Subject group type            | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed   | 8  | 11   |  |  |
| Units: percentage of subjects |  |  |  |  |
| number (not applicable)       | 37.5   | 45.5   |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Parts A and B: Median Duration of Response (DOR)

|                 |  |
|-----------------|--|
| End point title | Parts A and B: Median Duration of Response (DOR) |
|-----------------|--|

End point description:

DOR is defined as the time, in months, between date of the initial response (PR or CR) or date of first reduction of 50% in carbohydrate antigen 125 (CA-125), and date of the first documented disease

progression or death due to any cause, whichever occurs first. CR is defined by the disappearance of all target lesions and reduction of any pathological lymph nodes in short axis to <10 mm. PR is defined by at least a 30% decrease in the sum of diameters of target lesions taking as reference the baseline sum diameter. Data is reported as Kaplan-Meier product-limit estimates. Safety analysis set included all enrolled subjects who received at least one dose of any study drug. Number of subjects analysed indicates the censored subjects with at least a CR or PR. 9999= The median and the 95% confidence interval (CI) were not estimable due to insufficient number of subjects with events.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the start of study treatment until disease progression/recurrence was documented, a new systemic anti-cancer therapy was started or analysis cut-off, whichever occurred first (up to approximately 2.08 years in Part A and 2.05 years in Part B)

| End point values                 | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab |
|----------------------------------|---------------------------------------|---------------------------------------|--|---|
| Subject group type               | Reporting group                       | Reporting group                       | Reporting group  | Reporting group   |
| Number of subjects analysed      | 0 <sup>[6]</sup>                      | 2                                     | 0 <sup>[7]</sup>                                       | 0 <sup>[8]</sup>  |
| Units: months                    |                                       |                                       |  |   |
| median (confidence interval 95%) | ( to )                                | 9999 (9999 to 9999)                   | ( to )   | ( to )  |

Notes:

[6] - Only censored subjects with at least a CR or PR were analysed for this endpoint.

[7] - Only censored subjects with at least a CR or PR were analysed for this endpoint.

[8] - Only censored subjects with at least a CR or PR were analysed for this endpoint.

| End point values                 | Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab | PartB:Cohort4( Gynaecologic Cancers):Debio 1143 200 mg+Nivolumab |  |  |
|----------------------------------|--|--|--|--|
| Subject group type               | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed      | 0 <sup>[9]</sup>   | 1  |  |  |
| Units: months                    |  |  |  |  |
| median (confidence interval 95%) | ( to )   | 9999 (9999 to 9999)  |  |  |

Notes:

[9] - Only censored subjects with at least a CR or PR were analysed for this endpoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Parts A and B: Progression Free Survival (PFS)

|                 |  |
|-----------------|--|
| End point title | Parts A and B: Progression Free Survival (PFS) |
|-----------------|--|

End point description:

PFS duration is defined as the time, in months, elapsed between treatment initiation and tumor progression or death from any cause, whichever occurs first. Safety analysis set included all enrolled subjects who received at least one dose of any study drug. 9999= The upper limit of 95% CI was not estimable due to low number of subjects with events.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the start of study treatment until disease progression/recurrence or death from any cause, whichever occurs first (up to approximately 2.08 years in Part A and 2.05 years in Part B)

| End point values                 | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab |
|----------------------------------|---------------------------------------|---------------------------------------|--|---|
| Subject group type               | Reporting group                       | Reporting group                       | Reporting group  | Reporting group   |
| Number of subjects analysed      | 3                                     | 8                                     | 8  | 8   |
| Units: months                    |                                       |                                       |  |   |
| median (confidence interval 95%) | 2.3 (1.7 to 9999)                     | 2.3 (0.3 to 9999)                     | 1.8 (1.0 to 3.2)                                       | 1.9 (0.9 to 3.5)  |

| End point values                 | Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab | PartB:Cohort4( Gynaecologic Cancers):Debio 1143 200 mg+Nivolumab |  |  |
|----------------------------------|--|--|--|--|
| Subject group type               | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed      | 8  | 11   |  |  |
| Units: months                    |  |  |  |  |
| median (confidence interval 95%) | 1.2 (0.8 to 4.2)   | 1.8 (1.3 to 5.2)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Parts A and B: PFS Rate at Months 6 and 12

|                 |  |
|-----------------|--|
| End point title | Parts A and B: PFS Rate at Months 6 and 12 |
|-----------------|--|

End point description:

PFS is defined as duration elapsed between treatment initiation and tumor progression or death from any cause, whichever occurs first. Data for PFS rate is reported as Kaplan-Meier product-limit estimates and include Brookmeyer-Crowley confidence intervals. Safety analysis set included all enrolled subjects who received at least one dose of any study drug. 0.000 denotes that data was not available due to low number of subjects with events. n=number of subjects analysed at the given time point. 9999 denotes that data was not available due to all subjects discontinuing the study before the stipulated 12-month PFS duration i.e., no subjects were analysed at Month 12 in Part B.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Months 6 and 12



|                                  |                                       |                                       |  |   |
|----------------------------------|---------------------------------------|---------------------------------------|--|---|
| <b>End point values</b>          | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab |
| Subject group type               | Reporting group                       | Reporting group                       | Reporting group  | Reporting group   |
| Number of subjects analysed      | 3                                     | 8                                     | 8  | 8   |
| Units: proportion of subjects    |                                       |                                       |  |   |
| number (confidence interval 95%) |                                       |                                       |  |   |
| Month 6                          | 0.0 (0.000 to 0.000)                  | 0.2 (0.0 to 0.5)                      | 0.1 (0.0 to 0.4)                                       | 0.0 (0.000 to 0.000)                                    |
| Month 12 (n=3, 8, 0, 0, 0, 0)    | 0.0 (0.000 to 0.000)                  | 0.2 (0.0 to 0.5)                      | 9999 (9999 to 9999)                                    | 9999 (9999 to 9999)                                     |

|                                  |  |  |  |  |
|----------------------------------|--|--|--|--|
| <b>End point values</b>          | Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab | PartB:Cohort4( Gynaecologic Cancers):Debio 1143 200 mg+Nivolumab |  |  |
| Subject group type               | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed      | 8  | 11   |  |  |
| Units: proportion of subjects    |  |  |  |  |
| number (confidence interval 95%) |  |  |  |  |
| Month 6                          | 0.1 (0.0 to 0.4)   | 0.2 (0.0 to 0.4)   |  |  |
| Month 12 (n=3, 8, 0, 0, 0, 0)    | 9999 (9999 to 9999)  | 9999 (9999 to 9999)  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Parts A and B: Overall Survival (OS)

|                 |                                      |
|-----------------|--------------------------------------|
| End point title | Parts A and B: Overall Survival (OS) |
|-----------------|--------------------------------------|

End point description:

OS is defined as the time elapsed, in months, between treatment initiation and death from any cause. Safety analysis set included all enrolled subjects who received at least one dose of any study drug. 9999= The upper limit of 95% CI was not estimable due to low number of subjects with events.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the start of study treatment until death from any cause, whichever occurs first (up to approximately 2.08 years in Part A and 2.05 years in Part B)

| End point values                 | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab |
|----------------------------------|---------------------------------------|---------------------------------------|--|---|
| Subject group type               | Reporting group                       | Reporting group                       | Reporting group  | Reporting group   |
| Number of subjects analysed      | 3                                     | 8                                     | 8  | 8   |
| Units: months                    |                                       |                                       |  |   |
| median (confidence interval 95%) | 13.8 (12.5 to 9999)                   | 9999 (1.9 to 9999)                    | 17.5 (3.8 to 9999)                                     | 4.7 (0.9 to 13.4)                                       |

| End point values                 | Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab | PartB:Cohort4( Gynaecologic Cancers):Debio 1143 200 mg+Nivolumab |  |  |
|----------------------------------|--|--|--|--|
| Subject group type               | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed      | 8  | 11   |  |  |
| Units: months                    |  |  |  |  |
| median (confidence interval 95%) | 5.2 (1.9 to 9999)  | 11.7 (3.9 to 9999)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Parts A and B: OS Rate at Months 12 and 18

|                 |  |
|-----------------|--|
| End point title | Parts A and B: OS Rate at Months 12 and 18 |
|-----------------|--|

End point description:

OS is defined as the time elapsed, in months, between treatment initiation and death from any cause. Data for OS rate is reported as Kaplan-Meier product-limit estimates and includes Brookmeyer-Crowley confidence intervals. Safety analysis set included all enrolled subjects who received at least one dose of any study drug. 9999= The median and 95% CI were not estimable due to low number of subjects with events. n=number of subjects analysed at the given time point.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Months 12 and 18

| End point values                 | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab |
|----------------------------------|---------------------------------------|---------------------------------------|--|---|
| Subject group type               | Reporting group                       | Reporting group                       | Reporting group  | Reporting group   |
| Number of subjects analysed      | 3                                     | 8                                     | 8  | 8   |
| Units: proportion of subjects    |                                       |                                       |  |   |
| number (confidence interval 95%) |                                       |                                       |  |   |

|                                 |                     |                     |                  |                  |
|---------------------------------|---------------------|---------------------|------------------|------------------|
| Month 12                        | 1.0 (1.0 to 1.0)    | 0.5 (0.2 to 0.8)    | 0.9 (0.4 to 1.0) | 0.3 (0.0 to 0.6) |
| Month 18 (n= 1, 1, 8, 8, 8, 11) | 9999 (9999 to 9999) | 9999 (9999 to 9999) | 0.5 (0.2 to 0.8) | 0.1 (0.0 to 0.4) |

|                                  |  |  |  |  |
|----------------------------------|--|--|--|--|
| <b>End point values</b>          | Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab | PartB:Cohort4( Gynaecologic Cancers):Debio 1143 200 mg+Nivolumab |  |  |
| Subject group type               | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed      | 8  | 11   |  |  |
| Units: proportion of subjects    |  |  |  |  |
| number (confidence interval 95%) |  |  |  |  |
| Month 12                         | 0.4 (0.1 to 0.7)   | 0.4 (0.1 to 0.7)   |  |  |
| Month 18 (n= 1, 1, 8, 8, 8, 11)  | 0.4 (0.1 to 0.7)   | 0.3 (0.0 to 0.6)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Area Under the Curve From Time 0 to 4 Hours (AUC0-4H) of Debio 1143 and Debio 1143-MET1

|                 |   |
|-----------------|---|
| End point title | Part A: Area Under the Curve From Time 0 to 4 Hours (AUC0-4H) of Debio 1143 and Debio 1143-MET1 <sup>[10]</sup> |
|-----------------|---|

End point description:

Safety analysis set included all enrolled subjects who received at least one dose of any study drug in Part A. Number analysed (n) indicates the number of subjects with available data for analysis at the given timepoint.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Cycle 1: predose, 0.5, 1.5, 4 hours post-dose on Days 1 and 15, predose, 1.5, 4 hours post-dose on Days 8 and 22; Cycle 3: predose, 0.5, 1.5, 4 hours post-dose on Day 1 and predose, 1.5, 4 hours post-dose on Day 15 (each cycle=28 days)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was applicable only for Part A arm groups of the study.

|   |                                       |                                       |  |  |
|---|---------------------------------------|---------------------------------------|--|--|
| <b>End point values</b>                         | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab |  |  |
| Subject group type                              | Reporting group                       | Reporting group                       |  |  |
| Number of subjects analysed                     | 3                                     | 8                                     |  |  |
| Units: hours*nanograms per millilitre (h*ng/mL) |                                       |                                       |  |  |
| arithmetic mean (standard deviation)            |                                       |                                       |  |  |
| Debio 1143: Cycle 1 Day 1                       | 6200.28 (± 330.246)                   | 4907.15 (± 2496.914)                  |  |  |
| Debio 1143: Cycle 1 Day 8 (n=3, 7)              | 4321.40 (± 1127.611)                  | 5861.53 (± 3764.659)                  |  |  |

|  |                      |                      |  |  |
|--|----------------------|----------------------|--|--|
| Debio 1143: Cycle 1 Day 15 (n=3, 7)      | 5081.21 (± 868.905)  | 5114.03 (± 3168.408) |  |  |
| Debio 1143: Cycle 1 Day 22 (n=3, 5)      | 4517.00 (± 3539.938) | 4086.09 (± 2516.921) |  |  |
| Debio 1143: Cycle 3 Day 1 (n=3, 5)       | 4053.97 (± 3005.430) | 6844.02 (± 4940.667) |  |  |
| Debio 1143: Cycle 3 Day 15 (n=2, 4)      | 4725.37 (± 2033.252) | 5934.72 (± 2251.520) |  |  |
| Debio 1143-MET1: Cycle 1 Day 1           | 2624.48 (± 953.275)  | 1662.25 (± 957.856)  |  |  |
| Debio 1143-MET1: Cycle 1 Day 8 (n=3, 7)  | 3884.59 (± 565.589)  | 5133.24 (± 3794.465) |  |  |
| Debio 1143-MET1: Cycle 1 Day 15 (n=3, 7) | 2104.06 (± 325.456)  | 1673.48 (± 986.138)  |  |  |
| Debio 1143-MET1: Cycle 1 Day 22 (n=3, 5) | 3634.33 (± 1591.770) | 5064.61 (± 4242.170) |  |  |
| Debio 1143-MET1: Cycle 3 Day 1 (n=3, 5)  | 983.62 (± 501.515)   | 2617.59 (± 2250.993) |  |  |
| Debio 1143-MET1: Cycle 3 Day 15 (n=2, 4) | 3255.14 (± 513.699)  | 2208.80 (± 775.572)  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: AUC0-4H of Debio 1143 and Debio 1143-MET1

|                 |   |
|-----------------|---|
| End point title | Part B: AUC0-4H of Debio 1143 and Debio 1143-MET1 <sup>[11]</sup> |
|-----------------|---|

End point description:

Safety analysis set included all enrolled subjects who received at least one dose of any study drug in Part B. Number of subjects analysed indicates number of subjects available for analysis. Number analysed (n) indicates the number of subjects with available data for analysis at the given timepoint.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Cycle 1: predose, 1.5, 4 hours post-dose on Days 1 and 22; Cycle 3: predose, 1.5, 4 hours post-dose on Day 1 (each cycle = 28 days)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was applicable only for Part B arm groups of the study.

| End point values                       | Part B: Cohort 1 (SCLC):<br>Debio 1143<br>200 mg +<br>Nivolumab | Part B: Cohort 2 (SCCHN):<br>Debio 1143<br>200 mg +<br>Nivolumab | Part B: Cohort 3 (GI Cancers):<br>Debio 1143<br>200 mg +<br>Nivolumab | PartB:Cohort4(<br>Gynaecologic<br>Cancers):Debio<br>1143 200<br>mg+Nivolumab |
|--|---|--|---|--|
| Subject group type                     | Reporting group   | Reporting group  | Reporting group   | Reporting group  |
| Number of subjects analysed            | 7   | 7  | 8   | 10   |
| Units: h*ng/mL                         |   |  |   |  |
| arithmetic mean (standard deviation)   |   |  |   |  |
| Debio 1143: Cycle 1 Day 1              | 6842.88 (± 3251.994)  | 5552.70 (± 4559.658)   | 5149.10 (± 1922.588)  | 7619.75 (± 3287.399)   |
| Debio 1143: Cycle 1 Day 22 (n=7,6,5,8) | 7167.67 (± 4161.553)  | 5668.59 (± 3536.016)   | 3218.09 (± 1137.952)  | 6801.02 (± 1841.871)   |

|   |                      |                       |                      |                      |
|---|----------------------|-----------------------|----------------------|----------------------|
| Debio 1143: Cycle 3 Day 1 (n=2,2,3,7)       | 5674.83 (± 757.917)  | 3248.39 (± 3165.907)  | 2117.23 (± 970.849)  | 5920.77 (± 2206.953) |
| Debio 1143-MET1: Cycle 1 Day 1 (n=7,5,8,10) | 2737.56 (± 1280.628) | 3440.08 (± 2274.864)  | 2255.49 (± 1153.863) | 3140.29 (± 1139.965) |
| Debio 1143-MET1: Cycle 1 Day 22 (n=7,6,5,8) | 5938.44 (± 2187.477) | 10100.42 (± 3889.091) | 5404.44 (± 4032.522) | 7085.47 (± 5196.199) |
| Debio 1143-MET1: Cycle 3 Day 1 (n=2,2,3,7)  | 3409.44 (± 2059.973) | 1587.21 (± 1838.618)  | 2381.90 (± 2767.733) | 2128.83 (± 1581.498) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Area Under the Curve From Time 0 to 8 Hours (AUC0-8H) of Debio 1143 and Debio 1143-MET1

|                 |   |
|-----------------|---|
| End point title | Part A: Area Under the Curve From Time 0 to 8 Hours (AUC0-8H) of Debio 1143 and Debio 1143-MET1 <sup>[12]</sup> |
|-----------------|---|

End point description:

Safety analysis set included all enrolled subjects who received at least one dose of any study drug in Part A. Number of subjects analysed indicates number of subjects available for analysis. Number analysed (n) indicates the number of subjects with available data for analysis at the given timepoint.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Cycle 1: predose, 0.5, 1.5, 4, 8 hours post-dose on Days 1 and 15, and predose, 1.5, 4, 8 hours post-dose on Day 8; Cycle 3: predose, 0.5, 1.5, 4, 8 hours post-dose on Day 1 and predose, 1.5, 4, 8 hours post-dose on Day 15 (each cycle = 28 days)

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was applicable only for Part A arm groups of the study.

| End point values                     | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab |  |  |
|--------------------------------------|---------------------------------------|---------------------------------------|--|--|
| Subject group type                   | Reporting group                       | Reporting group                       |  |  |
| Number of subjects analysed          | 3                                     | 7                                     |  |  |
| Units: h*ng/mL                       |                                       |                                       |  |  |
| arithmetic mean (standard deviation) |                                       |                                       |  |  |
| Debio 1143: Cycle 1 Day 1            | 8954.45 (± 1347.640)                  | 8497.84 (± 3213.996)                  |  |  |
| Debio 1143: Cycle 1 Day 8            | 6699.18 (± 1315.190)                  | 9437.55 (± 6036.801)                  |  |  |
| Debio 1143: Cycle 1 Day 15           | 7280.65 (± 945.078)                   | 8024.00 (± 5036.125)                  |  |  |
| Debio 1143: Cycle 3 Day 1 (n=2, 4)   | 4623.23 (± 2089.994)                  | 10627.09 (± 6520.082)                 |  |  |
| Debio 1143: Cycle 3 Day 15 (n=2, 4)  | 6864.95 (± 1815.779)                  | 9072.05 (± 3529.268)                  |  |  |
| Debio 1143-MET1: Cycle 1 Day 1       | 5940.42 (± 2217.500)                  | 5128.38 (± 2307.490)                  |  |  |
| Debio 1143-MET1: Cycle 1 Day 8       | 7743.38 (± 1258.029)                  | 10646.90 (± 8177.450)                 |  |  |
| Debio 1143-MET1: Cycle 1 Day 15      | 4921.26 (± 741.691)                   | 4304.95 (± 2105.077)                  |  |  |

|  |                      |                      |  |  |
|--|----------------------|----------------------|--|--|
| Debio 1143-MET1: Cycle 3 Day 1 (n=2, 4)  | 2315.46 (± 1568.487) | 6632.52 (± 6610.503) |  |  |
| Debio 1143-MET1: Cycle 3 Day 15 (n=2, 4) | 6011.84 (± 429.313)  | 6225.18 (± 2315.768) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Maximum Observed Concentration (Cmax) of Debio 1143 and Debio 1143-MET1

|                 |   |
|-----------------|---|
| End point title | Part A: Maximum Observed Concentration (Cmax) of Debio 1143 and Debio 1143-MET1 <sup>[13]</sup> |
|-----------------|---|

End point description:

Safety analysis set included all enrolled subjects who received at least one dose of any study drug of Part A. Number analysed (n) indicates the number of subjects with available data for analysis at the given timepoint.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Cycle 1: Predose,0.5,1.5,4,8 hours post-dose (Days 1 and 15), predose,1.5,4,8 hours post-dose (Day 8), predose,1.5,4 hours post-dose (Day 22); Cycle 3: predose,0.5,1.5,4,8 hours post-dose (Day 1), predose,1.5,4,8 hours post-dose (Day 15) (Cycle=28 days)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was applicable only for Part A arm groups of the study.

| End point values                         | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab |  |  |
|--|---------------------------------------|---------------------------------------|--|--|
| Subject group type                       | Reporting group                       | Reporting group                       |  |  |
| Number of subjects analysed              | 3                                     | 8                                     |  |  |
| Units: ng/mL                             |                                       |                                       |  |  |
| arithmetic mean (standard deviation)     |                                       |                                       |  |  |
| Debio 1143: Cycle 1 Day 1                | 3063.33 (± 771.838)                   | 2020.63 (± 1015.945)                  |  |  |
| Debio 1143: Cycle 1 Day 8 (n=3, 7)       | 1656.67 (± 568.624)                   | 2132.71 (± 1346.859)                  |  |  |
| Debio 1143: Cycle 1 Day 15 (n=3, 7)      | 2426.67 (± 567.656)                   | 1956.29 (± 1137.771)                  |  |  |
| Debio 1143: Cycle 1 Day 22 (n=3, 5)      | 2037.00 (± 1637.415)                  | 1528.96 (± 910.236)                   |  |  |
| Debio 1143: Cycle 3 Day 1 (n=3, 5)       | 1954.00 (± 1119.459)                  | 3071.00 (± 1928.848)                  |  |  |
| Debio 1143: Cycle 3 Day 15 (n=2, 4)      | 1970.00 (± 1244.508)                  | 2265.00 (± 886.397)                   |  |  |
| Debio 1143-MET1: Cycle 1 Day 1           | 989.67 (± 344.515)                    | 972.50 (± 489.140)                    |  |  |
| Debio 1143-MET1: Cycle 1 Day 8 (n=3, 7)  | 1193.33 (± 222.336)                   | 1733.23 (± 1184.636)                  |  |  |
| Debio 1143-MET1: Cycle 1 Day 15 (n=3, 7) | 868.00 (± 117.051)                    | 915.86 (± 390.840)                    |  |  |
| Debio 1143-MET1: Cycle 1 Day 22 (n=3, 5) | 1088.33 (± 581.758)                   | 1658.68 (± 1339.093)                  |  |  |

|  |                     |                      |  |  |
|--|---------------------|----------------------|--|--|
| Debio 1143-MET1: Cycle 3 Day 1 (n=3, 5)  | 611.00 (± 376.227)  | 1343.60 (± 1078.400) |  |  |
| Debio 1143-MET1: Cycle 3 Day 15 (n=2, 4) | 1177.00 (± 272.943) | 1148.50 (± 458.398)  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part B: Cmax of Debio 1143 and Debio 1143-MET1

|                 |  |
|-----------------|--|
| End point title | Part B: Cmax of Debio 1143 and Debio 1143-MET1 <sup>[14]</sup> |
|-----------------|--|

End point description:

Safety analysis set included all enrolled subjects who received at least one dose of any study drug of Part B. Number analysed (n) indicates the number of subjects with available data for analysis at the given timepoint.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Cycle 1: predose, 1.5, 4 hours post-dose on Days 1 and 22; Cycle 3: predose, 1.5, 4 hours post-dose on Day 1 (each cycle = 28 days)

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was applicable only for Part B arm groups of the study.

| End point values                                | Part B: Cohort 1 (SCLC):<br>Debio 1143<br>200 mg +<br>Nivolumab | Part B: Cohort 2 (SCCHN):<br>Debio 1143<br>200 mg +<br>Nivolumab | Part B: Cohort 3 (GI Cancers):<br>Debio 1143<br>200 mg +<br>Nivolumab | PartB:Cohort4(<br>Gynaecologic<br>Cancers):Debio<br>1143 200<br>mg+Nivolumab |
|---|---|--|---|--|
| Subject group type                              | Reporting group   | Reporting group  | Reporting group   | Reporting group  |
| Number of subjects analysed                     | 8   | 8  | 8   | 11   |
| Units: ng/mL                                    |   |  |   |  |
| arithmetic mean (standard deviation)            |   |  |   |  |
| Debio 1143: Cycle 1 Day 1                       | 2839.5 (± 1293.43)  | 2266.1 (± 1830.74)   | 2331.3 (± 823.28)   | 2850.0 (± 1413.87)   |
| Debio 1143: Cycle 1 Day 22 (n=8, 6, 5, 10)      | 2786.3 (± 1591.66)  | 2065.8 (± 1205.31)   | 1327.0 (± 416.30)   | 2891.0 (± 860.28)  |
| Debio 1143: Cycle 3 Day 1 (n=3, 2, 3, 7)        | 2183.3 (± 496.42)   | 1726.0 (± 1094.60)   | 975.3 (± 179.70)  | 2271.4 (± 954.80)  |
| Debio 1143-MET1: Cycle 1 Day 1                  | 1077.38 (± 473.925)   | 1070.71 (± 808.979)  | 1190.00 (± 439.686)   | 1320.00 (± 483.919)  |
| Debio 1143-MET1: Cycle 1 Day 22 (n=8, 6, 5, 10) | 1888.50 (± 668.598)   | 2886.67 (± 915.394)  | 1782.80 (± 1074.434)  | 2289.10 (± 1414.128)   |
| Debio 1143-MET1: Cycle 3 Day 1 (n=3, 2, 3, 7)   | 808.67 (± 748.505)  | 738.00 (± 724.077)   | 965.33 (± 982.152)  | 891.29 (± 488.887)   |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Trough Concentration (Cmin) of Debio 1143 and Debio 1143-MET1

|                 |   |
|-----------------|---|
| End point title | Part A: Trough Concentration (Cmin) of Debio 1143 and Debio 1143-MET1 <sup>[15]</sup> |
|-----------------|---|

End point description:

Safety analysis set included all enrolled subjects who received at least one dose of any study drug of Part A. Number of subjects analysed indicates number of subjects available for analysis. Number analysed (n) indicates the number of subjects with available data for analysis at the given timepoint. 0.000= Data is not available as zero subjects were analysed at the given timepoint. 9999= The standard deviation cannot be calculated for 1 subject.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Cycle 1: predose on Days 3, 8, 15, 17 and 22; Cycle 3: predose on Days 1, 3, 15, 17; Cycle 6: predose on Day 1 (each cycle = 28 days)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was applicable only for Part A arm groups of the study.

| End point values                         | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab |  |  |
|--|---------------------------------------|---------------------------------------|--|--|
| Subject group type                       | Reporting group                       | Reporting group                       |  |  |
| Number of subjects analysed              | 3                                     | 8                                     |  |  |
| Units: ng/mL                             |                                       |                                       |  |  |
| arithmetic mean (standard deviation)     |                                       |                                       |  |  |
| Debio 1143: Cycle 1 Day 3                | 113.10 (± 31.892)                     | 169.50 (± 120.014)                    |  |  |
| Debio 1143: Cycle 1 Day 8                | 118.27 (± 30.751)                     | 173.35 (± 113.797)                    |  |  |
| Debio 1143: Cycle 1 Day 15 (n=1, 5)      | 7.34 (± 9999)                         | 5.22 (± 2.844)                        |  |  |
| Debio 1143: Cycle 1 Day 17               | 99.37 (± 19.290)                      | 133.57 (± 86.239)                     |  |  |
| Debio 1143: Cycle 1 Day 22 (n=3, 5)      | 83.53 (± 19.630)                      | 173.70 (± 135.079)                    |  |  |
| Debio 1143: Cycle 3 Day 1 (n=1, 2)       | 10.20 (± 9999)                        | 4.72 (± 0.410)                        |  |  |
| Debio 1143: Cycle 3 Day 3 (n=3, 2)       | 110.47 (± 13.808)                     | 97.20 (± 37.901)                      |  |  |
| Debio 1143: Cycle 3 Day 15 (n=0, 2)      | 0.000 (± 0.000)                       | 8.71 (± 6.640)                        |  |  |
| Debio 1143: Cycle 3 Day 17 (n=2, 3)      | 118.00 (± 16.971)                     | 136.37 (± 81.772)                     |  |  |
| Debio 1143: Cycle 6 Day 1 (n=0, 1)       | 0.000 (± 0.000)                       | 5.31 (± 9999)                         |  |  |
| Debio 1143-MET1: Cycle 1 Day 3           | 453.33 (± 180.059)                    | 620.10 (± 434.376)                    |  |  |
| Debio 1143-MET1: Cycle 1 Day 8           | 387.00 (± 145.812)                    | 793.65 (± 953.516)                    |  |  |
| Debio 1143-MET1: Cycle 1 Day 15 (n=1, 3) | 33.30 (± 9999)                        | 6.39 (± 3.241)                        |  |  |
| Debio 1143-MET1: Cycle 1 Day 17          | 543.00 (± 154.182)                    | 531.93 (± 560.633)                    |  |  |
| Debio 1143-MET1: Cycle 1 Day 22 (n=3, 5) | 367.33 (± 289.588)                    | 805.78 (± 961.228)                    |  |  |
| Debio 1143-MET1: Cycle 3 Day 1 (n=1, 2)  | 6.97 (± 9999)                         | 23.65 (± 27.655)                      |  |  |
| Debio 1143-MET1: Cycle 3 Day 3 (n=3, 2)  | 443.67 (± 172.631)                    | 1157.50 (± 1304.612)                  |  |  |



|  |                    |                    |  |  |
|--|--------------------|--------------------|--|--|
| Debio 1143-MET1: Cycle 3 Day 15 (n=0, 2) | 0.000 (± 0.000)    | 13.55 (± 9.687)    |  |  |
| Debio 1143-MET1: Cycle 3 Day 17 (n=2, 3) | 611.00 (± 322.441) | 639.67 (± 387.727) |  |  |
| Debio 1143-MET1: Cycle 6 Day 1 (n=0, 1)  | 0.000 (± 0.000)    | 3.15 (± 9999)      |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Trough Concentration (Cmin) of Debio 1143 and Debio 1143-MET1

|                 |   |
|-----------------|---|
| End point title | Part B: Trough Concentration (Cmin) of Debio 1143 and Debio 1143-MET1 <sup>[16]</sup> |
|-----------------|---|

End point description:

Safety analysis set included all enrolled subjects who received at least one dose of any study drug of Part B. Number of subjects analysed indicates number of subjects available for analysis. Number analysed (n) indicates the number of subjects with available data for analysis at the given timepoint. 0.000= Data is not available as zero subjects were analysed at the given timepoint.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Cycle 1: predose on Days 8 and 22; Cycle 3: predose on Day 1 (each cycle = 28 days)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was applicable only for Part B arm groups of the study.

| End point values                                | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab | Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab | PartB:Cohort4( Gynaecologic Cancers):Debio 1143 200 mg+Nivolumab |
|---|--|---|--|--|
| Subject group type                              | Reporting group  | Reporting group   | Reporting group  | Reporting group  |
| Number of subjects analysed                     | 8  | 8   | 7  | 10   |
| Units: ng/mL                                    |  |   |  |  |
| arithmetic mean (standard deviation)            |  |   |  |  |
| Debio 1143: Cycle 1 Day 8 (n=6, 7, 7, 10)       | 198.05 (± 143.494)                                     | 167.20 (± 112.649)                                      | 192.86 (± 130.457)   | 143.39 (± 44.663)  |
| Debio 1143: Cycle 1 Day 22 (n=8, 6, 5, 10)      | 150.29 (± 80.118)                                      | 221.60 (± 140.039)                                      | 130.92 (± 50.555)  | 146.39 (± 50.852)  |
| Debio 1143: Cycle 3 Day 1 (n=2, 2, 2, 5)        | 3.24 (± 0.721)   | 11.08 (± 12.056)  | 3.50 (± 0.318)   | 4.94 (± 2.137)   |
| Debio 1143-MET: Cycle 1 Day 8 (n=6, 8, 7, 10)   | 693.33 (± 983.009)                                     | 1917.89 (± 1826.669)                                    | 1005.20 (± 1150.843)   | 1118.40 (± 710.330)  |
| Debio 1143-MET1: Cycle 1 Day 22 (n=8, 6, 5, 10) | 658.50 (± 557.846)                                     | 2103.33 (± 1410.308)                                    | 830.20 (± 827.444)   | 1113.04 (± 811.962)  |
| Debio 1143-MET1: Cycle 3 Day 1 (n=2, 2, 0, 3)   | 2.84 (± 0.255)   | 14.35 (± 11.809)  | 0.000 (± 0.000)  | 10.30 (± 3.751)  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Serum Trough Concentration of Nivolumab

|                 |   |
|-----------------|---|
| End point title | Part A: Serum Trough Concentration of Nivolumab <sup>[17]</sup> |
|-----------------|---|

End point description:

Safety analysis set included all enrolled subjects who received at least one dose of any study drug of Part A. Number of subjects analysed indicates number of subjects available for analysis. Number analysed (n) indicates the number of subjects with available data for analysis at the given timepoint. 9999= the standard deviation cannot be calculated for 1 subject. 0.000=Data is not available as zero subjects were analysed at the given timepoint.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Cycle 1: predose, 1.5, 8 hours post-dose on Day 15; Cycle 3: predose, 0.5, 1.5, 8 hours post-dose on Day 1 and predose, 1.5 hours post-dose on Day 15 (each cycle = 28 days)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was applicable only for Part A arm groups of the study.

| End point values                     | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab |  |  |
|--------------------------------------|---------------------------------------|---------------------------------------|--|--|
| Subject group type                   | Reporting group                       | Reporting group                       |  |  |
| Number of subjects analysed          | 3                                     | 7                                     |  |  |
| Units: ng/mL                         |                                       |                                       |  |  |
| arithmetic mean (standard deviation) |                                       |                                       |  |  |
| Cycle 1 Day 15                       | 21366.67 (± 4808.673)                 | 22271.43 (± 7553.744)                 |  |  |
| Cycle 3 Day 1 (n=1, 1)               | 43500.00 (± 9999)                     | 32700.00 (± 9999)                     |  |  |
| Cycle 3 Day 15 (n=0, 1)              | 0.000 (± 0.000)                       | 27100.00 (± 9999)                     |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part B: Serum Trough Concentration of Nivolumab

|                 |   |
|-----------------|---|
| End point title | Part B: Serum Trough Concentration of Nivolumab <sup>[18]</sup> |
|-----------------|---|

End point description:

Safety analysis set included all enrolled subjects who received at least one dose of any study drug of Part B. Number of subjects analysed indicates number of subjects available for analysis. Number analysed (n) indicates the number of subjects with available data for analysis at the given timepoint. 9999= the standard deviation cannot be calculated for 1 subject. 0.000= Data is not available as zero subjects were analysed at the given timepoint.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Cycle 1: predose, 1.5 hours post-dose on Day 15; Cycle 3: predose, 1.5 hours post-dose on Day 1 and Day 15; Cycle 6: predose on Day 1 (each cycle = 28 days)

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was applicable only for Part B arm groups of the study.

| End point values                     | Part B: Cohort 1 (SCLC):<br>Debio 1143<br>200 mg +<br>Nivolumab | Part B: Cohort 2 (SCCHN):<br>Debio 1143<br>200 mg +<br>Nivolumab | Part B: Cohort 3 (GI Cancers):<br>Debio 1143<br>200 mg +<br>Nivolumab | PartB:Cohort4(<br>Gynaecologic<br>Cancers):Debio<br>1143 200<br>mg+Nivolumab |
|--------------------------------------|---|--|---|--|
| Subject group type                   | Reporting group   | Reporting group  | Reporting group   | Reporting group  |
| Number of subjects analysed          | 8   | 7  | 8   | 10   |
| Units: ng/mL                         |   |  |   |  |
| arithmetic mean (standard deviation) |   |  |   |  |
| Cycle 1 Day 15                       | 21312.5 (±<br>2942.51)  | 25414.3 (±<br>8766.68)   | 33725.0 (±<br>17751.28)   | 22332.0 (±<br>8864.61)   |
| Cycle 3 Day 1 (n=1, 1, 0, 6)         | 34100.0 (±<br>9999)   | 40600.0 (±<br>9999)  | 0.000 (±<br>0.000)  | 43866.7 (±<br>11670.08)  |
| Cycle 3 Day 15 (n=0, 1, 0, 4)        | 0.000 (±<br>0.000)  | 45400.0 (±<br>9999)  | 0.000 (±<br>0.000)  | 58400.0 (±<br>10492.22)  |
| Cycle 6 Day 1 (n=0, 1, 0, 0)         | 0.000 (±<br>0.000)  | 40400.0 (±<br>9999)  | 0.000 (±<br>0.000)  | 0.000 (±<br>0.000)   |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Parts A and B: Time to Response (TTR)

|   |                                       |
|---|---------------------------------------|
| End point title   | Parts A and B: Time to Response (TTR) |
| End point description:  |                                       |
| The average of the time taken in days for PR is reported. PR is defined by at least a 30% decrease in the sum of diameters of target lesions taking as reference the baseline sum diameter. Safety analysis set included all enrolled subjects who received at least one dose of any study drug. Number of subjects analysed indicates number of subjects with at least a CR or PR. |                                       |
| End point type  | Secondary                             |
| End point timeframe:  |                                       |
| From the start of study treatment until disease progression/recurrence was documented, a new systemic anti-cancer therapy was started or analysis cut-off, whichever occurred first (up to approximately 2.08 years in Part A and 2.05 years in Part B)   |                                       |

| End point values                       | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab | Part B: Cohort 1 (SCLC):<br>Debio 1143<br>200 mg +<br>Nivolumab | Part B: Cohort 2 (SCCHN):<br>Debio 1143<br>200 mg +<br>Nivolumab |
|--|---------------------------------------|---------------------------------------|---|--|
| Subject group type                     | Reporting group                       | Reporting group                       | Reporting group   | Reporting group  |
| Number of subjects analysed            | 0 <sup>[19]</sup>                     | 2                                     | 0 <sup>[20]</sup>   | 0 <sup>[21]</sup>  |
| Units: days                            |                                       |                                       |   |  |
| arithmetic mean (full range (min-max)) | ( to )                                | 82 (56 to 108)                        | ( to )  | ( to )   |

Notes:

[19] - This endpoint was analysed only in subjects who had a response.

[20] - This endpoint was analysed only in subjects who had a response.

[21] - This endpoint was analysed only in subjects who had a response.

| <b>End point values</b>                | Part B: Cohort 3 (GI Cancers):<br>Debio 1143<br>200 mg +<br>Nivolumab | PartB:Cohort4(<br>Gynaecologic<br>Cancers):Debio<br>1143 200<br>mg+Nivolumab |  |  |
|--|---|--|--|--|
| Subject group type                     | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed            | 0 <sup>[22]</sup>   | 1  |  |  |
| Units: days                            |   |  |  |  |
| arithmetic mean (full range (min-max)) | ( to )  | 52 (52 to 52)  |  |  |

Notes:

[22] - This endpoint was analysed only in subjects who had a response.

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From after the first study drug administration and up to 5 months after last nivolumab infusion, or the earliest date of new anticancer therapy -1 day, whichever occurs first (up to approximately 2.08 years in Part A and 2.05 years in Part B)

Adverse event reporting additional description:

Safety analysis set included all enrolled subjects who received at least one dose of any study drug.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

### Reporting groups

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Part A: Debio 1143 150 mg + Nivolumab |
|-----------------------|---------------------------------------|

Reporting group description:

Subjects received Debio 1143, 150 milligrams (mg) capsules, orally once on Days 1 to 10 and Days 15 to 24 of each 28-day treatment cycle along with nivolumab 240 mg, intravenous (IV) infusion over 30 minutes on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Part A: Debio 1143 200 mg + Nivolumab |
|-----------------------|---------------------------------------|

Reporting group description:

Subjects received Debio 1143, 200 mg capsules, orally once on Days 1 to 10 and Days 15 to 24 of each 28-day treatment cycle along with nivolumab 240 mg, IV infusion on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.

|                       |  |
|-----------------------|--|
| Reporting group title | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab |
|-----------------------|--|

Reporting group description:

Subjects with small-cell lung cancer (SCLC) received Debio 1143, 200 mg capsules, orally once on Days 1 to 28 in each 28-day treatment cycle along with nivolumab 240 mg, IV infusion on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.

|                       |   |
|-----------------------|---|
| Reporting group title | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab |
|-----------------------|---|

Reporting group description:

Subjects with squamous cell carcinoma of the head and neck (SCCHN) received Debio 1143, 200mg capsules, orally once on Days 1 to 28 in each 28-day treatment cycle along with nivolumab, 240mg, IV infusion on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.

|                       |  |
|-----------------------|--|
| Reporting group title | Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab |
|-----------------------|--|

Reporting group description:

Subjects with gastrointestinal (GI) cancers received Debio 1143, 200mg capsules, orally once on Days 1 to 28 in each 28-day treatment cycle along with nivolumab 240mg, IV infusion on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.

|                       |   |
|-----------------------|---|
| Reporting group title | Part B: Cohort 4 (Gynaecologic Cancers): Debio 1143 200mg + Nivolumab |
|-----------------------|---|

Reporting group description:

Subjects with gynaecologic cancers received Debio 1143, 200 mg capsules, orally once on Days 1 to 28 in each 28-day treatment cycle along with nivolumab 240 mg, IV infusion on Days 1 and 15 of each 28-day treatment cycle allowed for a maximum of 26 cycles.

| Serious adverse events                            | Part A: Debio 1143 150 mg + Nivolumab | Part A: Debio 1143 200 mg + Nivolumab | Part B: Cohort 1 (SCLC): Debio 1143 200 mg + Nivolumab |
|---|---------------------------------------|---------------------------------------|--|
| Total subjects affected by serious adverse events |                                       |                                       |  |
| subjects affected / exposed                       | 0 / 3 (0.00%)                         | 8 / 8 (100.00%)                       | 0 / 8 (0.00%)  |

|   |               |                |               |
|---|---------------|----------------|---------------|
| number of deaths (all causes)                                       | 2             | 4              | 5             |
| number of deaths resulting from adverse events                      | 0             | 0              | 0             |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |               |                |               |
| Glioblastoma  |               |                |               |
| subjects affected / exposed   | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all                          | 0 / 0         | 0 / 0          | 0 / 0         |
| Malignant neoplasm progression                                      |               |                |               |
| subjects affected / exposed   | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all                          | 0 / 0         | 0 / 0          | 0 / 0         |
| Nervous system disorders  |               |                |               |
| Disturbance in attention  |               |                |               |
| subjects affected / exposed   | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all                          | 0 / 0         | 0 / 0          | 0 / 0         |
| General disorders and administration site conditions                |               |                |               |
| Disease progression   |               |                |               |
| subjects affected / exposed   | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all                          | 0 / 0         | 0 / 1          | 0 / 0         |
| Fatigue   |               |                |               |
| subjects affected / exposed   | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all                          | 0 / 0         | 0 / 0          | 0 / 0         |
| Pyrexia   |               |                |               |
| subjects affected / exposed   | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all                          | 0 / 0         | 0 / 0          | 0 / 0         |
| Immune system disorders   |               |                |               |
| Drug hypersensitivity   |               |                |               |
| subjects affected / exposed   | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all                          | 0 / 0         | 0 / 0          | 0 / 0         |

|   |               |                |               |
|---|---------------|----------------|---------------|
| Gastrointestinal disorders                      |               |                |               |
| Abdominal pain                                  |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Dysphagia                                       |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pancreatitis acute                              |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Reproductive system and breast disorders        |               |                |               |
| Pelvic pain                                     |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Hepatobiliary disorders                         |               |                |               |
| Bile duct stone                                 |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Biliary obstruction                             |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Hepatic failure                                 |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 1          | 0 / 0         |
| Hyperbilirubinaemia                             |               |                |               |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Portal vein thrombosis                          |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Respiratory, thoracic and mediastinal disorders |               |                |               |
| Dyspnoea  |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pleural effusion                                |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pulmonary embolism                              |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Respiratory failure                             |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Renal and urinary disorders                     |               |                |               |
| Acute kidney injury                             |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Musculoskeletal and connective tissue disorders |               |                |               |
| Myositis  |               |                |               |



|  |                |                |                 |
|--|----------------|----------------|-----------------|
| subjects affected / exposed                                  | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 0 / 8 (0.00%)   |
| occurrences causally related to treatment / all              | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all                   | 0 / 0          | 0 / 0          | 0 / 0           |
| <b>Infections and infestations</b>                           |                |                |                 |
| Cellulitis   |                |                |                 |
| subjects affected / exposed                                  | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 0 / 8 (0.00%)   |
| occurrences causally related to treatment / all              | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all                   | 0 / 0          | 0 / 0          | 0 / 0           |
| Pneumonia  |                |                |                 |
| subjects affected / exposed                                  | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 0 / 8 (0.00%)   |
| occurrences causally related to treatment / all              | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all                   | 0 / 0          | 0 / 0          | 0 / 0           |
| Sepsis   |                |                |                 |
| subjects affected / exposed                                  | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 0 / 8 (0.00%)   |
| occurrences causally related to treatment / all              | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all                   | 0 / 0          | 0 / 0          | 0 / 0           |
| Upper respiratory tract infection                            |                |                |                 |
| subjects affected / exposed                                  | 0 / 3 (0.00%)  | 1 / 8 (12.50%) | 0 / 8 (0.00%)   |
| occurrences causally related to treatment / all              | 0 / 0          | 0 / 1          | 0 / 0           |
| deaths causally related to treatment / all                   | 0 / 0          | 0 / 0          | 0 / 0           |
| <b>Metabolism and nutrition disorders</b>                    |                |                |                 |
| Hypercalcaemia   |                |                |                 |
| subjects affected / exposed                                  | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 0 / 8 (0.00%)   |
| occurrences causally related to treatment / all              | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all                   | 0 / 0          | 0 / 0          | 0 / 0           |
| Hyponatraemia  |                |                |                 |
| subjects affected / exposed                                  | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 0 / 8 (0.00%)   |
| occurrences causally related to treatment / all              | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all                   | 0 / 0          | 0 / 0          | 0 / 0           |
| <b>Serious adverse events</b>                                |                |                |                 |
| Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab      |                |                |                 |
| Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab |                |                |                 |
| Part B: Cohort 4 (Gynaecologic Cancers): Debio 1143          |                |                |                 |
| <b>Total subjects affected by serious adverse events</b>     |                |                |                 |
| subjects affected / exposed                                  | 6 / 8 (75.00%) | 5 / 8 (62.50%) | 5 / 11 (45.45%) |

|   |                |                |                |
|---|----------------|----------------|----------------|
| number of deaths (all causes)                                       | 7              | 6              | 7              |
| number of deaths resulting from adverse events                      | 3              | 0              | 0              |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                |                |
| Glioblastoma  |                |                |                |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Malignant neoplasm progression                                      |                |                |                |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 1 / 8 (12.50%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 1          | 0 / 0          |
| Nervous system disorders  |                |                |                |
| Disturbance in attention  |                |                |                |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions                |                |                |                |
| Disease progression   |                |                |                |
| subjects affected / exposed   | 1 / 8 (12.50%) | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 1          | 0 / 0          | 0 / 0          |
| Fatigue   |                |                |                |
| subjects affected / exposed   | 2 / 8 (25.00%) | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 2          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Pyrexia   |                |                |                |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Immune system disorders   |                |                |                |
| Drug hypersensitivity   |                |                |                |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Gastrointestinal disorders                      |                |                |                |
| Abdominal pain                                  |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 1 / 8 (12.50%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Dysphagia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 1 / 8 (12.50%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pancreatitis acute                              |                |                |                |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Reproductive system and breast disorders        |                |                |                |
| Pelvic pain                                     |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                         |                |                |                |
| Bile duct stone                                 |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Biliary obstruction                             |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatic failure                                 |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hyperbilirubinaemia                             |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Portal vein thrombosis                          |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Dyspnoea  |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 1 / 8 (12.50%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pleural effusion                                |                |                |                |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 1 / 8 (12.50%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary embolism                              |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 1 / 8 (12.50%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory failure                             |                |                |                |
| subjects affected / exposed                     | 2 / 8 (25.00%) | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 2          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |                |                |                |
| Acute kidney injury                             |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Myositis  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Infections and infestations</b>              |                |                |                |
| Cellulitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| Sepsis  |                |                |                |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Upper respiratory tract infection               |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Metabolism and nutrition disorders</b>       |                |                |                |
| Hypercalcaemia                                  |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hyponatraemia                                   |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 1 / 8 (12.50%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

Frequency threshold for reporting non-serious adverse events: 5 %

| <b>Non-serious adverse events</b>   | Part A: Debio 1143<br>150 mg +<br>Nivolumab   | Part A: Debio 1143<br>200 mg +<br>Nivolumab   | Part B: Cohort 1<br>(SCLC): Debio 1143<br>200 mg +<br>Nivolumab  |
|---|---|---|--|
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed   | 3 / 3 (100.00%)   | 8 / 8 (100.00%)   | 8 / 8 (100.00%)  |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps)<br>Tumour pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1  |
| Vascular disorders<br>Lymphoedema<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0   |
| General disorders and administration<br>site conditions<br>Asthenia<br>subjects affected / exposed<br>occurrences (all)<br><br>Chills<br>subjects affected / exposed<br>occurrences (all)<br><br>Facial pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Fatigue<br>subjects affected / exposed<br>occurrences (all)<br><br>Generalised oedema<br>subjects affected / exposed<br>occurrences (all)<br><br>Pyrexia<br>subjects affected / exposed<br>occurrences (all)<br><br>Mucosal inflammation<br>subjects affected / exposed<br>occurrences (all)<br><br>Malaise | 0 / 3 (0.00%)<br>0<br><br>0 / 3 (0.00%)<br>0<br><br>0 / 3 (0.00%)<br>0<br><br>1 / 3 (33.33%)<br>1<br><br>0 / 3 (0.00%)<br>0<br><br>0 / 3 (0.00%)<br>0<br><br>0 / 3 (0.00%)<br>0 | 2 / 8 (25.00%)<br>3<br><br>0 / 8 (0.00%)<br>0<br><br>0 / 8 (0.00%)<br>0<br><br>1 / 8 (12.50%)<br>1<br><br>0 / 8 (0.00%)<br>0<br><br>1 / 8 (12.50%)<br>2 | 1 / 8 (12.50%)<br>1<br><br>1 / 8 (12.50%)<br>1<br><br>0 / 8 (0.00%)<br>0<br><br>6 / 8 (75.00%)<br>6<br><br>0 / 8 (0.00%)<br>0<br><br>1 / 8 (12.50%)<br>1<br><br>0 / 8 (0.00%)<br>0 |

|  |                    |                    |                    |
|--|--------------------|--------------------|--------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0 |
| Reproductive system and breast disorders         |                    |                    |                    |
| Intermenstrual bleeding                          |                    |                    |                    |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 8 (0.00%)      | 0 / 8 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Pelvic pain                                      |                    |                    |                    |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 8 (0.00%)      | 0 / 8 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Vaginal fistula                                  |                    |                    |                    |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 8 (0.00%)      | 0 / 8 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Vulvovaginal pruritus                            |                    |                    |                    |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 8 (0.00%)      | 0 / 8 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Respiratory, thoracic and mediastinal disorders  |                    |                    |                    |
| Catarrh  |                    |                    |                    |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 1 / 8 (12.50%)     | 0 / 8 (0.00%)      |
| occurrences (all)                                | 0                  | 1                  | 0                  |
| Cough  |                    |                    |                    |
| subjects affected / exposed                      | 1 / 3 (33.33%)     | 1 / 8 (12.50%)     | 2 / 8 (25.00%)     |
| occurrences (all)                                | 1                  | 1                  | 3                  |
| Pneumonitis                                      |                    |                    |                    |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 1 / 8 (12.50%)     | 0 / 8 (0.00%)      |
| occurrences (all)                                | 0                  | 1                  | 0                  |
| Hypoxia  |                    |                    |                    |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 8 (0.00%)      | 1 / 8 (12.50%)     |
| occurrences (all)                                | 0                  | 0                  | 1                  |
| Productive cough                                 |                    |                    |                    |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 8 (0.00%)      | 0 / 8 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Rhinitis allergic                                |                    |                    |                    |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 8 (0.00%)      | 1 / 8 (12.50%)     |
| occurrences (all)                                | 0                  | 0                  | 1                  |
| Rhinorrhoea                                      |                    |                    |                    |

|  |                    |                     |                     |
|--|--------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Throat irritation<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 3 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 |
| Psychiatric disorders<br>Agitation<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 3 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Anxiety<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Depression<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Investigations<br>Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 | 2 / 8 (25.00%)<br>2 |
| Amylase increased<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 3 (0.00%)<br>0 | 2 / 8 (25.00%)<br>2 | 1 / 8 (12.50%)<br>1 |
| Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 3 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 | 1 / 8 (12.50%)<br>3 |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 3 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 | 0 / 8 (0.00%)<br>0  |
| Lipase increased   |                    |                     |                     |



|  |               |                |                |
|--|---------------|----------------|----------------|
| subjects affected / exposed                    | 0 / 3 (0.00%) | 2 / 8 (25.00%) | 2 / 8 (25.00%) |
| occurrences (all)                              | 0             | 2              | 2              |
| Weight decreased                               |               |                |                |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 1 / 8 (12.50%) |
| occurrences (all)                              | 0             | 1              | 1              |
| Blood alkaline phosphatase increased           |               |                |                |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0             | 0              | 0              |
| Blood corticotrophin decreased                 |               |                |                |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                              | 0             | 0              | 1              |
| Blood creatine increased                       |               |                |                |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                              | 0             | 0              | 1              |
| C-reactive protein increased                   |               |                |                |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0             | 0              | 0              |
| Cortisol decreased                             |               |                |                |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                              | 0             | 0              | 1              |
| Electrocardiogram QT prolonged                 |               |                |                |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                              | 0             | 0              | 1              |
| Gamma-glutamyltransferase increased            |               |                |                |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0             | 0              | 0              |
| Lymphocyte count decreased                     |               |                |                |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0             | 0              | 0              |
| Neutrophil count decreased                     |               |                |                |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                              | 0             | 0              | 1              |
| Injury, poisoning and procedural complications |               |                |                |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| Subdural haematoma<br>subjects affected / exposed<br>occurrences (all)                       | 1 / 3 (33.33%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Craniocerebral injury<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 3 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| VIth nerve injury<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 3 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Cardiac disorders<br>Angina pectoris<br>subjects affected / exposed<br>occurrences (all)     | 0 / 3 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 3 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Nervous system disorders<br>Bell's palsy<br>subjects affected / exposed<br>occurrences (all) | 1 / 3 (33.33%)<br>1 | 0 / 8 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                                | 1 / 3 (33.33%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Sciatica<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 3 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 | 0 / 8 (0.00%)<br>0  |
| Dysgeusia<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 3 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 |
| Headache<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 3 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Memory impairment<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 3 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Neuralgia  |                     |                     |                     |

|                                      |               |                |                |
|--------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed          | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                    | 0             | 0              | 1              |
| Somnolence                           |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Vocal cord paralysis                 |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Blood and lymphatic system disorders |               |                |                |
| Anaemia                              |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 3 / 8 (37.50%) | 1 / 8 (12.50%) |
| occurrences (all)                    | 0             | 5              | 2              |
| Hyperleukocytosis                    |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Lymph node pain                      |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Lymphadenopathy                      |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                    | 0             | 0              | 1              |
| Thrombocytopenia                     |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Ear and labyrinth disorders          |               |                |                |
| Hypoacusis                           |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Eye disorders                        |               |                |                |
| Vision blurred                       |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Gastrointestinal disorders           |               |                |                |
| Constipation                         |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 2 / 8 (25.00%) | 2 / 8 (25.00%) |
| occurrences (all)                    | 0             | 2              | 2              |
| Diarrhoea                            |               |                |                |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed            | 0 / 3 (0.00%)  | 2 / 8 (25.00%) | 3 / 8 (37.50%) |
| occurrences (all)                      | 0              | 2              | 4              |
| Dry mouth                              |                |                |                |
| subjects affected / exposed            | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Dysphagia                              |                |                |                |
| subjects affected / exposed            | 1 / 3 (33.33%) | 0 / 8 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                      | 1              | 0              | 1              |
| Gingival pain                          |                |                |                |
| subjects affected / exposed            | 1 / 3 (33.33%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                      | 2              | 0              | 0              |
| Haemorrhoids                           |                |                |                |
| subjects affected / exposed            | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Nausea                                 |                |                |                |
| subjects affected / exposed            | 0 / 3 (0.00%)  | 2 / 8 (25.00%) | 2 / 8 (25.00%) |
| occurrences (all)                      | 0              | 2              | 2              |
| Oral pain                              |                |                |                |
| subjects affected / exposed            | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Stomatitis                             |                |                |                |
| subjects affected / exposed            | 1 / 3 (33.33%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                      | 1              | 0              | 0              |
| Vomiting                               |                |                |                |
| subjects affected / exposed            | 0 / 3 (0.00%)  | 1 / 8 (12.50%) | 1 / 8 (12.50%) |
| occurrences (all)                      | 0              | 3              | 1              |
| Hepatobiliary disorders                |                |                |                |
| Hepatic cytolysis                      |                |                |                |
| subjects affected / exposed            | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Skin and subcutaneous tissue disorders |                |                |                |
| Dry skin                               |                |                |                |
| subjects affected / exposed            | 1 / 3 (33.33%) | 0 / 8 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                      | 1              | 0              | 1              |
| Dermatitis                             |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| Erythema                                    |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 1 / 8 (12.50%) | 0 / 8 (0.00%)  |
| occurrences (all)                           | 0              | 1              | 0              |
| Leukoplakia                                 |                |                |                |
| subjects affected / exposed                 | 1 / 3 (33.33%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                           | 1              | 0              | 0              |
| Pruritus                                    |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 3 / 8 (37.50%) | 4 / 8 (50.00%) |
| occurrences (all)                           | 0              | 4              | 4              |
| Rash maculo-papular                         |                |                |                |
| subjects affected / exposed                 | 1 / 3 (33.33%) | 0 / 8 (0.00%)  | 3 / 8 (37.50%) |
| occurrences (all)                           | 1              | 0              | 3              |
| Skin exfoliation                            |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 1 / 8 (12.50%) | 0 / 8 (0.00%)  |
| occurrences (all)                           | 0              | 1              | 0              |
| Palmar-plantar erythrodysaesthesia syndrome |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| Pemphigoid                                  |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                           | 0              | 0              | 1              |
| Rash macular                                |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| Rash  |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                           | 0              | 0              | 1              |
| Skin lesion                                 |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| Skin reaction                               |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| Urticaria<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 3 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Renal and urinary disorders  |                     |                     |                     |
| Dysuria<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 3 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Haematuria<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 3 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Renal failure<br>subjects affected / exposed<br>occurrences (all)              | 0 / 3 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Urinary incontinence<br>subjects affected / exposed<br>occurrences (all)       | 0 / 3 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Urinary retention<br>subjects affected / exposed<br>occurrences (all)          | 0 / 3 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 |
| Endocrine disorders  |                     |                     |                     |
| Hyperthyroidism<br>subjects affected / exposed<br>occurrences (all)            | 0 / 3 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 | 0 / 8 (0.00%)<br>0  |
| Hypothyroidism<br>subjects affected / exposed<br>occurrences (all)             | 0 / 3 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 |
| Musculoskeletal and connective tissue disorders                                |                     |                     |                     |
| Back pain<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 3 (33.33%)<br>1 | 1 / 8 (12.50%)<br>1 | 2 / 8 (25.00%)<br>2 |
| Musculoskeletal chest pain<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 | 0 / 8 (0.00%)<br>0  |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 3 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 |

|                                   |                |                |                |
|-----------------------------------|----------------|----------------|----------------|
| Myalgia                           |                |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                 | 0              | 0              | 1              |
| Pain in extremity                 |                |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                 | 0              | 0              | 0              |
| Polymyalgia rheumatica            |                |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                 | 0              | 0              | 0              |
| Sacral pain                       |                |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                 | 0              | 0              | 0              |
| Infections and infestations       |                |                |                |
| Ear infection                     |                |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%)  | 1 / 8 (12.50%) | 0 / 8 (0.00%)  |
| occurrences (all)                 | 0              | 1              | 0              |
| Fungal foot infection             |                |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%)  | 1 / 8 (12.50%) | 0 / 8 (0.00%)  |
| occurrences (all)                 | 0              | 1              | 0              |
| Lip infection                     |                |                |                |
| subjects affected / exposed       | 1 / 3 (33.33%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                 | 1              | 0              | 0              |
| Mucosal infection                 |                |                |                |
| subjects affected / exposed       | 1 / 3 (33.33%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                 | 1              | 0              | 0              |
| Oral candidiasis                  |                |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%)  | 1 / 8 (12.50%) | 0 / 8 (0.00%)  |
| occurrences (all)                 | 0              | 1              | 0              |
| Upper respiratory tract infection |                |                |                |
| subjects affected / exposed       | 1 / 3 (33.33%) | 2 / 8 (25.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                 | 1              | 2              | 0              |
| Bronchitis                        |                |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%)  | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                 | 0              | 0              | 0              |
| Candida infection                 |                |                |                |

|                                    |               |                |                |
|------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed        | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                  | 0             | 0              | 0              |
| Gingivitis                         |               |                |                |
| subjects affected / exposed        | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                  | 0             | 0              | 0              |
| Listeria encephalitis              |               |                |                |
| subjects affected / exposed        | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                  | 0             | 0              | 0              |
| Oral fungal infection              |               |                |                |
| subjects affected / exposed        | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                  | 0             | 0              | 0              |
| Pseudomonas infection              |               |                |                |
| subjects affected / exposed        | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                  | 0             | 0              | 0              |
| Skin infection                     |               |                |                |
| subjects affected / exposed        | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                  | 0             | 0              | 0              |
| Soft tissue infection              |               |                |                |
| subjects affected / exposed        | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                  | 0             | 0              | 0              |
| Urinary tract infection            |               |                |                |
| subjects affected / exposed        | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                  | 0             | 0              | 0              |
| Metabolism and nutrition disorders |               |                |                |
| Decreased appetite                 |               |                |                |
| subjects affected / exposed        | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 3 / 8 (37.50%) |
| occurrences (all)                  | 0             | 2              | 3              |
| Hypercalcaemia                     |               |                |                |
| subjects affected / exposed        | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                  | 0             | 0              | 0              |
| Hyperglycaemia                     |               |                |                |
| subjects affected / exposed        | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                  | 0             | 0              | 0              |
| Hypertriglyceridaemia              |               |                |                |
| subjects affected / exposed        | 0 / 3 (0.00%) | 0 / 8 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                  | 0             | 0              | 1              |



|                             |               |               |                |
|-----------------------------|---------------|---------------|----------------|
| Hypokalaemia                |               |               |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0             | 0              |
| Hypomagnesaemia             |               |               |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0             | 0              |
| Hyponatraemia               |               |               |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all)           | 0             | 0             | 1              |
| Hypophosphataemia           |               |               |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all)           | 0             | 0             | 1              |

| <b>Non-serious adverse events</b>                                   | Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab | Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab | Part B: Cohort 4 (Gynaecologic Cancers): Debio 1143 |
|---|---|--|---|
| Total subjects affected by non-serious adverse events               |   |  |   |
| subjects affected / exposed   | 8 / 8 (100.00%)   | 8 / 8 (100.00%)  | 11 / 11 (100.00%)                                   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |  |   |
| Tumour pain   |   |  |   |
| subjects affected / exposed   | 0 / 8 (0.00%)   | 1 / 8 (12.50%)   | 0 / 11 (0.00%)                                      |
| occurrences (all)   | 0   | 1  | 0   |
| Vascular disorders  |   |  |   |
| Lymphoedema   |   |  |   |
| subjects affected / exposed   | 0 / 8 (0.00%)   | 0 / 8 (0.00%)  | 1 / 11 (9.09%)                                      |
| occurrences (all)   | 0   | 0  | 1   |
| General disorders and administration site conditions                |   |  |   |
| Asthenia  |   |  |   |
| subjects affected / exposed   | 0 / 8 (0.00%)   | 0 / 8 (0.00%)  | 2 / 11 (18.18%)                                     |
| occurrences (all)   | 0   | 0  | 3   |
| Chills  |   |  |   |
| subjects affected / exposed   | 0 / 8 (0.00%)   | 0 / 8 (0.00%)  | 1 / 11 (9.09%)                                      |
| occurrences (all)   | 0   | 0  | 1   |
| Facial pain   |   |  |   |
| subjects affected / exposed   | 1 / 8 (12.50%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%)                                      |
| occurrences (all)   | 1   | 0  | 0   |
| Fatigue   |   |  |   |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 3 / 8 (37.50%) | 2 / 8 (25.00%) | 2 / 11 (18.18%) |
| occurrences (all)                               | 3              | 2              | 2               |
| Generalised oedema                              |                |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 1 / 8 (12.50%) | 0 / 11 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0               |
| Pyrexia   |                |                |                 |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 8 (0.00%)  | 3 / 11 (27.27%) |
| occurrences (all)                               | 1              | 0              | 3               |
| Mucosal inflammation                            |                |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%)  |
| occurrences (all)                               | 0              | 0              | 1               |
| Malaise   |                |                |                 |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 8 (0.00%)  | 0 / 11 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0               |
| Reproductive system and breast disorders        |                |                |                 |
| Intermenstrual bleeding                         |                |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%)  |
| occurrences (all)                               | 0              | 0              | 2               |
| Pelvic pain                                     |                |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%)  |
| occurrences (all)                               | 0              | 0              | 1               |
| Vaginal fistula                                 |                |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%)  |
| occurrences (all)                               | 0              | 0              | 1               |
| Vulvovaginal pruritus                           |                |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%)  |
| occurrences (all)                               | 0              | 0              | 1               |
| Respiratory, thoracic and mediastinal disorders |                |                |                 |
| Catarrh   |                |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Cough   |                |                |                 |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 1 / 8 (12.50%) | 1 / 11 (9.09%)  |
| occurrences (all)                               | 1              | 1              | 1               |
| Pneumonitis                                     |                |                |                 |

|                                    |                |                |                |
|------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0              |
| Hypoxia                            |                |                |                |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0              |
| Productive cough                   |                |                |                |
| subjects affected / exposed        | 1 / 8 (12.50%) | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences (all)                  | 1              | 0              | 0              |
| Rhinitis allergic                  |                |                |                |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0              |
| Rhinorrhoea                        |                |                |                |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%) |
| occurrences (all)                  | 0              | 0              | 1              |
| Throat irritation                  |                |                |                |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%) |
| occurrences (all)                  | 0              | 0              | 1              |
| Dyspnoea                           |                |                |                |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 1 / 8 (12.50%) | 1 / 11 (9.09%) |
| occurrences (all)                  | 0              | 1              | 1              |
| Psychiatric disorders              |                |                |                |
| Agitation                          |                |                |                |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 1 / 8 (12.50%) | 0 / 11 (0.00%) |
| occurrences (all)                  | 0              | 1              | 0              |
| Anxiety                            |                |                |                |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 1 / 8 (12.50%) | 0 / 11 (0.00%) |
| occurrences (all)                  | 0              | 1              | 0              |
| Depression                         |                |                |                |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%) |
| occurrences (all)                  | 0              | 0              | 1              |
| Insomnia                           |                |                |                |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 1 / 8 (12.50%) | 1 / 11 (9.09%) |
| occurrences (all)                  | 0              | 1              | 1              |
| Investigations                     |                |                |                |
| Alanine aminotransferase increased |                |                |                |

|                                      |                |                |                 |
|--------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed          | 1 / 8 (12.50%) | 1 / 8 (12.50%) | 5 / 11 (45.45%) |
| occurrences (all)                    | 2              | 1              | 5               |
| Amylase increased                    |                |                |                 |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 2 / 11 (18.18%) |
| occurrences (all)                    | 0              | 0              | 2               |
| Aspartate aminotransferase increased |                |                |                 |
| subjects affected / exposed          | 1 / 8 (12.50%) | 1 / 8 (12.50%) | 4 / 11 (36.36%) |
| occurrences (all)                    | 2              | 1              | 4               |
| Blood creatinine increased           |                |                |                 |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%)  |
| occurrences (all)                    | 0              | 0              | 2               |
| Lipase increased                     |                |                |                 |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 8 (0.00%)  | 1 / 11 (9.09%)  |
| occurrences (all)                    | 1              | 0              | 1               |
| Weight decreased                     |                |                |                 |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 8 (0.00%)  | 1 / 11 (9.09%)  |
| occurrences (all)                    | 1              | 0              | 1               |
| Blood alkaline phosphatase increased |                |                |                 |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 8 (0.00%)  | 0 / 11 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0               |
| Blood corticotrophin decreased       |                |                |                 |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Blood creatine increased             |                |                |                 |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 1 / 8 (12.50%) | 0 / 11 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0               |
| C-reactive protein increased         |                |                |                 |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 8 (0.00%)  | 0 / 11 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0               |
| Cortisol decreased                   |                |                |                 |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Electrocardiogram QT prolonged       |                |                |                 |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 8 (0.00%)  | 1 / 11 (9.09%)  |
| occurrences (all)                    | 1              | 0              | 1               |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| Gamma-glutamyltransferase increased<br>subjects affected / exposed<br>occurrences (all)                                  | 1 / 8 (12.50%)<br>1 | 0 / 8 (0.00%)<br>0  | 1 / 11 (9.09%)<br>1 |
| Lymphocyte count decreased<br>subjects affected / exposed<br>occurrences (all)   | 1 / 8 (12.50%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 |
| Neutrophil count decreased<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 |
| Injury, poisoning and procedural complications<br>Subdural haematoma<br>subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 |
| Craniocerebral injury<br>subjects affected / exposed<br>occurrences (all)  | 1 / 8 (12.50%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 |
| Vlth nerve injury<br>subjects affected / exposed<br>occurrences (all)  | 1 / 8 (12.50%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 |
| Cardiac disorders<br>Angina pectoris<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 8 (0.00%)<br>0  | 1 / 8 (12.50%)<br>2 | 0 / 11 (0.00%)<br>0 |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)  | 1 / 8 (12.50%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 |
| Nervous system disorders<br>Bell's palsy<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)  | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 1 / 11 (9.09%)<br>1 |
| Sciatica<br>subjects affected / exposed<br>occurrences (all)   | 1 / 8 (12.50%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 |

|                                      |                |                |                 |
|--------------------------------------|----------------|----------------|-----------------|
| Dysgeusia                            |                |                |                 |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Headache                             |                |                |                 |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 8 (0.00%)  | 0 / 11 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0               |
| Memory impairment                    |                |                |                 |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 1 / 8 (12.50%) | 0 / 11 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0               |
| Neuralgia                            |                |                |                 |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Somnolence                           |                |                |                 |
| subjects affected / exposed          | 2 / 8 (25.00%) | 0 / 8 (0.00%)  | 0 / 11 (0.00%)  |
| occurrences (all)                    | 2              | 0              | 0               |
| Vocal cord paralysis                 |                |                |                 |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%)  |
| occurrences (all)                    | 0              | 0              | 1               |
| Blood and lymphatic system disorders |                |                |                 |
| Anaemia                              |                |                |                 |
| subjects affected / exposed          | 2 / 8 (25.00%) | 2 / 8 (25.00%) | 4 / 11 (36.36%) |
| occurrences (all)                    | 2              | 2              | 4               |
| Hyperleukocytosis                    |                |                |                 |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 8 (0.00%)  | 0 / 11 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0               |
| Lymph node pain                      |                |                |                 |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%)  |
| occurrences (all)                    | 0              | 0              | 1               |
| Lymphadenopathy                      |                |                |                 |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Thrombocytopenia                     |                |                |                 |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%)  |
| occurrences (all)                    | 0              | 0              | 1               |
| Ear and labyrinth disorders          |                |                |                 |

|  |                     |                     |                      |
|--|---------------------|---------------------|----------------------|
| Hypoacusis<br>subjects affected / exposed<br>occurrences (all)                                 | 1 / 8 (12.50%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  |
| Eye disorders<br>Vision blurred<br>subjects affected / exposed<br>occurrences (all)            | 0 / 8 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 | 0 / 11 (0.00%)<br>0  |
| Gastrointestinal disorders<br>Constipation<br>subjects affected / exposed<br>occurrences (all) | 1 / 8 (12.50%)<br>1 | 1 / 8 (12.50%)<br>1 | 3 / 11 (27.27%)<br>4 |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                                  | 1 / 8 (12.50%)<br>1 | 0 / 8 (0.00%)<br>0  | 3 / 11 (27.27%)<br>3 |
| Dry mouth<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 2 / 11 (18.18%)<br>2 |
| Dysphagia<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  |
| Gingival pain<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  |
| Haemorrhoids<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 1 / 11 (9.09%)<br>1  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                                     | 2 / 8 (25.00%)<br>2 | 3 / 8 (37.50%)<br>3 | 2 / 11 (18.18%)<br>2 |
| Oral pain<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 1 / 11 (9.09%)<br>1  |
| Stomatitis<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 2 / 11 (18.18%)<br>2 |
| Vomiting   |                     |                     |                      |

|  |                     |                     |                      |
|--|---------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)   | 1 / 8 (12.50%)<br>2 | 1 / 8 (12.50%)<br>1 | 0 / 11 (0.00%)<br>0  |
| Hepatobiliary disorders<br>Hepatic cytolysis<br>subjects affected / exposed<br>occurrences (all)       | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 1 / 11 (9.09%)<br>1  |
| Skin and subcutaneous tissue disorders<br>Dry skin<br>subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  |
| Dermatitis<br>subjects affected / exposed<br>occurrences (all)   | 1 / 8 (12.50%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  |
| Erythema<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  |
| Leukoplakia<br>subjects affected / exposed<br>occurrences (all)  | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)   | 2 / 8 (25.00%)<br>2 | 2 / 8 (25.00%)<br>3 | 3 / 11 (27.27%)<br>3 |
| Rash maculo-papular<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 8 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 | 1 / 11 (9.09%)<br>1  |
| Skin exfoliation<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  |
| Palmar-plantar erythrodysesthesia<br>syndrome<br>subjects affected / exposed<br>occurrences (all)      | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 1 / 11 (9.09%)<br>1  |
| Pemphigoid<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  |
| Rash macular   |                     |                     |                      |



|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 2 / 11 (18.18%) |
| occurrences (all)           | 0              | 0              | 2               |
| Rash                        |                |                |                 |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 8 (12.50%) | 0 / 11 (0.00%)  |
| occurrences (all)           | 2              | 1              | 0               |
| Skin lesion                 |                |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%)  | 1 / 8 (12.50%) | 0 / 11 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Skin reaction               |                |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Urticaria                   |                |                |                 |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 8 (0.00%)  | 0 / 11 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0               |
| Renal and urinary disorders |                |                |                 |
| Dysuria                     |                |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Haematuria                  |                |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Renal failure               |                |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%)  | 1 / 8 (12.50%) | 2 / 11 (18.18%) |
| occurrences (all)           | 0              | 1              | 2               |
| Urinary incontinence        |                |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 2 / 11 (18.18%) |
| occurrences (all)           | 0              | 0              | 2               |
| Urinary retention           |                |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Endocrine disorders         |                |                |                 |
| Hyperthyroidism             |                |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Hypothyroidism              |                |                |                 |

|  |                     |                    |                     |
|--|---------------------|--------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 1 / 8 (12.50%)<br>1 | 0 / 8 (0.00%)<br>0 | 1 / 11 (9.09%)<br>1 |
| Musculoskeletal and connective tissue disorders  |                     |                    |                     |
| Back pain  |                     |                    |                     |
| subjects affected / exposed                      | 0 / 8 (0.00%)       | 0 / 8 (0.00%)      | 1 / 11 (9.09%)      |
| occurrences (all)                                | 0                   | 0                  | 1                   |
| Musculoskeletal chest pain                       |                     |                    |                     |
| subjects affected / exposed                      | 0 / 8 (0.00%)       | 0 / 8 (0.00%)      | 0 / 11 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                   |
| Arthralgia                                       |                     |                    |                     |
| subjects affected / exposed                      | 0 / 8 (0.00%)       | 1 / 8 (12.50%)     | 1 / 11 (9.09%)      |
| occurrences (all)                                | 0                   | 1                  | 3                   |
| Myalgia  |                     |                    |                     |
| subjects affected / exposed                      | 0 / 8 (0.00%)       | 1 / 8 (12.50%)     | 0 / 11 (0.00%)      |
| occurrences (all)                                | 0                   | 1                  | 0                   |
| Pain in extremity                                |                     |                    |                     |
| subjects affected / exposed                      | 0 / 8 (0.00%)       | 0 / 8 (0.00%)      | 1 / 11 (9.09%)      |
| occurrences (all)                                | 0                   | 0                  | 1                   |
| Polymyalgia rheumatica                           |                     |                    |                     |
| subjects affected / exposed                      | 0 / 8 (0.00%)       | 0 / 8 (0.00%)      | 1 / 11 (9.09%)      |
| occurrences (all)                                | 0                   | 0                  | 1                   |
| Sacral pain                                      |                     |                    |                     |
| subjects affected / exposed                      | 0 / 8 (0.00%)       | 1 / 8 (12.50%)     | 0 / 11 (0.00%)      |
| occurrences (all)                                | 0                   | 1                  | 0                   |
| Infections and infestations                      |                     |                    |                     |
| Ear infection                                    |                     |                    |                     |
| subjects affected / exposed                      | 0 / 8 (0.00%)       | 0 / 8 (0.00%)      | 0 / 11 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                   |
| Fungal foot infection                            |                     |                    |                     |
| subjects affected / exposed                      | 0 / 8 (0.00%)       | 0 / 8 (0.00%)      | 0 / 11 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                   |
| Lip infection                                    |                     |                    |                     |
| subjects affected / exposed                      | 0 / 8 (0.00%)       | 0 / 8 (0.00%)      | 0 / 11 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                   |
| Mucosal infection                                |                     |                    |                     |

|                                    |                |                |                |
|------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0              |
| Oral candidiasis                   |                |                |                |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0              |
| Upper respiratory tract infection  |                |                |                |
| subjects affected / exposed        | 1 / 8 (12.50%) | 1 / 8 (12.50%) | 0 / 11 (0.00%) |
| occurrences (all)                  | 1              | 1              | 0              |
| Bronchitis                         |                |                |                |
| subjects affected / exposed        | 1 / 8 (12.50%) | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences (all)                  | 1              | 0              | 0              |
| Candida infection                  |                |                |                |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%) |
| occurrences (all)                  | 0              | 0              | 1              |
| Gingivitis                         |                |                |                |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%) |
| occurrences (all)                  | 0              | 0              | 1              |
| Listeria encephalitis              |                |                |                |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%) |
| occurrences (all)                  | 0              | 0              | 1              |
| Oral fungal infection              |                |                |                |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%) |
| occurrences (all)                  | 0              | 0              | 1              |
| Pseudomonas infection              |                |                |                |
| subjects affected / exposed        | 1 / 8 (12.50%) | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences (all)                  | 1              | 0              | 0              |
| Skin infection                     |                |                |                |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%) |
| occurrences (all)                  | 0              | 0              | 1              |
| Soft tissue infection              |                |                |                |
| subjects affected / exposed        | 1 / 8 (12.50%) | 0 / 8 (0.00%)  | 0 / 11 (0.00%) |
| occurrences (all)                  | 1              | 0              | 0              |
| Urinary tract infection            |                |                |                |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 8 (0.00%)  | 1 / 11 (9.09%) |
| occurrences (all)                  | 0              | 0              | 1              |
| Metabolism and nutrition disorders |                |                |                |

|   |                     |                     |                      |
|---|---------------------|---------------------|----------------------|
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)    | 3 / 8 (37.50%)<br>3 | 1 / 8 (12.50%)<br>1 | 1 / 11 (9.09%)<br>1  |
| Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all)        | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 1 / 11 (9.09%)<br>1  |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)        | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 1 / 11 (9.09%)<br>1  |
| Hypertriglyceridaemia<br>subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all)          | 1 / 8 (12.50%)<br>1 | 0 / 8 (0.00%)<br>0  | 2 / 11 (18.18%)<br>4 |
| Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all)       | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 2 / 11 (18.18%)<br>2 |
| Hyponatraemia<br>subjects affected / exposed<br>occurrences (all)         | 1 / 8 (12.50%)<br>1 | 1 / 8 (12.50%)<br>1 | 3 / 11 (27.27%)<br>3 |
| Hypophosphataemia<br>subjects affected / exposed<br>occurrences (all)     | 0 / 8 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 14 January 2019  | <ul style="list-style-type: none"><li>• Added that the subjects should have had no established standard therapeutic alternatives to the cancer treatment.</li><li>• Advised that subjects with active ongoing infection requiring systemic antibiotic therapy, including active tuberculosis, were not eligible for enrolment.</li><li>• Changed the duration of safety follow-up, TEAE monitoring, and SAE reporting period for withdrawn subjects to 5 months (previously, 90 days) after the last nivolumab infusion.</li><li>• Expanded the list of prohibited medications.</li></ul>   |
| 07 November 2019 | <ul style="list-style-type: none"><li>• Allowed the inclusion of subjects with haemoglobin levels of <math>\geq 9.0</math> grams/decilitre (g/dL).</li><li>• Adjusted the subject population for Cohort 1 to allow the inclusion of subjects with extrapulmonary small-cell carcinomas or large cell neuroendocrine lung carcinoma.</li><li>• Clarified that nasopharyngeal carcinoma was not allowed in Cohort 2.</li><li>• Shortened the time window of thoracic or head and neck radiation <math>&gt;30</math> Gray (Gy) from within 3 months to 6 weeks prior to the start of treatment.</li><li>• Allowed inclusion of subjects with vitiligo <math>&gt;</math>Grade 1 as an ongoing toxicity of prior antineoplastic therapies.</li><li>• Shortened the time window for blood transfusion from up to 4 weeks to 2 weeks prior to the start of treatment.</li></ul>  |
| 03 April 2020    | <ul style="list-style-type: none"><li>• Added the clarification of the study treatment duration and the conditions under which treatment duration could be prolonged by 1 year for subjects who exceptionally continued study treatment beyond 13 cycles.</li><li>• Added the clarification of the schedule of assessments for subjects who exceptionally continued study treatment beyond 13 cycles.</li><li>• Added the clarification that the final analysis would be conducted 18 months after the last subject was included in the study (LPI) or 60 days from last subject last visit (LPLV), whichever occurs first.</li><li>• Updated the inclusion criteria to align the washout period of previous investigational monoclonal antibodies (mAbs) to 4 weeks or at least the duration of 1 treatment cycle whichever is the longest to prevent a potential carry-over effect.</li><li>• Updated language for prohibited concomitant medication for strong P-glycoprotein (P-gp) inhibitors/inducers and cytochrome P450 (CYP) 3A substrates. CYP 2B6 and 1A2 substrates were added as drugs to be used with caution and closely monitored based on new data. In addition, drugs with a known risk of QTc prolongation were added as medications to be used with caution. Furthermore, language on possible drug-drug interaction (DDI) concerning hormonal contraception was corrected.</li></ul> |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported