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	• Correction of full data set 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
Arm title	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.

Arm title	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.

Arm title	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.

Arm title	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.

Arm title	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.

Arm title	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 150 mg + Nivolumab	Part A: Debio 1143 200 mg + Nivolumab	Part B: Cohort 1 (SCLC): Debio 1143 200 mg + 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 (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
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:	
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 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:	
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, 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:	
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	PartB:Cohort4(Gynaecologic Cancers):Debio1143 200 mg+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.	

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			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	71.0	55.5	65.5
standard deviation	± 11.36	± 16.70	± 5.37
Gender categorical			
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

Reporting group values	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

Reporting group values	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:	
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 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:	
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, 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:	
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	PartB:Cohort4(Gynaecologic Cancers):Debio1143 200 mg+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.	

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

End point title	Part A: Number of Subjects With Dose-Limiting Toxicities (DLTs)[1][2]
End point description:	
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:	
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.

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	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)[3][4]

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.

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	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)]: ≤ 90 mmHg OR change from baseline ≤ -20 mmHg, ≥ 140 mmHg OR change from baseline ≥ 20 mmHg; DBP (mmHg): ≤ 60 mmHg OR change from baseline ≤ -20 mmHg, ≥ 90 mmHg OR change from baseline ≥ 20 mmHg; Heart rate [beats per minute (bpm)]: ≤ 50 bpm OR change from baseline ≤ -20 bpm, ≥ 100 bpm OR change from baseline ≥ 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)

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	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: 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)

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	0	2	1	1

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	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)

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	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

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				
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 200 mg + Nivolumab	Debio1143 200 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 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 Leading to Discontinuation of Debio 1143	1	1	0	3
TEAEs Leading to Discontinuation of Nivolumab	1	1	0	3
TEAEs Leading to Dose Modification of Debio 1143	2	5	5	5
TEAEs Leading to Dose Modification of Nivolumab	2	6	4	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: subjects				
TEAEs Leading to Discontinuation of Debio 1143	1	2		
TEAEs Leading to Discontinuation of Nivolumab	1	2		
TEAEs Leading to Dose Modification of Debio 1143	3	4		
TEAEs Leading to Dose Modification of 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)[5]

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.

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: 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[6]	2	0[7]	0[8]
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[9]	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

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 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)

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

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: proportion of subjects				
number (confidence interval 95%)				
Month 12 Month 18 (n= 1, 1, 8, 8, 8, 11)	0.4 (0.1 to 0.7) 0.4 (0.1 to 0.7)	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[10]

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.

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: hours*nanograms per millilitre (h*ng/mL)				
arithmetic mean (standard deviation)				
Debio 1143: Cycle 1 Day 1 Debio 1143: Cycle 1 Day 8 (n=3, 7)	6200.28 (± 330.246) 4321.40 (± 1127.611)	4907.15 (± 2496.914) 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[11]

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): 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	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[12]

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[13]

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[14]

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): 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: 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[15]

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[16]

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[17]

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[18]

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): 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	7	8	10
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 15	21312.5 (± 2942.51)	25414.3 (± 8766.68)	33725.0 (± 17751.28)	22332.0 (± 8864.61)
Cycle 3 Day 1 (n=1, 1, 0, 6)	34100.0 (± 9999)	40600.0 (± 9999)	0.000 (± 0.000)	43866.7 (± 11670.08)
Cycle 3 Day 15 (n=0, 1, 0, 4)	0.000 (± 0.000)	45400.0 (± 9999)	0.000 (± 0.000)	58400.0 (± 10492.22)
Cycle 6 Day 1 (n=0, 1, 0, 0)	0.000 (± 0.000)	40400.0 (± 9999)	0.000 (± 0.000)	0.000 (± 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): 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[19]	2	0[20]	0[21]
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.

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[22]	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 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:Cohort4(Gynaecologic Cancers):Debio1143 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
Infections and infestations			
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
Metabolism and nutrition disorders			
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

Serious adverse events	Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab	Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab	Part B:Cohort4(Gynaecologic Cancers):Debio1143
Total subjects affected by serious adverse events			
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
Infections and infestations			
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
Metabolism and nutrition disorders			
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 %

Non-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 non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	8 / 8 (100.00%)	8 / 8 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Vascular disorders			
Lymphoedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 8 (25.00%)	1 / 8 (12.50%)
occurrences (all)	0	3	1
Chills			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Facial pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	1 / 8 (12.50%)	6 / 8 (75.00%)
occurrences (all)	1	1	6
Generalised oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	0	2	1
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Malaise			

subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	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	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	2 / 8 (25.00%)
occurrences (all)	0	1	2
Amylase increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 8 (25.00%)	1 / 8 (12.50%)
occurrences (all)	0	2	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	0	1	3
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	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			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Craniocerebral injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
VIth nerve injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Bell's palsy			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Dizziness			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Memory impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	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			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hypothyroidism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 8 (12.50%)	2 / 8 (25.00%)
occurrences (all)	1	1	2
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	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

Non-serious adverse events	Part B: Cohort 2 (SCCHN): Debio 1143 200 mg + Nivolumab	Part B: Cohort 3 (GI Cancers): Debio 1143 200 mg + Nivolumab	Part B:Cohort4(Gynaecologic Cancers):Debio1143
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			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Lymphocyte count decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Subdural haematoma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Craniocerebral injury			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
VIth nerve injury			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Atrial fibrillation			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Bell's palsy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Sciatica			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	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			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	3 / 11 (27.27%)
occurrences (all)	1	1	4
Diarrhoea			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	3 / 11 (27.27%)
occurrences (all)	1	0	3
Dry mouth			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Dysphagia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gingival pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	2 / 8 (25.00%)	3 / 8 (37.50%)	2 / 11 (18.18%)
occurrences (all)	2	3	2
Oral pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Vomiting			

subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	0 / 11 (0.00%)
occurrences (all)	2	1	0
Hepatobiliary disorders			
Hepatic cytolysis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Leukoplakia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	2 / 8 (25.00%)	2 / 8 (25.00%)	3 / 11 (27.27%)
occurrences (all)	2	3	3
Rash maculo-papular			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Skin exfoliation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Pemphigoid			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	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	1 / 8 (12.50%)	0 / 8 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	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			
subjects affected / exposed	3 / 8 (37.50%)	1 / 8 (12.50%)	1 / 11 (9.09%)
occurrences (all)	3	1	1
Hypercalcaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Hyperglycaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Hypertriglyceridaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	2 / 11 (18.18%)
occurrences (all)	1	0	4
Hypomagnesaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Hyponatraemia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	3 / 11 (27.27%)
occurrences (all)	1	1	3
Hypophosphataemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 January 2019	• Added that the subjects should have had no established standard therapeutic alternatives to the cancer treatment. • Advised that subjects with active ongoing infection requiring systemic antibiotic therapy, including active tuberculosis, were not eligible for enrolment. • 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. • Expanded the list of prohibited medications.
07 November 2019	• Allowed the inclusion of subjects with haemoglobin levels of ≥9.0 grams/decilitre (g/dL). • Adjusted the subject population for Cohort 1 to allow the inclusion of subjects with extrapulmonary small-cell carcinomas or large cell neuroendocrine lung carcinoma. • Clarified that nasopharyngeal carcinoma was not allowed in Cohort 2. • Shortened the time window of thoracic or head and neck radiation >30 Gray (Gy) from within 3 months to 6 weeks prior to the start of treatment. • Allowed inclusion of subjects with vitiligo >Grade 1 as an ongoing toxicity of prior antineoplastic therapies. • Shortened the time window for blood transfusion from up to 4 weeks to 2 weeks prior to the start of treatment.
03 April 2020	• 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. • Added the clarification of the schedule of assessments for subjects who exceptionally continued study treatment beyond 13 cycles. • 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. • 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. • 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.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported