Clinical trial results:
A randomized, double-blind placebo-controlled, Phase 3 study of Debio 1143 in combination with platinum-based chemotherapy and standard fractionation intensity-modulated radiotherapy in patients with locally advanced squamous cell carcinoma of the head and neck, suitable for definitive chemoradiotherapy (TrilynX)

Summary

EudraCT number	2020-000377-25
Trial protocol	FR DE HU PT AT BE CZ GR IT
Global end of trial date	18 September 2024

Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	MS202359_0006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04459715
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Healthcare KGaA, Darmstadt Germany, an affiliate of Merck KGaA, Darmstadt, Germany
Sponsor organisation address	Frankfurter Strasse 250, Darmstadt, Germany,
Public contact	Communication Center, Merck Healthcare KGaA, Darmstadt Germany, an affiliate of Merck KGaA, Darmstadt, Germany, +49 6151725200, service@emdgroup.com
Scientific contact	Communication Center, Merck Healthcare KGaA, Darmstadt Germany, an affiliate of Merck KGaA, Darmstadt, Germany, +49 6151725200, service@emdgroup.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 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 September 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 September 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to demonstrate superior efficacy of Xevinapant (Debio 1143) vs placebo when added to chemoradiotherapy (CRT) in locally advanced squamous cell carcinoma of the head and neck (LA-SCCHN).

Protection of trial subjects:

Subject protection was ensured by following high medical and ethical standards in accordance with the principles laid down in the Declaration of Helsinki, and that are consistent with Good Clinical Practice and applicable regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 August 2020
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	China: 49
Country: Number of subjects enrolled	Japan: 38
Country: Number of subjects enrolled	Korea, Republic of: 10
Country: Number of subjects enrolled	Taiwan: 21
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Czechia: 1
Country: Number of subjects enrolled	Georgia: 45
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Poland: 39
Country: Number of subjects enrolled	Russian Federation: 9
Country: Number of subjects enrolled	Ukraine: 2
Country: Number of subjects enrolled	Israel: 9
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	Argentina: 22
Country: Number of subjects enrolled	Brazil: 55
Country: Number of subjects enrolled	Austria: 7
Country: Number of subjects enrolled	Belgium: 31
Country: Number of subjects enrolled	France: 149
Country: Number of subjects enrolled	Germany: 20

Country: Number of subjects enrolled	Greece: 16
Country: Number of subjects enrolled	Italy: 22
Country: Number of subjects enrolled	Portugal: 26
Country: Number of subjects enrolled	Spain: 58
Country: Number of subjects enrolled	Switzerland: 11
Country: Number of subjects enrolled	United Kingdom: 22
Country: Number of subjects enrolled	United States: 41
Worldwide total number of subjects	730
EEA total number of subjects	384

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)	496
From 65 to 84 years	234
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 1237 subjects were screened out of which only 730 received a study intervention.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Sequence 1: Debio 1143 + CRT

Arm description:

Subjects received a combination of Debio 1143 along with Chemoradiotherapy (CRT): Radiotherapy +Cisplatin + Xevinapant (Debio 1143). Subjects received 6 cycles of oral solution of Xevinapant at a dose of 200 milligrams per day (mg/day) once daily from Day 1 to 14, per 3-week cycle in combination with 70 Gray (Gy) of intensity modulated radiation therapy (IMRT) in 35 fractions, 2 Gy/fraction, over 7 weeks, and High-dose cisplatin (100 Milligram per square meter (mg/m2) on Day 2 of a 3-week cycle per 3 cycles (combination therapy period). If high-dose cisplatin 100 mg/m2 was not tolerated after the first dose, subjects could be switched to carboplatin (10 Milligrams per milliliter [mg/mL], intravenous [iv] infusion), followed by 3 cycles of monotherapy of Xevinapant at a dose of 200 mg/day from Day 1 to 14, per 3-week cycle (monotherapy period).

Arm type	Experimental
Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin administered as an IV infusion every 3 weeks (Q3W).

Investigational medicinal product name	Xevinapant
Investigational medicinal product code	
Other name	Debio 1143
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Xevinapant (Debio 1143) administrated as oral solution from Day 1 to 14, every 21-day cycle.

Arm title	Sequence 2: Placebo + CRT

Arm description:

Subjects received a combination of placebo matched to Debio 1143 along with Chemoradiotherapy(CRT): Radiotherapy +Cisplatin+ placebo matched to Xevinapant (Debio 1143). Subjects received 6 cycles of oral solution of placebo matched to Xevinapant once daily from Day 1 to 14, per 3-week cycle in combination with 70 Gray (Gy) of intensity modulated radiation therapy (IMRT) in 35 fractions, 2 Gy/fraction, over 7 weeks, and High-dose cisplatin (100 mg/m2) on Day 2 of a 3-week cycle per 3 cycles(combination therapy period).If high-dose cisplatin 100 mg/m2 was not tolerated after the first dose, subjects could be switched to carboplatin (10mg/mL, iv infusion), followed by 3 cycles of monotherapy of placebo matched to Xevinapant from Day 1 to 14, per 3-week cycle (monotherapy period).

Arm type	Experimental

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Matched placebo administrated as oral solution from Day 1 to 14, every 21-day cycle.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin administered as an IV infusion every 3 weeks (Q3W).

Number of subjects in period 1	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT
Started	364	366
Completed	0	0
Not completed	364	366
Adverse event, serious fatal	111	93
Consent withdrawn by subject	22	22
Adverse event, non-fatal	3	3
RANDOMIZED BY MISTAKE	-	1
STUDY TERMINATED BY SPONSOR	214	232
Lost to follow-up	10	9
PROTOCOL DEVIATION	4	5

Baseline characteristics

Reporting groups	
Reporting group title	Sequence 1: Debio 1143 + CRT
Reporting group description:	
Subjects received a combination of Debio 1143 along with Chemoradiotherapy (CRT): Radiotherapy +Cisplatin + Xevinapant (Debio 1143). Subjects received 6 cycles of oral solution of Xevinapant at a dose of 200 milligrams per day (mg/day) once daily from Day 1 to 14, per 3-week cycle in combination with 70 Gray (Gy) of intensity modulated radiation therapy (IMRT) in 35 fractions, 2 Gy/fraction, over 7 weeks, and High-dose cisplatin (100 Milligram per square meter (mg/m2) on Day 2 of a 3-week cycle per 3 cycles (combination therapy period). If high-dose cisplatin 100 mg/m2 was not tolerated after the first dose, subjects could be switched to carboplatin (10 Milligrams per milliliter [mg/mL], intravenous [iv] infusion), followed by 3 cycles of monotherapy of Xevinapant at a dose of 200 mg/day from Day 1 to 14, per 3-week cycle (monotherapy period).	
Reporting group title	Sequence 2: Placebo + CRT
Reporting group description:	
Subjects received a combination of placebo matched to Debio 1143 along with Chemoradiotherapy(CRT): Radiotherapy +Cisplatin+ placebo matched to Xevinapant (Debio 1143). Subjects received 6 cycles of oral solution of placebo matched to Xevinapant once daily from Day 1 to 14, per 3-week cycle in combination with 70 Gray (Gy) of intensity modulated radiation therapy (IMRT) in 35 fractions, 2 Gy/fraction, over 7 weeks, and High-dose cisplatin (100 mg/m2) on Day 2 of a 3-week cycle per 3 cycles(combination therapy period).If high-dose cisplatin 100 mg/m2 was not tolerated after the first dose, subjects could be switched to carboplatin (10mg/mL, iv infusion), followed by 3 cycles of monotherapy of placebo matched to Xevinapant from Day 1 to 14, per 3-week cycle (monotherapy period).	

Reporting group values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT	Total
Number of subjects	364	366	730
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	243	253	496
From 65-84 years	121	113	234
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	60	60	
standard deviation	± 8.01	± 8.53	-
Sex: Female, Male Units: subjects			
Female	64	57	121
Male	300	309	609
Ethnicity Units: Subjects			
Hispanic or Latino	41	46	87
Not Hispanic or Latino	264	273	537
Missing	59	47	106

Race Units: Subjects			
Asian	59	60	119
American Indian or Alaska Native	0	0	0
Black or African American	5	6	11
Native Hawaiian or Other Pacific Islander	0	0	0
White	253	256	509
Other	5	9	14
Missing	42	35	77

End points

End points reporting groups

Reporting group title	Sequence 1: Debio 1143 + CRT

Reporting group description:

Subjects received a combination of Debio 1143 along with Chemoradiotherapy (CRT): Radiotherapy +Cisplatin + Xevinapant (Debio 1143). Subjects received 6 cycles of oral solution of Xevinapant at a dose of 200 milligrams per day (mg/day) once daily from Day 1 to 14, per 3-week cycle in combination with 70 Gray (Gy) of intensity modulated radiation therapy (IMRT) in 35 fractions, 2 Gy/fraction, over 7 weeks, and High-dose cisplatin (100 Milligram per square meter (mg/m2) on Day 2 of a 3-week cycle per 3 cycles (combination therapy period). If high-dose cisplatin 100 mg/m2 was not tolerated after the first dose, subjects could be switched to carboplatin (10 Milligrams per milliliter [mg/mL], intravenous [iv] infusion), followed by 3 cycles of monotherapy of Xevinapant at a dose of 200 mg/day from Day 1 to 14, per 3-week cycle (monotherapy period).

Reporting group title	Sequence 2: Placebo + CRT

Reporting group description:

Subjects received a combination of placebo matched to Debio 1143 along with Chemoradiotherapy(CRT): Radiotherapy +Cisplatin+ placebo matched to Xevinapant (Debio 1143). Subjects received 6 cycles of oral solution of placebo matched to Xevinapant once daily from Day 1 to 14, per 3-week cycle in combination with 70 Gray (Gy) of intensity modulated radiation therapy (IMRT) in 35 fractions, 2 Gy/fraction, over 7 weeks, and High-dose cisplatin (100 mg/m2) on Day 2 of a 3-week cycle per 3 cycles(combination therapy period).If high-dose cisplatin 100 mg/m2 was not tolerated after the first dose, subjects could be switched to carboplatin (10mg/mL, iv infusion), followed by 3 cycles of monotherapy of placebo matched to Xevinapant from Day 1 to 14, per 3-week cycle (monotherapy period).

Primary: Event-Free Survival (EFS) as assessed by Blinded Independent Review Committee (BIRC)

End point title	Event-Free Survival (EFS) as assessed by Blinded Independent Review Committee (BIRC)[1]

End point description:

Event-Free Survival (EFS) as assessed by BIRC is the time from randomization to the first of: (1) Death from any cause; (2) Progression: either radiological (per RECIST v1.1) or clinical (with/without radiologic proof, assessed endoscopically); (3) Primary treatment failure prior to complete response (CR): requirement for radical salvage surgery at primary tumor site with viable tumor confirmed histologically, even without RECIST progression; (4) Relapse after CR (locoregional): including radical salvage surgery or elective neck dissection/biopsy more than equal to (>=) 22 weeks post-randomization showing viable tumor cells regardless of radiologic status; (5) Second cancers, unless histology excludes squamous origin. Calculated via Kaplan Meier method. The Intention To Treat (ITT) set included all randomized subjects.

End point type	Primary

End point timeframe:

From randomization to the earliest between any EFS event or End of Study (EOS) (up to 188 weeks and 5 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: No statistical and comparison analysis were performed in single arm for this endpoint.

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364[2]	366[3]		
Units: months				
median (confidence interval 95%)	19.4 (14.46 to 99999)	33.1 (20.99 to 99999)		

Notes:

[2] - 99999 = no data; 95% CI upper limit for median not estimable due to few events.

[3] - 99999 = no data; 95% CI upper limit for median not estimable due to few events.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) According to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 as Assessed by Blinded Independent Review Committee (BIRC)

End point title	Progression Free Survival (PFS) According to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 as Assessed by Blinded Independent Review Committee (BIRC)

End point description:

PFS according to RECIST v1.1 defined as the time from randomization to the first occurrence of progression (radiological or clinical, as assessed by the BIRC) or death from any cause. According to RECIST 1.1, progressive disease (PD) was defined as a 20% relative increase in the sum of diameters (SOD) of target lesions, taking as reference the nadir SOD and an absolute increase of >5 millimeter (mm) in the SOD, or the appearance of new lesions. Calculated via Kaplan Meier method. The ITT set included all randomized subjects. Subjects were analyzed according to the randomized treatment (assigned arm) assignment following the intention-to-treat principle.

End point type	Secondary

End point timeframe:

From randomization to the first occurrence of progression (radiological or clinical, as assessed by the BIRC) or death from any cause or EOS (up to 188 weeks and 5 days)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364[4]	366[5]		
Units: months				
median (confidence interval 95%)	26.8 (15.93 to 99999)	33.1 (22.83 to 99999)		

Notes:

[4] - 9.9999 = no observation; median not derived due to limited number of events.

[5] - 9.9999 = no observation; median not derived due to limited number of events.

Statistical analyses

No statistical analyses for this end point

Secondary: Locoregional control (LRC) Time

End point title	Locoregional control (LRC) Time

End point description:

LRC time is defined as the time from randomization to the first occurrence of progression at the site of the primary tumor or the locoregional lymph nodes, either according to RECIST v1.1 or based on clinical assessment (radiological or clinical, as assessed by the Investigator). According to RECIST 1.1, progressive disease (PD) was defined as a 20% relative increase in the sum of diameters (SOD) of target lesions, taking as reference the nadir SOD and an absolute increase of >5 millimeter (mm) in the SOD, or the appearance of new lesions. Calculated via Kaplan Meier method. The ITT set included all

randomized subjects. Subjects were analyzed according to the randomized treatment (assigned arm) assignment following the intention-to-treat principle.

End point type	Secondary

End point timeframe:

From randomization to the first occurrence of progression at the site of the primary tumor or the locoregional lymph nodes or End Of Study (EOS) (188 weeks and 5 days)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364[6]	366[7]		
Units: months				
median (full range (min-max))	9.9999 (0.0 to 37.0)	9.9999 (0.0 to 38.2)		

Notes:

[6] - 9.9999 = no observation; median not derived due to limited number of events.

[7] - 9.9999 = no observation; median not derived due to limited number of events.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall survival is defined as the time from randomization to the date of death. Calculated via Kaplan Meier method. The ITT set included all randomized subjects. Subjects were analyzed according to the randomized treatment (assigned arm) assignment following the intention-to-treat principle.

End point type	Secondary

End point timeframe:

From randomization to the earliest between death or EOS (up to 188 weeks and 5 days)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364[8]	366[9]		
Units: months				
median (full range (min-max))	9.9999 (0.0 to 37.6)	9.9999 (0.0 to 39.4)		

Notes:

[8] - 9.9999 = no observation; median not derived due to limited number of events.

[9] - 9.9999 = no observation; median not derived due to limited number of events.

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) as Assessed by BIRC

End point title	Objective Response Rate (ORR) as Assessed by BIRC

End point description:

Objective response rate was defined as percentage of subjects with either a confirmed complete response (CR) or partial response (PR). CR: Disappearance of all target and non-target lesions. PR: At least a 30 percent (%) decrease in the sum of diameters of target lesions, taking as reference the baseline sum of their diameters, and no unequivocal progression of non-target lesions. Progression is defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on the study, or unequivocal progression of non-target lesions, or appearance of any new lesion. The ITT set included all randomized subjects. Subjects were analyzed according to the randomized treatment (assigned arm) assignment following the intention-to-treat principle.

End point type	Secondary

End point timeframe:

At 9 and 12 months post randomization

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	366		
Units: percentage of subjects				
number (not applicable)				
9 Months Post Randomization	73.4	77.3		
12 Months Post Randomization	73.6	77.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Radical Salvage Surgery

End point title	Number of Subjects with Radical Salvage Surgery

End point description:

Number of subjects with Radical Salvage Surgery (excluding elective neck dissection without anatomopathological evidence of residual malignant cells) was reported. The ITT set included all randomized subjects. Subjects were analyzed according to the randomized treatment (assigned arm) assignment following the intention-to-treat principle.

End point type	Secondary

End point timeframe:

At 9, 12, 24 and 36 months post randomization

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	366		
Units: subjects				
Month 9	10	3		

Month 12	19	5		
Month 24	23	9		
Month 36	23	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Response Rate (CRR)

End point title	Complete Response Rate (CRR)

End point description:

CRR defined as the number of subjects with Complete Response by RECIST v1.1, as assessed by the BIRC. Complete response is defined as disappearance of all target and non-target lesions. The ITT set included all randomized subjects. Subjects were analyzed according to the randomized treatment (assigned arm) assignment following the intention-to-treat principle.

End point type	Secondary

End point timeframe:

At 9 and 12 months post randomization

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	366		
Units: subjects				
9 Months Post Randomization	187	212		
12 Months Post Randomization	194	222		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

Duration of response (DoR) defined as the time from the first evidence of response (partial or complete, as assessed by the BIRC according to RECIST v1.1) to the first occurrence of progression (radiological or clinical, as assessed by the BIRC) or death from any cause. Kaplan Meier method was used for calculation. The ITT set included all randomized subjects. Subjects were analyzed according to the randomized treatment (assigned arm) assignment following the intention-to-treat principle. "Number of subjects analyzed" signifies subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Time from first evidence of response to the first occurrence of progression or death from any cause, assessed up to 24 months

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	269[10]	287[11]		
Units: months				
median (full range (min-max))	9.9999 (0.0 to 33.5)	9.9999 (0.0 to 33.7)		

Notes:

[10] - 9.9999 = no observation; median not derived due to limited number of events.

[11] - 9.9999 = no observation; median not derived due to limited number of events.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs), Serious TEAEs, Adverse Events (AEs) of Special Interest

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs), Serious TEAEs, Adverse Events (AEs) of Special Interest

End point description:

An AE is any unfavorable/unintended sign symptom or disease temporally linked to study drug, whether or not related. A serious AE leads to death, is life-threatening, causes significant/persistent disability, hospitalization, congenital anomaly, or is medically important. TEAEs include both serious and non-serious AEs after treatment. AESIs are events of clinical interest needing close monitoring. The safety analysis set (SAF set) included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT).

End point type	Secondary

End point timeframe:

From signed informed consent to EOS (up to 188 weeks and 5 days)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	356		
Units: subjects				
TEAEs	362	351		
Serious TEAEs	194	129		
AESI	357	342		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Subsequent Systemic Cancer Treatments

End point title	Time to Subsequent Systemic Cancer Treatments

End point description:

Time to new subsequent systemic cancer treatment (in months) was derived as (date of event/censoring – randomization date +1) / 30.4375. Calculated via kaplan meier method. The ITT set included all randomized subjects. Subjects were analyzed according to the randomized treatment (assigned arm) assignment following the intention-to-treat principle.

End point type	Secondary

End point timeframe:

Up to 188 weeks and 5 days post randomization

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364[12]	366[13]		
Units: months				
median (confidence interval 95%)	9.9999 (9.9999 to 9.9999)	9.9999 (9.9999 to 9.9999)		

Notes:

[12] - 9.9999 = no observation; median not derived due to limited number of events.

[13] - 9.9999 = no observation; median not derived due to limited number of events.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Severity of Grade Greater or Equal to 3 TEAEs

End point title	Number of Subjects With Severity of Grade Greater or Equal to 3 TEAEs

End point description:

Severity of TEAEs were evaluated using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version. The grade are as follows: grade 1 : mild grade 2 : moderate grade 3 : severe or medically significant but not immediately life-threatening grade 4 : life threatening or disabling grade 5 : death related to AE. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT).

End point type	Secondary

End point timeframe:

From signed informed consent to EOS (up to 188 weeks and 5 days)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	356		
Units: subjects	320	286		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Laboratory Parameters: Basophils, Leukocytes, Lymphocytes, Monocytes, Neutrophils, Platelets

End point title	Change from Baseline in Laboratory Parameters: Basophils, Leukocytes, Lymphocytes, Monocytes, Neutrophils, Platelets

End point description:

Change from Baseline in Laboratory Parameters: Basophils, Leukocytes, Lymphocytes, Monocytes, Neutrophils, Platelets was reported. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "overall number of subjects analyzed signified" subjects who were evaluable for this outcome measure and "number analyzed" or "n" signifies subjects who were evaluable at specified timepoints. Please note Sequence 1= S1, Sequence 2= S2, Basophils = BP, Leukocytes= Leuko, Lymphocyte = Lympho, Monocyte = mono, Neutrophils = Neutro, Platelets = Plt and Maximum on treatment change = max change.

End point type	Secondary

End point timeframe:

At Baseline, Cycle 3 Day 1 (C3D1) (combination period), EOT (15 days after last study treatment administration) and baseline upto event free survival (EFS) follow up Month 18 after EOT (max on treatment change)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	363	352		
Units: 10^9 cells per liter				
arithmetic mean (standard deviation)				
Basophils: Baseline	0.052 (± 0.0343)	0.054 (± 0.0367)		
Baso: C3D1 (n= S1-283, S2-288)	-0.032 (± 0.0367)	-0.041 (± 0.0362)		
Baso: EOT (n= S1-280, S2-287)	-0.021 (± 0.0367)	-0.023 (± 0.0312)		
Baso: Max change (n= S1-357, S2-345)	-0.022 (± 0.0673)	-0.031 (± 0.0618)		
Leukos: Baseline (n= S1-363, S2-352)	8.175 (± 2.9656)	8.105 (± 2.6725)		
Leuko: C3D1 (n= S1-288, S2-290)	-4.065 (± 3.1244)	-4.597 (± 2.9352)		
Leuko: EOT (n=S1-282, S2-287)	-2.129 (± 3.2074)	-2.354 (± 2.4137)		
Leuko: Max change (n= S1-357, S2-345)	-3.045 (± 7.5455)	-3.444 (± 6.7059)		
Lympho: Baseline (n= S1-363,S2-352)	1.753 (± 0.5734)	1.753 (± 0.6367)		
Lympho: C3D1 (283, 288)	-1.168 (± 0.5804)	-1.251 (± 0.5742)		

Lympho: EOT (n= S1-280, S2-287)	-0.884 (± 0.5485)	-0.901 (± 0.5536)		
Lympho: Max change (n=S1-357, S2-345)	-1.382 (± 0.6359)	-1.356 (± 0.6150)		
Mono: Baseline (n= S1-363, S2- 352)	0.518 (± 0.2156)	0.506 (± 0.2072)		
Mono: C3D1 (n= S1-283, S2-288)	-0.139 (± 0.2389)	-0.169 (± 0.2063)		
Mono: EOT (n= S1-280, S2-287)	-0.114 (± 0.1991)	-0.100 (± 0.1683)		
Mono: Max change (n= S1-357, S2-345)	-0.175 (± 0.4050)	-0.152 (± 0.3870)		
Neutro: Baseline (n= S1-363, S2-352)	5.669 (± 2.6589)	5.610 (± 2.3663)		
Neutro: C3D1 (n= S1-283, S2-288)	-2.646 (± 2.8532)	-3.018 (± 2.6744)		
Neutro: EOT (n= S1-280, S2-287)	-1.081 (± 2.9287)	-1.275 (± 2.2696)		
Neutro: Max change (n= S1-357, S2-345)	-0.528 (± 7.2775)	-1.095 (± 6.3143)		
Plt: Baseline (n= S1-362, S2-351)	292.6 (± 104.86)	287.7 (± 107.38)		
Plt: C3D1 (n= S1-282, S2-277)	-48.2 (± 112.13)	-56.5 (± 109.52)		
Plt: EOT (n= S1-278, S2-284)	-24.8 (± 94.59)	-38.6 (± 87.16)		
Plt: Max change (n=S1-356, S2-344)	-63.2 (± 203.40)	-88.7 (± 171.61)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in Laboratory Parameters: Basophils/Leukocytes, Eosinophils/Leukocytes, Lymphocytes/Leukocytes, Monocytes/Leukocytes, Neutrophils/Leukocytes

End point title	Percent Change from Baseline in Laboratory Parameters: Basophils/Leukocytes, Eosinophils/Leukocytes, Lymphocytes/Leukocytes, Monocytes/Leukocytes, Neutrophils/Leukocytes

End point description:

Percent change from Baseline in Laboratory Parameters: Basophils/Leukocytes, Eosinophils/Leukocytes, Lymphocytes/Leukocytes, Monocytes/Leukocytes, Neutrophils/Leukocytes was reported. Here "overall number of subjects analyzed signified" subjects who were evaluable for this outcome measure and "number analyzed" or "n" signifies subjects who were evaluable at specified timepoints. Please note Sequence 1= S1, Sequence 2= S2, Basophils = BP, Leukocytes= Leuko, Lymphocyte = Lympho, Monocyte = mono, Neutrophils = Neutro and Maximum on treatment change = max change.

End point type	Secondary

End point timeframe:

At Cycle 3 Day 1 (C3D1) (combination period), EOT (15 days after last study treatment administration) and baseline upto event free survival (EFS) follow up Month 18 after EOT (max on treatment change)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	363	352		
Units: percent change				
arithmetic mean (standard deviation)				
C3D1: Baso/Leuko (n= S1-283, S2-288)	-0.21 (± 0.551)	-0.29 (± 0.527)		
EOT: Baso/Leuko (n=S1-280,S2-287)	-0.14 (± 0.502)	-0.13 (± 0.483)		
Max change: Baso/Leuko (n=S1-357,S2-345)	0.03 (± 0.985)	0.00 (± 1.032)		
C3D1: Eosino/Leuko (n=S1-283,S2-288)	-0.04 (± 2.874)	-0.39 (± 2.147)		
EOT: Eosino/Leuko (n=S1-280,S2-287)	0.60 (± 3.435)	0.07 (± 1.878)		
Max change: Eosino/Leuko (n=S1-357,S2-345)	1.32 (± 5.005)	0.04 (± 3.308)		
C3D1: Lympho/Leuko (n=S1-283,S2-288)	-6.89 (± 10.604)	-5.80 (± 10.086)		
EOT:Lympho/Leuko (n=S1-280,S2-287)	-6.85 (± 8.855)	-6.91 (± 7.850)		
Max change: Lympho/Leuko (n=S1-357,S2-345)	-11.39 (± 15.553)	-10.07 (± 15.985)		
C3D1: Mono/Leuko (n=S1-283,S2-288)	3.65 (± 4.502)	3.90 (± 3.840)		
EOT: Mono/Leuko (n=S1-280,S2-287)	0.64 (± 2.666)	0.89 (± 2.454)		
Max change: Mono/Leuko (n=S1-280,S2-287)	5.87 (± 6.060)	6.26 (± 5.631)		
C3D1: Neutro/Leuko (n=S1-283,S2-288)	2.67 (± 14.064)	2.33 (± 12.467)		
EOT: Neutro/Leuko (n=S1-280,S2-287)	5.75 (± 10.651)	6.08 (± 9.086)		
Max change: Neutro/Leuko (n=S1-357,S2-345)	6.80 (± 24.388)	7.45 (± 21.764)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Laboratory Parameters: Erythrocytes

End point title	Change from Baseline in Laboratory Parameters: Erythrocytes

End point description:

Change from Baseline in Laboratory Parameters: Erythrocytes was reported. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "number analyzed" or "n" signifies subjects who were evaluable at specified timepoints. Please note S1- Sequence 1, S2- Sequence 2 and Max on treatment change - Max change.

End point type	Secondary

End point timeframe:

At Baseline, Cycle 3 Day 1 (C3D1) (combination period), EOT (15 days after last study treatment administration) and baseline upto event free survival (EFS) follow up Month 18 after EOT (max on treatment change)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	363	352		
Units: 10^12 cells per liter				
arithmetic mean (standard deviation)				
Baseline	4.27 (± 0.507)	4.37 (± 0.477)		
C3D1 (n=S1- 288, S2-290)	-0.81 (± 0.456)	-0.82 (± 0.433)		
EOT (n=S1- 282, S2-287)	-0.70 (± 0.575)	-0.59 (± 0.464)		
Max change (n=S1- 357, S2-345)	-1.14 (± 0.636)	-1.19 (± 0.605)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Laboratory Parameters: Hemoglobin, Albumin, Protein

End point title	Change from Baseline in Laboratory Parameters: Hemoglobin, Albumin, Protein

End point description:

Change from Baseline in Laboratory Parameters: Hemoglobin, Albumin, Protein was reported. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "overall number of subjects analyzed signified" subjects who were evaluable for this outcome measure and "number analyzed" or "n" signifies subjects who were evaluable at specified timepoints. Please note Sequence 1= S1, Sequence 2= S2, hemoglobin - Hb, Albumin- Alb, Protein - Prt and Maximum on treatment change = max change.

End point type	Secondary

End point timeframe:

At Baseline, Cycle 3 Day 1 (C3D1) (combination period), EOT (15 days after last study treatment administration) and baseline upto event free survival (EFS) follow up Month 18 after EOT (max on treatment change)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	356		
Units: grams per liters (g/L)				
arithmetic mean (standard deviation)				
Hb: Baseline(n= S1- 363,S2-352)	132.9 (± 15.08)	135.4 (± 14.34)		
Hb: C3D1(n= S1- 288,S2-290)	-25.7 (± 14.24)	-25.2 (± 13.75)		
Hb: EOT(n= S1- 282,S2-287)	-19.1 (± 17.73)	-14.4 (± 14.44)		
Hb: Max change(n= S1- 357,S2-345)	-34.8 (± 19.83)	-35.8 (± 18.82)		
Alb: Baseline(n= S1- 364,S2-352)	43.2 (± 3.95)	43.6 (± 3.55)		

Alb: C3D1(n= S1- 304,S2-314)	-4.0 (± 4.33)	-2.6 (± 3.61)		
Alb: EOT (n= S1- 309,S2-314)	-1.1 (± 4.43)	0.4 (± 4.02)		
Alb: Max change (n= S1- 351,S2-343)	-4.8 (± 6.38)	-2.6 (± 5.90)		
Prt: Baseline(n= S1- 363,S2-356)	70.1 (± 5.11)	70.5 (± 4.78)		
Prt: C3D1(n= S1- 300,S2-313)	-4.5 (± 5.73)	-4.3 (± 5.24)		
Prt: EOT(n= S1- 306,S2-312)	-0.3 (± 6.10)	-0.7 (± 5.32)		
Prt: Max change (n= S1- 350,S2-343)	-4.7 (± 9.12)	-5.0 (± 8.03)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Laboratory Parameters: Alanine Aminotransferase, Alkaline Phosphatase, Amylase, Aspartate Aminotransferase, Lipase

End point title	Change from Baseline in Laboratory Parameters: Alanine Aminotransferase, Alkaline Phosphatase, Amylase, Aspartate Aminotransferase, Lipase

End point description:

Change from Baseline in Laboratory Parameters: Alanine Aminotransferase, Alkaline Phosphatase, Amylase, Aspartate Aminotransferase, Lipase was reported. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "overall number of subjects analyzed signified" subjects who were evaluable for this outcome measure and "number analyzed" or "n" signifies subjects who were evaluable at specified timepoints. Please note Sequence 1= S1, Sequence 2= S2, Alanine aminotransferase - ALT, Alkaline Phosphatase- ALP, Aspartate Aminotransferase-AST and Maximum on treatment change = max change.

End point type	Secondary

End point timeframe:

At Baseline, Cycle 3 Day 1 (C3D1) (combination period), EOT (15 days after last study treatment administration) and baseline upto event free survival (EFS) follow up Month 18 after EOT (max on treatment change)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	356		
Units: microgram per liter (mcg/L)				
arithmetic mean (standard deviation)				
ALT: Baseline (n= S1-363, S2-353)	18.9 (± 12.10)	19.4 (± 12.66)		
ALT: C3D1 (n= S1-295, S2-300)	0.5 (± 16.77)	-4.6 (± 13.53)		
ALT: EOT (n= S1-297, S2-297)	-2.0 (± 18.25)	-3.4 (± 15.87)		
ALT: Max change (n= S1-356, S2-346)	55.8 (± 70.73)	26.5 (± 45.39)		
ALP: Baseline (n= S1-363, S2-356)	79.3 (± 24.48)	78.0 (± 23.20)		
ALP: C3D1 (n= S1-301, S2-312)	-0.8 (± 19.94)	-1.0 (± 21.89)		
ALP: EOT (n= S1-305, S2-311)	-2.2 (± 28.14)	-5.6 (± 18.79)		
ALP: Max change (n= S1-364, S2-356)	12.7 (± 47.38)	5.6 (± 49.27)		
Amylase: Baseline (n= S1-, S2-)	70.0 (± 42.81)	67.8 (± 61.61)		
Amylase: C3D1 (n= S1-304, S2-310)	-14.0 (± 38.07)	-14.0 (± 32.85)		

Amylase: EOT (n= S1-308, S2-313)	-13.5 (± 40.51)	-13.5 (± 33.79)		
Amylase: Max change (n= S1-359, S2-350)	125.8 (± 205.22)	60.4 (± 119.29)		
AST: Baseline (n= S1-363, S2-356)	19.8 (± 11.10)	19.8 (± 8.31)		
AST: C3D1 (n= S1-302, S2-311)	-2.4 (± 12.30)	-3.5 (± 8.63)		
AST: EOT (n= S1-304, S2-312)	0.4 (± 19.01)	0.9 (± 18.80)		
AST: Max change (n= S1-356, S2-350)	20.0 (± 37.35)	9.7 (± 25.02)		
Lipase: Baseline (n= S1-364, S2-356)	35.4 (± 48.01)	29.8 (± 19.37)		
Lipase: C3D1 (n= S1-305, S2-309)	-4.0 (± 39.69)	-4.0 (± 23.64)		
Lipase: EOT (n= S1-308, S2-314)	-1.8 (± 47.38)	-1.0 (± 21.69)		
Lipase: Max change (n= S1-359, S2-350)	87.3 (± 196.87)	25.0 (± 60.54)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Laboratory Parameters: Bilirubin, Creatinine, Direct Bilirubin, Urate

End point title	Change from Baseline in Laboratory Parameters: Bilirubin, Creatinine, Direct Bilirubin, Urate

End point description:

Change from Baseline in Laboratory Parameters: Bilirubin, Creatinine, Direct Bilirubin, Urate was reported. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "overall number of subjects analyzed signified" subjects who were evaluable for this outcome measure and "number analyzed" or "n" signifies subjects who were evaluable at specified timepoints. Please note Bilirubin - Bil, Creatine- Creat, Direct Bilirubin-DB, Sequence 1-S1, Sequence 2-S2 and Max on treatment change - max change

End point type	Secondary

End point timeframe:

At Baseline, Cycle 3 Day 1 (C3D1) (combination period), EOT (15 days after last study treatment administration) and baseline upto event free survival (EFS) follow up Month 18 after EOT (max on treatment change)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364[14]	356[15]		
Units: micromole per liter (mcmol/L)				
arithmetic mean (standard deviation)				
Bil: Baseline(n= S1-364,S2-355)	7.4 (± 4.03)	7.8 (± 4.06)		
Bil: C3D1(n= S1-304,S2-312)	-1.8 (± 3.74)	-1.5 (± 3.68)		
Bil: EOT(n= S1-309,S2-314)	-2.0 (± 3.85)	-1.3 (± 3.52)		
Bil: Max change(n= S1-359,S2-349)	1.1 (± 7.49)	0.1 (± 6.83)		
Creat: Baseline(n= S1-363,S2-356)	67.884 (± 15.1427)	70.612 (± 15.3405)		
Creat: C3D1(n= S1-301,S2-312)	11.771 (± 27.4012)	11.740 (± 26.2545)		

Creat: EOT(n= S1-306,S2-313)	17.660 (± 49.3934)	16.243 (± 32.1216)		
Creat: Max change(n= S1-358,S2-350)	292.808 (± 4199.9623)	360.521 (± 5664.5213)		
DB: Baseline(n= S1-6,S2-9)	4.8 (± 0.75)	5.6 (± 1.33)		
DB: C3D1(n= S1-0,S2-1)	99999 (± 99999)	3.0 (± 99999)		
DB: EOT(n= S1-0,S2-2)	99999 (± 99999)	0.0 (± 1.41)		
DB: Max change(n= S1-2,S2-8)	2.5 (± 2.12)	1.0 (± 2.14)		
Urate: Baseline(n= S1-363,S2-356)	303.1 (± 79.62)	305.9 (± 82.79)		
Urate: C3D1(n= S1-301,S2-313)	-25.4 (± 90.93)	-21.5 (± 91.07)		
Urate: EOT(n= S1-306,S2-313)	25.9 (± 85.01)	33.1 (± 80.07)		
Urate: Max change(n= S1-350,S2-343)	1.2 (± 140.44)	12.7 (± 137.74)		

Notes:

[14] - 99999 denotes no observation.no participants were analyzed and no data was collected

[15] - 99999 denotes no observation.no participants were analyzed and no data was collected

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Laboratory Parameters: C Reactive Protein

End point title	Change from Baseline in Laboratory Parameters: C Reactive Protein

End point description:

Change from Baseline in Laboratory Parameters: C Reactive Protein was reported. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "number analyzed" or "n" signifies subjects who were evaluable at specified timepoints. Please note Maximum on-treatment change - max change, Sequence 1 - S1 and Sequence 2- S2)

End point type	Secondary

End point timeframe:

At Baseline, Cycle 3 Day 1 (C3D1) (combination period), EOT (15 days after last study treatment administration) and baseline upto event free survival (EFS) follow up Month 18 after EOT (max on treatment change)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	356		
Units: milligrams per liter (mg/L)				
arithmetic mean (standard deviation)				
Baseline	15.80 (± 24.655)	13.78 (± 21.780)		
C3D1 (n=S1-304, S2-307)	25.30 (± 50.259)	11.66 (± 36.791)		
EOT (n=S1-306, S2-314)	1.26 (± 31.784)	1.22 (± 27.720)		
Max change (n=S1-351, S2-343)	43.91 (± 66.024)	27.90 (± 56.262)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Laboratory Parameters: Calcium, Magnesium, Potassium, Sodium, Urea

End point title	Change from Baseline in Laboratory Parameters: Calcium, Magnesium, Potassium, Sodium, Urea

End point description:

Change from Baseline in Laboratory Parameters: Calcium, Magnesium, Potassium, Sodium, Urea was reported. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "overall number of subjects analyzed signified" subjects who were evaluable for this outcome measure and "number analyzed" or "n" signifies subjects who were evaluable at specified timepoints. Please note Sequence 1- S1, Sequence 2-S2, Calcium - Ca, Magnesium - Mg, Potassium - K, Sodium - Na and maximum on treatment change - max change.

End point type	Secondary

End point timeframe:

At Baseline, Cycle 3 Day 1 (C3D1) (combination period), EOT (15 days after last study treatment administration) and baseline upto event free survival (EFS) follow up Month 18 after EOT (max on treatment change)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	356		
Units: millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)				
Ca: Baseline(n=S1-364,S2-356)	2.4065 (± 0.14050)	2.4043 (± 0.11777)		
Ca: C3D1(n=S1-304,S2-314)	-0.1054 (± 0.16830)	-0.0574 (± 0.12989)		
Ca: EOT(n=S1-309,S2-314)	0.0006 (± 0.15586)	0.0136 (± 0.12258)		
Ca: Max change(n=S1-351,S2-346)	-0.1182 (± 0.64226)	-0.0575 (± 0.63941)		
Mg: Baseline(n=S1-363,S2-356)	0.8731 (± 0.08816)	0.8718 (± 0.08800)		
Mg: C3D1(n=S1-301,S2-313)	-0.0871 (± 0.11743)	-0.0719 (± 0.11889)		
Mg: EOT(n=S1-306,S2-313)	-0.0588 (± 0.10612)	-0.0372 (± 0.08725)		
Mg: Max change(n=S1-350,S2-345)	-0.1231 (± 0.21711)	-0.0860 (± 0.21948)		
K: Baseline(n=S1-363,S2-356)	4.4270 (± 0.41610)	4.4534 (± 0.44584)		
K: C3D1(n=S1-301,S2-309)	-0.1226 (± 0.60007)	-0.0877 (± 0.58424)		

K: EOT(n=S1-302,S2-311)	-0.0374 (± 0.52898)	0.0170 (± 0.58221)		
K: Max change(n=S1-356,S2-350)	-0.2845 (± 1.13356)	-0.2551 (± 1.14282)		
Na: Baseline(n=S1-363,S2-356)	139.3333 (± 2.72935)	139.1798 (± 3.19705)		
Na: C3D1(n=S1-302,S2-313)	-2.0828 (± 3.96368)	-1.5527 (± 3.73110)		
Na: EOT(n=S1-306,S2-313)	-0.9510 (± 3.53728)	-0.9521 (± 3.71944)		
Na: Max change(n=S1-358,S2-350)	-4.7482 (± 9.86512)	-4.6627 (± 14.14911)		
Urea: Baseline(n=S1-363,S2-356)	5.22 (± 1.885)	5.23 (± 2.068)		
Urea: C3D1(n=S1-302,S2-312)	1.89 (± 3.302)	1.87 (± 3.961)		
Urea: EOT(n=S1-306,S2-313)	1.73 (± 3.266)	1.40 (± 2.922)		
Urea: Max change (n=S1-358,S2-350)	8.51 (± 7.226)	6.18 (± 6.110)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Estimated Glomerular Filtration Rate

End point title	Change from Baseline in Estimated Glomerular Filtration Rate

End point description:

Change from baseline in biochemistry parameter eGFR was reported. The Glomerular Filtration Rate was measured as milliliter per minute per 1.73 square meter (mL/min/1.73m^2). The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "number analyzed" or "n" signifies subjects who were evaluable at specified timepoints. Please note Sequence 1- S1, Sequence 2-S2, Max on treatment change - max change.

End point type	Secondary

End point timeframe:

At Baseline, Cycle 3 Day 1 (C3D1) (combination period), EOT (15 days after last study treatment administration) and baseline upto event free survival (EFS) follow up Month 18 after EOT (max on treatment change)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	361	356		
Units: mL/min/1.73m*2				
arithmetic mean (standard deviation)				
Baseline	96.956 (± 14.2212)	95.244 (± 14.1290)		
C3D1(n=S1-299, S2-312)	-8.799 (± 19.0295)	-9.205 (± 18.5178)		
EOT(n=S1-304, S2-313)	-11.385 (± 20.6015)	-12.594 (± 18.0053)		
Max change(n=S1-348, S2-346)	-19.439 (± 27.3672)	-19.528 (± 25.7099)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Activated partial thromboplastin time (PTT)/ Standard and Prothrombin Time

End point title	Change from Baseline in Activated partial thromboplastin time (PTT)/ Standard and Prothrombin Time

End point description:

Change from Baseline in coagulation parameter activated PTT/standard and prothrombin Time was reported. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "overall number of subjects analyzed signified" subjects who were evaluable for this outcome measure and "number analyzed" or "n" signifies subjects who were evaluable at specified timepoints. Please note Sequence 1 - S1, Sequence 2- S2, Activated PTT/Standard - APTT/S, Prothrombin Time- PT and Maximum on treatment change - Max change.

End point type	Secondary

End point timeframe:

At Baseline, Cycle 3 Day 1 (C3D1) (combination period), EOT (15 days after last study treatment administration) and baseline upto event free survival (EFS) follow up Month 18 after EOT (max on treatment change)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	349	344		
Units: seconds (Sec)				
arithmetic mean (standard deviation)				
APTT/S: Baseline	26.15 (± 2.349)	26.25 (± 2.540)		
APTT/S: C3D1(n=S1-269,S2-273)	-0.80 (± 3.132)	-0.91 (± 2.324)		
APTT/S: EOT(n=S1-260,S2-268)	-0.29 (± 2.812)	-0.09 (± 2.419)		
APTT/S: Max change(n=S1-331,S2-322)	-1.01 (± 4.165)	-0.87 (± 3.509)		
PT: Baseline(n=S1-349,S2-344)	10.50 (± 0.730)	10.73 (± 1.696)		
PT: C3D1(n=S1-274,S2-284)	0.11 (± 1.730)	-0.17 (± 1.543)		
PT: EOT(n=S1-266,S2-283)	0.17 (± 1.757)	-0.04 (± 1.697)		
PT: Max change(n=S1-334,S2-329)	0.35 (± 2.364)	-0.01 (± 1.838)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Fibrinogen

End point title	Change from Baseline in Fibrinogen

End point description:

Change from Baseline in coagulation parameter fibrinogen was reported. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "number of subjects analyzed signified" participants who were evaluable for this outcome measure and "n=number analyzed" signifies participants who were evaluable at specified timepoints. Please note Sequence 1-S1, Sequence 2-S2, Maximum on treatment change - Max change.

End point type	Secondary

End point timeframe:

At Baseline, Cycle 3 Day 1 (C3D1) (combination period), EOT (15 days after last study treatment administration) and baseline upto event free survival (EFS) follow up Month 18 after EOT (max on treatment change)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	348	343		
Units: milligrams per deciliter (mg/dl)				
arithmetic mean (standard deviation)				
Baseline	486.9 (± 140.35)	467.7 (± 119.14)		
C3D1 (n=S1-273,S2-282)	121.3 (± 164.05)	109.8 (± 157.03)		
EOT (n=S1-265,S2-283)	17.8 (± 150.78)	1.0 (± 138.69)		
Max change (n=S1-333,S2-328)	112.6 (± 212.46)	122.4 (± 207.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Prothrombin International Normalized Ratio

End point title	Change from Baseline in Prothrombin International Normalized Ratio

End point description:

Change from baseline in coagulation parameters prothrombin international normalized ratio was reported. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Please note Sequence 1-S1, Sequence 2-S2, Maximum on treatment change - Max change.

End point type	Secondary

End point timeframe:

At Baseline, Cycle 3 Day 1 (C3D1) (combination period), EOT (15 days after last study treatment administration) and baseline upto event free survival (EFS) follow up Month 18 after EOT (max on treatment change)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	349	344		
Units: ratio				
arithmetic mean (standard deviation)				
Baseline	0.96 (± 0.090)	0.99 (± 0.188)		
C3D1 (n=S1-274,S2-284)	0.01 (± 0.195)	-0.02 (± 0.175)		
EOT (n=S1-266,S2-283)	0.02 (± 0.197)	0.00 (± 0.195)		
Max change (n=S1-334,S2-329)	0.04 (± 0.265)	0.00 (± 0.212)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Vital Signs: Systolic Blood Pressure, Diastolic Blood Pressure

End point title	Change from Baseline in Vital Signs: Systolic Blood Pressure, Diastolic Blood Pressure

End point description:

Change from Baseline in Vital Signs: Systolic Blood Pressure, Diastolic Blood Pressure was reported. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "overall number of subjects analyzed signified" subjects who were evaluable for this outcome measure and "number analyzed" signifies subjects who were evaluable at specified timepoints. Please note Sequence 1-S1, Sequence 2-S2, Maximum on treatment change - Max change, Systolic Blood Pressure - SBP and Diastolic Blood Pressure - DBP.

End point type	Secondary

End point timeframe:

At Baseline, Cycle 3 Day 1 (C3D1) (combination period), EOT (15 days after last study treatment administration) and baseline upto event free survival (EFS) follow up Month 18 after EOT (max on treatment increase & decrease)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	356		
Units: millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
SBP: Baseline(n= S1-364 , S2-356)	128.0 (± 18.08)	128.2 (± 16.96)		
SBP: C3D1 (n= S1-320, S2-326)	-10.1 (± 19.36)	-7.9 (± 17.53)		
SBP: EOT (n= S1-320, S2-323)	-5.8 (± 20.47)	-3.4 (± 20.03)		

SBP: Max increase(n= S1-249 , S2-274)	15.6 (± 12.89)	16.5 (± 12.43)		
SBP: Max decrease(n= S1-328, S2-323)	-24.7 (± 15.85)	-21.9 (± 14.48)		
DBP: Baseline(n= S1- , S2-)	77.4 (± 10.60)	77.5 (± 9.75)		
DBP: C3D1(n= S1-320, S2-326)	-5.6 (± 12.04)	-4.0 (± 10.65)		
DBP: EOT(n= S1-320, S2-323)	-1.8 (± 12.02)	-1.2 (± 11.55)		
DBP: Max increase(n= S1-241, S2-250)	11.1 (± 7.54)	11.2 (± 8.09)		
DBP: Max decrease(n= S1-323, S2-319)	-15.2 (± 9.43)	-13.2 (± 8.42)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Vital Signs: Heart Rate

End point title	Change from Baseline in Vital Signs: Heart Rate

End point description:

Change from Baseline in Vital Signs: Heart Rate was reported. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "number analyzed" signifies subjects who were evaluable at specified timepoints. Please note Sequence 1-S1, Sequence 2-S2, Maximum on treatment change - Max change and Heart Rate - HR.

End point type	Secondary

End point timeframe:

At Baseline, Cycle 3 Day 1 (C3D1) (combination period), EOT (15 days after last study treatment administration) and baseline upto event free survival (EFS) follow up Month 18 after EOT (max on treatment increase & decrease)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	356		
Units: beats/minute				
arithmetic mean (standard deviation)				
HR: Baseline(n=S1-364,S2-356)	77.6 (± 12.35)	76.1 (± 12.60)		
HR: C3D1(n=S1-320,S2-326)	5.2 (± 13.71)	3.4 (± 13.92)		
HR: EOT(n=S1-318,S2-323)	2.8 (± 14.33)	2.2 (± 13.51)		
HR: Max increase(n=S1-316,S2-304)	17.8 (± 12.30)	16.7 (± 10.97)		
HR: Max decrease(n=S1-274,S2-280)	-11.7 (± 9.00)	-12.2 (± 9.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Vital Signs: Respiratory Rate

End point title	Change from Baseline in Vital Signs: Respiratory Rate

End point description:

Change from Baseline in Vital Signs: Respiratory Rate was reported. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "number analyzed" signifies subjects who were evaluable at specified timepoints. Please note Sequence 1-S1, Sequence 2-S2, Maximum on treatment change - Max change and Respiratory Rate - RR.

End point type	Secondary

End point timeframe:

At Baseline, Cycle 3 Day 1 (C3D1) (combination period), EOT (15 days after last study treatment administration) and baseline upto event free survival (EFS) follow up Month 18 after EOT (max on treatment increase & decrease)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	359	355		
Units: breaths/minute				
arithmetic mean (standard deviation)				
RR: Baseline(n=S1-359,S2-355)	16.8 (± 2.38)	16.7 (± 2.98)		
RR: C3D1(n=S1-304,S2-319)	-0.1 (± 2.65)	0.0 (± 2.76)		
RR: EOT(n=S1-308,S2-317)	-0.1 (± 2.83)	-0.1 (± 3.01)		
RR: Max increase(n=S1-208,S2-316)	3.2 (± 2.66)	2.7 (± 2.13)		
RR: Max decrease(n=S1-208,S2-216)	-3.1 (± 2.52)	-2.7 (± 2.88)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Vital Signs: Body Temperature

End point title	Change from Baseline in Vital Signs: Body Temperature

End point description:

Change from Baseline in Vital Signs: Body Temperature was reported. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "number analyzed" signifies subjects who were evaluable at specified timepoints. Please note Sequence 1-S1, Sequence 2-S2, Maximum on treatment change - Max channge.

End point type	Secondary

End point timeframe:

At Baseline, Cycle 3 Day 1 (C3D1) (combination period), EOT (15 days after last study treatment administration) and baseline upto event free survival (EFS) follow up Month 18 after EOT (max on treatment increase)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	355		
Units: degree Celsius				
arithmetic mean (standard deviation)				
Baseline(n=S1-364,s2-355)	36.44 (± 0.443)	36.41 (± 0.432)		
C3D1(n=S1-318,s2-325)	0.10 (± 36.49)	0.07 (± 0.476)		
EOT(n=S1-317,s2-320)	0.00 (± 0.463)	0.00 (± 0.453)		
Max increase(n=S1-292,s2-295)	0.57 (± 0.445)	0.51 (± 0.413)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in ECG Parameters

End point title	Change from Baseline in ECG Parameters

End point description:

The 12-lead ECGs were recorded after the subjects have rested for at least 5 minutes in supine position. The parameters included Respiratory Rate (RR), Pulse Rate (PR), QRS, QT and QTcF calculated by the Bazett formula. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "number analyzed" signifies subjects who were evaluable for each specific category. Please note Sequence 1-S1, Sequence 2-S2, Maximum on treatment change - Max change, PR Interval - PRI, QRS Duration - QRSD, QT Interval - QRI, RR Interval - RRI, QTcF Interval - QRcFI.

End point type	Secondary

End point timeframe:

At Baseline, and upto event free survival (EFS) follow up Month 18 after EOT (max on treatment increase)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	356		
Units: millisecond				
arithmetic mean (standard deviation)				
PRI: Baseline(n=S1-361,S2-353)	154.6 (± 28.05)	159.2 (± 29.85)		
PRI: Max increase(n=S1-273,S2-247)	15.2 (± 16.48)	15.8 (± 19.90)		
QRSD: Baseline(n=S1-364,S2-355)	90.4 (± 14.78)	91.9 (± 14.48)		
QRSD: Max increase(n=S1-267,S2-268)	9.8 (± 9.87)	9.8 (± 21.97)		
QTI: Baseline(n=S1-364,S2-356)	381.9 (± 30.29)	385.7 (± 33.47)		
QTI: Max increase(n=S1-307,S2-278)	33.3 (± 26.91)	26.9 (± 21.78)		
RRI: Baseline(n=S1-359,S2-349)	824.5 (± 163.43)	858.0 (± 153.30)		
RRI: Max increase(n=S1-291,S2-266)	139.5 (± 125.19)	117.2 (± 87.11)		

QTcFI: Baseline(n=S1-364,S2-356)	406.3 (± 22.78)	406.6 (± 25.06)		
QTcFI: Max increase(n=S1-305,S2-279)	24.9 (± 21.27)	19.7 (± 19.17)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Vital Signs: Body Weight

End point title	Change from Baseline in Vital Signs: Body Weight

End point description:

Change from Baseline in Vital Signs: Body Weight was reported. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "number analyzed" signifies subjects who were evaluable at specified timepoints. Please note Sequence 1-S1, Sequence 2-S2, Maximum on treatment change - Max change.

End point type	Secondary

End point timeframe:

At Baseline, C3D1 (combination period), EOT (15 days after last study treatment administration) and baseline upto event free survival (EFS) follow up Month 18 after EOT (max on treatment increase & decrease)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	356		
Units: kilograms (kg)				
arithmetic mean (standard deviation)				
Baseline(n=S1-364,S2-356)	69.552 (± 16.8493)	70.261 (± 15.2793)		
C3D1(n=S1-321,S2-327)	-4.762 (± 3.9129)	-4.331 (± 3.6001)		
EOT(n=S1-319,S2-328)	-6.282 (± 6.1160)	-4.819 (± 5.9718)		
Max increase(n=S1-86,S2-104)	2.497 (± 2.1157)	2.549 (± 2.7503)		
Max decrease(n=S1-340,S2-331)	-8.182 (± 5.1605)	-7.379 (± 4.8001)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who Completed Cycle 1, 2, 3, 4, 5 and 6

End point title	Number of Subjects who Completed Cycle 1, 2, 3, 4, 5 and 6

End point description:

Number of subjects who completed cycle 1, 2, 3, 4, 5 or 6 of xevinapant/matched placebo were reported. The SAF set included all subjects who received any dose of any of the study intervention

(xevinapant/matched placebo, cisplatin/carboplatin, IMRT).

End point type	Secondary

End point timeframe:

Cycle 1, 2, 3, 4, 5 and 6 (each cycle is of 3 weeks)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	356		
Units: count of subjects				
Cycle 1	363	355		
Cycle 2	325	335		
Cycle 3	290	314		
Cycle 4	266	210		
Cycle 5	263	307		
Cycle 6	246	297		

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Duration

End point title	Treatment Duration

End point description:

Treatment duration is calculated by study treatment component as (last dose date minus first dose date plus x)/7, where x=8 for xevinapant/matched placebo, x=21 for cisplatin/carboplatin, x=3 for IMRT.The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "number analyzed" signifies subjects who were evaluable for each specific category.

End point type	Secondary

End point timeframe:

Up to end of study (up to 188weeks and 5 days)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	356		
Units: weeks				
median (full range (min-max))				
Xevinapant/matched placebo	18.00 (10.71 to 18.14)	18.00 (18.00 to 18.29)		
Cisplatin(n=S1-360,S2-351)	8.86 (6.00 to 9.00)	9.00 (6.00 to 9.00)		
Carboplatin(n=S1-55,s2-60)	3.00 (3.00 to 6.00)	3.00 (3.00 to 6.00)		

IMRT(n=S1-364,S2-355)	7.43 (7.21 to 7.86)	7.43 (7.29 to 7.71)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Cumulative Dose of Cisplatin

End point title	Total Cumulative Dose of Cisplatin

End point description:

Total cumulative dose of cisplatin was reported. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here" overall number of subjects analyzed signified" subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Up to end of treatment (Day 134)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	360	351		
Units: milligrams per square meter (mg/m^2)				
arithmetic mean (standard deviation)	223.3 (± 76.26)	236.3 (± 73.14)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Cumulative Dose of Xevinapant/ Matched Placebo

End point title	Total Cumulative Dose of Xevinapant/ Matched Placebo

End point description:

Total cumulative dose of Xevinapant/ Matched Placebo was reported in form of mean and standard deviation. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "overall number of subjects analyzed signified" subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Up to end of treatment (Day 134)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	355		
Units: milligrams (mg)				
arithmetic mean (standard deviation)	12383.6 (± 5375.66)	14417.0 (± 4288.55)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Cumulative Dose of Carboplatin

End point title	Total Cumulative Dose of Carboplatin

End point description:

Total cumulative dose of carboplatin was reported as mean and standard deviation. The SAF set included all participants who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "overall number of subjects analyzed signified" subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Up to end of treatment (Day 134)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	60		
Units: Area under curve (AUC)				
arithmetic mean (standard deviation)	6.9 (± 2.37)	6.6 (± 2.26)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Cumulative Dose of Intensity-Modulated Radiation Therapy (IMRT)

End point title	Total Cumulative Dose of Intensity-Modulated Radiation Therapy (IMRT)

End point description:

Total cumulative dose of IMRT were reported in form of mean and standard deviation. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here" overall number of subjects analyzed signified" subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Up to end of treatment (Day 134)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	355		
Units: Gray (Gy)				
arithmetic mean (standard deviation)	66.4 (± 12.32)	67.9 (± 9.74)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Dose intensity of Carboplatin

End point title	Overall Dose intensity of Carboplatin

End point description:

Overall dose intensity of Carboplatin is calculated as the mean of the dose intensities of the individual cycles. This was reported with unit of measure Milligrams per minute per milliliter per week (mg min/mL/week). The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT).Here "overall number of subjects analyzed signified" subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Cycle 1, 2, 3, 4 5, 6 (each cycle is of 3 weeks) or End of Treatment (Day 134)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	60		
Units: mg min/mL/week				
arithmetic mean (standard deviation)	1.59 (± 0.136)	1.60 (± 0.123)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Dose Intensity of Xevinapant/Matched Placebo

End point title	Overall Dose Intensity of Xevinapant/Matched Placebo

End point description:

Overall dose intensity of Xevinapant/ matched placebo is calculated as the mean of the dose intensities of the individual cycles. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT).Here "overall number of subjects analyzed signified" subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Cycle 1, 2, 3, 4 5, 6 (each cycle is of 3 weeks) or End of Treatment (Day 134)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	355		
Units: milligrams per day (mg/day)				
arithmetic mean (standard deviation)	122.72 (± 18.274)	126.56 (± 16.495)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Dose intensity of Cisplatin

End point title	Overall Dose intensity of Cisplatin

End point description:

Overall dose intensity of Cisplatin is calculated as the mean of the dose intensities of the individual cycles. This was reported with the unit of measure milligrams per meter square per week (mg/m2/week). The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "overall number of participants analyzed signified" subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Cycle 1, 2, 3, 4 5, 6 (each cycle is of 3 weeks) or End of Treatment (Day 134)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	360	351		
Units: mg/m2/week				
arithmetic mean (standard deviation)	32.33 (± 3.053)	32.55 (± 2.301)		

Statistical analyses

No statistical analyses for this end point

Secondary: Relative Dose Intensity

End point title	Relative Dose Intensity

End point description:

Relative dose intensity (RDI) represents the percentage of the amount of a drug actually delivered [actual dose intensity (DI)] to the amount planned (planned DI). The purpose of calculating RDI is to evaluate whether the planned DI of an anti-cancer treatment was actually achieved which may suggest the feasibility of planned treatment regimen. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "number analyzed" signifies subjects who were evaluable for each specific category.

End point type	Secondary

End point timeframe:

Up to 50 months

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	363	355		
Units: percentage (%) of dose intensity				
arithmetic mean (standard deviation)				
Xevinapant/matched placebo	92.04 (± 13.706)	94.92 (± 12.372)		
Cisplatin	96.98 (± 9.159)	97.65 (± 6.904)		
Carboplatin	95.19 (± 8.182)	96.17 (± 7.386)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment Interruption, Treatment Reduction and Treatment Discontinuation for Xevinapant/ Matched Placebo

End point title	Number of Subjects with Treatment Interruption, Treatment Reduction and Treatment Discontinuation for Xevinapant/ Matched Placebo

End point description:

Number of subjects with Treatment Interruption, Treatment Reduction and Treatment Discontinuation was reported. The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT). Here "number analyzed" signifies subjects who were evaluable for each specific category.

End point type	Secondary

End point timeframe:

Up to end of treatment (Day 134)

End point values	Sequence 1: Debio 1143 + CRT	Sequence 2: Placebo + CRT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	356		
Units: subjects				
Treatment Interruption-xevinapant/Placebo	206	147		
Treatment Reduction-xevinapant/placebo	34	17		
Treatment Discontinuation-xevinapant/placebo	71	30		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs were be collected from the time of Informed Consent Form signature until the End Of Treatment(EOT)visit (Day134).From the EOT visit until the End Of Study visit(Up to 44 months),only SAEs and late onset AEs of Special Interest were collected

Adverse event reporting additional description:

The SAF set included all subjects who received any dose of any of the study intervention (xevinapant/matched placebo, cisplatin/carboplatin, IMRT).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Sequence 2: Placebo + CRT

Reporting group description:

Subjects received a combination of placebo matched to Debio 1143 along with Chemoradiotherapy(CRT): Radiotherapy +Cisplatin+ placebo matched to Xevinapant (Debio 1143). Subjects received 6 cycles of oral solution of placebo matched to Xevinapant once daily from Day 1 to 14, per 3-week cycle in combination with 70 Gray (Gy) of intensity modulated radiation therapy (IMRT) in 35 fractions, 2 Gy/fraction, over 7 weeks, and High-dose cisplatin (100 mg/m2) on Day 2 of a 3-week cycle per 3 cycles(combination therapy period).If high-dose cisplatin 100 mg/m2 was not tolerated after the first dose, subjects could be switched to carboplatin (10mg/mL, iv infusion), followed by 3 cycles of monotherapy of placebo matched to Xevinapant from Day 1 to 14, per 3-week cycle (monotherapy period).

Reporting group title	Sequence 1: Debio 1143 + CRT

Reporting group description:

Subjects received a combination of Debio 1143 along with Chemoradiotherapy (CRT): Radiotherapy +Cisplatin + Xevinapant (Debio 1143). Subjects received 6 cycles of oral solution of Xevinapant at a dose of 200 milligrams per day (mg/day) once daily from Day 1 to 14, per 3-week cycle in combination with 70 Gray (Gy) of intensity modulated radiation therapy (IMRT) in 35 fractions, 2 Gy/fraction, over 7 weeks, and High-dose cisplatin (100 mg/m2) on Day 2 of a 3-week cycle per 3 cycles (combination therapy period). If high-dose cisplatin 100 mg/m2 was not tolerated after the first dose, subjects could be switched to carboplatin (10mg/mL, iv infusion), followed by 3 cycles of monotherapy of Xevinapant at a dose of 200 mg/day from Day 1 to 14, per 3-week cycle (monotherapy period).

Serious adverse events	Sequence 2: Placebo + CRT	Sequence 1: Debio 1143 + CRT	
Total subjects affected by serious adverse events			
subjects affected / exposed	129 / 356 (36.24%)	194 / 364 (53.30%)	
number of deaths (all causes)	93	111	
number of deaths resulting from adverse events	13	22	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	6 / 356 (1.69%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	3 / 7	0 / 2	
deaths causally related to treatment / all	1 / 1	0 / 0	
Tumour rupture			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Vascular disorders			
Peripheral vein thrombus extension			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic thrombosis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	0 / 356 (0.00%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurogenic shock			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Shock			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Malaise			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 356 (0.56%)	8 / 364 (2.20%)	
occurrences causally related to treatment / all	0 / 2	6 / 8	
deaths causally related to treatment / all	0 / 0	1 / 2	
Fatigue			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	2 / 356 (0.56%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Death			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 356 (0.56%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	1 / 2	1 / 2	
Multiple organ dysfunction syndrome			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Asthenia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 356 (0.56%)	5 / 364 (1.37%)	
occurrences causally related to treatment / all	2 / 2	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyrexia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 356 (0.56%)	5 / 364 (1.37%)	
occurrences causally related to treatment / all	2 / 2	3 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	0 / 356 (0.00%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Prostatitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	1 / 356 (0.28%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal oedema			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	3 / 356 (0.84%)	3 / 364 (0.82%)	
occurrences causally related to treatment / all	2 / 4	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal haemorrhage			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asphyxia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung disorder			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal haemorrhage			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal inflammation			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumothorax			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary oedema			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 356 (0.56%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	2 / 2	0 / 2	
deaths causally related to treatment / all	1 / 1	0 / 0	
Respiratory distress			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Stridor			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 356 (0.56%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	2 / 356 (0.56%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device malfunction			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Amylase increased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 356 (0.56%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	5 / 356 (1.40%)	12 / 364 (3.30%)	
occurrences causally related to treatment / all	5 / 5	11 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood potassium decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram QT prolonged			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	4 / 364 (1.10%)	
occurrences causally related to treatment / all	0 / 0	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerular filtration rate decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipase increased			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	3 / 356 (0.84%)	4 / 364 (1.10%)	
occurrences causally related to treatment / all	2 / 3	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight increased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell count decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Gastrostomy tube site complication			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrostomy failure			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stoma site discharge			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	3 / 364 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Unintentional medical device removal			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Bradycardia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Atrial fibrillation			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Ischaemic cardiomyopathy			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Cardio-respiratory arrest			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Nervous system disorders			
Bell's palsy			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coma			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplegia			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Guillain-Barre syndrome			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle spasticity			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peroneal nerve palsy			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Seizure			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord paralysis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	7 / 356 (1.97%)	7 / 364 (1.92%)	
occurrences causally related to treatment / all	7 / 7	6 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile bone marrow aplasia			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Agranulocytosis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	4 / 356 (1.12%)	8 / 364 (2.20%)	
occurrences causally related to treatment / all	4 / 4	8 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphopenia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	3 / 356 (0.84%)	7 / 364 (1.92%)	
occurrences causally related to treatment / all	3 / 3	7 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	3 / 356 (0.84%)	7 / 364 (1.92%)	
occurrences causally related to treatment / all	2 / 3	7 / 7	
deaths causally related to treatment / all	0 / 0	1 / 1	

Leukopenia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Ototoxicity			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoacusis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Constipation			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	1 / 356 (0.28%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Odynophagia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	5 / 364 (1.37%)	
occurrences causally related to treatment / all	0 / 0	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	8 / 356 (2.25%)	5 / 364 (1.37%)	
occurrences causally related to treatment / all	8 / 9	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth haemorrhage			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Melaena			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric perforation			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	9 / 356 (2.53%)	21 / 364 (5.77%)	
occurrences causally related to treatment / all	8 / 9	20 / 21	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	4 / 356 (1.12%)	6 / 364 (1.65%)	
occurrences causally related to treatment / all	4 / 5	5 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Upper gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue ulceration			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	6 / 356 (1.69%)	15 / 364 (4.12%)	
occurrences causally related to treatment / all	6 / 6	15 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumoperitoneum			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hepatobiliary disorders			
Hepatic failure			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Skin and subcutaneous tissue disorders			
Dermatitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angioedema			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis acneiform			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis exfoliative generalised			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erythema multiforme			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash macular			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	1 / 356 (0.28%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	3 / 364 (0.82%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin exfoliation			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	19 / 356 (5.34%)	25 / 364 (6.87%)	
occurrences causally related to treatment / all	19 / 20	24 / 31	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal injury			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy toxic			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prerenal failure			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	6 / 356 (1.69%)	10 / 364 (2.75%)	
occurrences causally related to treatment / all	5 / 7	8 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcapsular renal haematoma			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 356 (0.56%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Endocrine disorders			
Central hypothyroidism			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adrenal insufficiency			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in jaw			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Device related infection			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			

alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis bacterial			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	3 / 356 (0.84%)	4 / 364 (1.10%)	
occurrences causally related to treatment / all	0 / 3	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess jaw			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral infection			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 356 (0.56%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiglottic abscess			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parotitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumonia necrotising			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia legionella			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia escherichia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	4 / 356 (1.12%)	8 / 364 (2.20%)	
occurrences causally related to treatment / all	2 / 4	4 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	14 / 356 (3.93%)	23 / 364 (6.32%)	
occurrences causally related to treatment / all	7 / 14	11 / 24	
deaths causally related to treatment / all	0 / 1	3 / 6	
Peritonitis			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	3 / 364 (0.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	3 / 356 (0.84%)	8 / 364 (2.20%)	
occurrences causally related to treatment / all	1 / 3	5 / 8	
deaths causally related to treatment / all	1 / 2	1 / 2	
Stoma site infection			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	5 / 364 (1.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vascular device infection			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 356 (0.56%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	5 / 364 (1.37%)	
occurrences causally related to treatment / all	1 / 1	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	3 / 356 (0.84%)	7 / 364 (1.92%)	
occurrences causally related to treatment / all	2 / 3	5 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemic hyperosmolar nonketotic syndrome			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	4 / 356 (1.12%)	7 / 364 (1.92%)	
occurrences causally related to treatment / all	3 / 5	6 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomagnesaemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	3 / 356 (0.84%)	7 / 364 (1.92%)	
occurrences causally related to treatment / all	2 / 4	3 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophagia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 356 (0.28%)	0 / 364 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 356 (0.56%)	2 / 364 (0.55%)	
occurrences causally related to treatment / all	2 / 3	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypernatraemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 356 (0.00%)	1 / 364 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Sequence 2: Placebo + CRT	Sequence 1: Debio 1143 + CRT	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	350 / 356 (98.31%)	360 / 364 (98.90%)	
Vascular disorders			
Hypertension			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	20 / 356 (5.62%)	14 / 364 (3.85%)	
occurrences (all)	26	15	
General disorders and administration site conditions			
Pyrexia			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	35 / 356 (9.83%)	58 / 364 (15.93%)	
occurrences (all)	42	72	
Asthenia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	68 / 356 (19.10%)	98 / 364 (26.92%)	
occurrences (all)	88	108	
Fatigue			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	66 / 356 (18.54%)	58 / 364 (15.93%)	
occurrences (all)	75	71	
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	42 / 356 (11.80%)	36 / 364 (9.89%)	
occurrences (all)	45	38	
Cough			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	45 / 356 (12.64%)	36 / 364 (9.89%)	
occurrences (all)	48	38	
Dyspnoea			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	18 / 356 (5.06%)	19 / 364 (5.22%)	
occurrences (all)	20	22	
Hiccups			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	28 / 356 (7.87%)	21 / 364 (5.77%)	
occurrences (all)	33	24	
Oropharyngeal pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	62 / 356 (17.42%)	56 / 364 (15.38%)	
occurrences (all)	65	60	
Pharyngeal inflammation			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	13 / 356 (3.65%)	21 / 364 (5.77%)	
occurrences (all)	13	23	
Productive cough			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	23 / 356 (6.46%)	23 / 364 (6.32%)	
occurrences (all)	23	23	
Psychiatric disorders			
Insomnia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	26 / 356 (7.30%)	37 / 364 (10.16%)	
occurrences (all)	27	37	
Investigations			
Amylase increased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	44 / 356 (12.36%)	84 / 364 (23.08%)	
occurrences (all)	50	110	
Alanine aminotransferase increased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	40 / 356 (11.24%)	78 / 364 (21.43%)	
occurrences (all)	54	115	
C-reactive protein increased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	17 / 356 (4.78%)	24 / 364 (6.59%)	
occurrences (all)	21	26	
Blood urea increased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	17 / 356 (4.78%)	20 / 364 (5.49%)	
occurrences (all)	28	27	
Blood creatinine increased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	81 / 356 (22.75%)	87 / 364 (23.90%)	
occurrences (all)	106	119	
Aspartate aminotransferase increased			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	30 / 356 (8.43%)	47 / 364 (12.91%)	
occurrences (all)	43	56	
Electrocardiogram QT prolonged			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	14 / 356 (3.93%)	26 / 364 (7.14%)	
occurrences (all)	14	29	
White blood cell count decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	65 / 356 (18.26%)	63 / 364 (17.31%)	
occurrences (all)	127	113	
Weight decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	157 / 356 (44.10%)	187 / 364 (51.37%)	
occurrences (all)	171	201	
Platelet count decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	46 / 356 (12.92%)	57 / 364 (15.66%)	
occurrences (all)	71	82	
Neutrophil count decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	76 / 356 (21.35%)	78 / 364 (21.43%)	
occurrences (all)	122	118	
Lymphocyte count decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	30 / 356 (8.43%)	45 / 364 (12.36%)	
occurrences (all)	39	63	
Lipase increased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	23 / 356 (6.46%)	56 / 364 (15.38%)	
occurrences (all)	32	76	
Gamma-glutamyltransferase increased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	19 / 356 (5.34%)	23 / 364 (6.32%)	
occurrences (all)	22	26	

Injury, poisoning and procedural complications			
Radiation skin injury			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	160 / 356 (44.94%)	165 / 364 (45.33%)	
occurrences (all)	166	175	
Radiation mucositis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	23 / 356 (6.46%)	20 / 364 (5.49%)	
occurrences (all)	23	20	
Nervous system disorders			
Headache			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	22 / 356 (6.18%)	23 / 364 (6.32%)	
occurrences (all)	24	24	
Dysgeusia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	111 / 356 (31.18%)	106 / 364 (29.12%)	
occurrences (all)	117	109	
Dizziness			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	18 / 356 (5.06%)	20 / 364 (5.49%)	
occurrences (all)	19	22	
Blood and lymphatic system disorders			
Neutropenia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	100 / 356 (28.09%)	110 / 364 (30.22%)	
occurrences (all)	136	141	
Lymphopenia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	42 / 356 (11.80%)	39 / 364 (10.71%)	
occurrences (all)	46	48	
Thrombocytopenia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	45 / 356 (12.64%)	63 / 364 (17.31%)	
occurrences (all)	61	79	

Anaemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	180 / 356 (50.56%)	199 / 364 (54.67%)	
occurrences (all)	212	244	
Leukopenia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	44 / 356 (12.36%)	57 / 364 (15.66%)	
occurrences (all)	69	79	
Ear and labyrinth disorders			
Tinnitus			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	65 / 356 (18.26%)	59 / 364 (16.21%)	
occurrences (all)	70	67	
Hypoacusis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	30 / 356 (8.43%)	21 / 364 (5.77%)	
occurrences (all)	33	21	
Deafness			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	18 / 356 (5.06%)	19 / 364 (5.22%)	
occurrences (all)	18	19	
Gastrointestinal disorders			
Odynophagia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	77 / 356 (21.63%)	66 / 364 (18.13%)	
occurrences (all)	84	69	
Nausea			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	162 / 356 (45.51%)	144 / 364 (39.56%)	
occurrences (all)	238	188	
Dysphagia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	97 / 356 (27.25%)	138 / 364 (37.91%)	
occurrences (all)	103	154	
Dry mouth			

alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	124 / 356 (34.83%)	138 / 364 (37.91%)	
occurrences (all)	131	143	
Diarrhoea			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	46 / 356 (12.92%)	40 / 364 (10.99%)	
occurrences (all)	51	44	
Constipation			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	125 / 356 (35.11%)	126 / 364 (34.62%)	
occurrences (all)	146	144	
Vomiting			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	84 / 356 (23.60%)	66 / 364 (18.13%)	
occurrences (all)	112	85	
Stomatitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	160 / 356 (44.94%)	193 / 364 (53.02%)	
occurrences (all)	173	224	
Salivary hypersecretion			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	12 / 356 (3.37%)	20 / 364 (5.49%)	
occurrences (all)	13	20	
Skin and subcutaneous tissue disorders			
Rash			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	13 / 356 (3.65%)	40 / 364 (10.99%)	
occurrences (all)	15	49	
Dermatitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	54 / 356 (15.17%)	57 / 364 (15.66%)	
occurrences (all)	58	60	
Musculoskeletal and connective tissue disorders			

Neck pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	21 / 356 (5.90%)	20 / 364 (5.49%)	
occurrences (all)	21	23	
Infections and infestations			
Oral candidiasis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	20 / 356 (5.62%)	18 / 364 (4.95%)	
occurrences (all)	26	19	
COVID-19			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	22 / 356 (6.18%)	27 / 364 (7.42%)	
occurrences (all)	22	27	
Metabolism and nutrition disorders			
Decreased appetite			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	97 / 356 (27.25%)	65 / 364 (17.86%)	
occurrences (all)	115	76	
Dehydration			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	17 / 356 (4.78%)	19 / 364 (5.22%)	
occurrences (all)	22	20	
Hyperkalaemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	17 / 356 (4.78%)	25 / 364 (6.87%)	
occurrences (all)	21	34	
Hypoalbuminaemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	22 / 356 (6.18%)	31 / 364 (8.52%)	
occurrences (all)	30	40	
Hypocalcaemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	12 / 356 (3.37%)	26 / 364 (7.14%)	
occurrences (all)	14	36	
Hypokalaemia			

alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	63 / 356 (17.70%)	71 / 364 (19.51%)	
occurrences (all)	83	103	
Hypomagnesaemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	43 / 356 (12.08%)	54 / 364 (14.84%)	
occurrences (all)	52	64	
Hyponatraemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	42 / 356 (11.80%)	64 / 364 (17.58%)	
occurrences (all)	49	97	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 May 2020	The protocol for study Debio 1143-SCCHN-301 was amended to correct a typo in the gender specific QTcF values mentioned in the exclusion criterion.
02 July 2020	The protocol for study Debio 1143-SCCHN-301 was amended to 1. To add a recommendation on cryoconservation of sperm prior to treatment because of the possibility of infertility due to therapy with cisplatin, carboplatin or Debio 1143. 2. The addition of an ECG examination 3. The addition in the prohibited medication list of live-attenuated vaccinations 4. Two modifications in the management of grade 4 anemia and grade 3/4 thrombocytopenia potentially related to study treatment 5. A clarification of the assumptions used for the sample size calculation 6. A clarification of dynamic allocation 7. Correction regarding laboratory assessments.
06 December 2020	The following modifications were made to the protocol: • Exclusion of patients with hypersensitivity to the active substances or other compounds containing platinum. • Additional information on the management and dose modification of the Investigational Medicinal Products in case of hemolytic uremic syndrome. • Additional information on the management and dose modification of the Investigational Medicinal Products in case of allergic reactions. • Addition of an optional audiogram before each new cycle of cisplatin throughout the study, as required per the cisplatin prescribing information. • Additional information on the prohibited medications and medications to be used with caution in combination with cisplatin and carboplatin, following the prescribing information of these products. These modifications are considered substantial because an exclusion criterion and some clinical follow-up instructions have been modified.
28 June 2021	The protocol for study Debio 1143-SCCHN-301 version 7.0 dated 28 June 2021 was amended to reflect the following changes: 1. Modification of inclusion criterion number 2. Granulocyte-Colony Stimulating Factors (G-CSF) use 3. Abnormal QTcF prolongation and ECG changes
08 November 2021	Version 8.0 dated 08 November 2021 has been amended to include a modified hierarchical testing procedure of secondary endpoints and to update EOS definition taking into account an event driven OS analysis. In addition, clear guidance on close monitoring of renal function was added by including additional local laboratory assessment timepoints.
31 January 2022	Version 8 .0 dated 8 November 2021 was amended (for China only) to include an additional, China-specific extension cohort to increase the sample size of the overall Chinese population analysis to approximately 15 % (106 subjects) of the global ITT population in order to adequately represent the Chinese population. Statistical evaluations of the global ITT population will remain unchanged; a separate analysis of the overall Chinese population included in the study will be performed as described in this amendment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported