



Clinical trial results:

A Phase II Basket Study of the Oral Selective Pan-FGFR Inhibitor Debio 1347 in Subjects With Solid Tumors Harboring a Fusion of FGFR1, FGFR2 or FGFR3

Summary

EudraCT number	2018-003584-53
Trial protocol	FR GR AT NL GB CZ DK NO BG FI ES HR RO
Global end of trial date	04 January 2022

Results information

Result version number	v1
This version publication date	19 January 2023
First version publication date	19 January 2023

Trial information

Trial identification

Sponsor protocol code	Debio 1347-201
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03834220
WHO universal trial number (UTN)	-
Other trial identifiers	IND number: 118244

Notes:

Sponsors

Sponsor organisation name	Debiopharm International S.A.
Sponsor organisation address	Chemin Messidor 5-7, Lausanne, Switzerland, CH - 1002
Public contact	Clinical Department, Debiopharm International SA, 0041 21 321 01 11, ClinicalTrials@debiopharm.com
Scientific contact	Clinical Department, Debiopharm International SA, 0041 21 321 01 11, ClinicalTrials@debiopharm.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 January 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 January 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study was to assess the efficacy of Debio 1347 in terms of objective response rate (ORR) in subjects with solid tumors harboring fibroblast growth factor receptor (FGFR) 1-3 gene fusion/rearrangement.

Protection of trial subjects:

All study subjects were required to read and sign an informed consent form (ICF).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 March 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Norway: 1
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Bulgaria: 1
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	Finland: 2
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	United States: 39
Country: Number of subjects enrolled	Korea, Republic of: 2
Country: Number of subjects enrolled	Singapore: 2
Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	Taiwan: 1
Worldwide total number of subjects	63
EEA total number of subjects	16

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)	40
From 65 to 84 years	23
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 63 subjects were enrolled at 31 investigational sites in the United States, France, Spain, Finland, Korea, Singapore, Australia, Bulgaria, Denmark, Norway, Russian Federation, Taiwan, and the United Kingdom from 22 March 2019 to 04 January 2022.

Pre-assignment

Screening details:

A total of 63 subjects with solid tumors harboring FGFR1-3 gene fusion/rearrangement were enrolled into one of the 3 cohorts: Cohort 1: Biliary Tract Cancer (N=30), Cohort 2: Urothelial Cancer (N=4), Cohort 3: All Other Solid Tumor Histologies (N=29) to receive Debio 1347.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Debio 1347 (Biliary Tract Cancer)

Arm description:

Subjects with biliary tract cancer were included in this cohort to receive Debio 1347 80 milligrams (mg) tablets, orally, once daily (QD), from Day 1 to Day 28 in 28-day cycles until the occurrence of disease progression or unacceptable toxicity (up to a median of 20 weeks).

Arm type	Experimental
Investigational medicinal product name	Debio 1347
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Debio 1347 tablets administered orally from Day 1 to Day 28 in 28-day cycles.

Arm title	Cohort 2: Debio 1347 (Urothelial Cancer)
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Arm description:

Subjects with urothelial cancer were included in this cohort to receive Debio 1347 80 mg tablets, orally, QD, from Day 1 to Day 28 in 28-day cycles until the occurrence of disease progression or unacceptable toxicity (up to a median of 5.86 weeks).

Arm type	Experimental
Investigational medicinal product name	Debio 1347
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Debio 1347 tablets administered orally from Day 1 to Day 28 in 28-day cycles.

Arm title	Cohort 3: Debio 1347 (All Other Solid Tumor Histologies)
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Arm description:

Subjects with all other solid tumor histologies were included in this cohort to receive Debio 1347 80 mg tablets, orally, QD, from Day 1 to Day 28 in 28-day cycles until the occurrence of disease progression or unacceptable toxicity (up to a median of 8.14 weeks).

Arm type	Experimental
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Investigational medicinal product name	Debio 1347
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Debio 1347 tablets administered orally from Day 1 to Day 28 in 28-day cycles.

Number of subjects in period 1	Cohort 1: Debio 1347 (Biliary Tract Cancer)	Cohort 2: Debio 1347 (Urothelial Cancer)	Cohort 3: Debio 1347 (All Other Solid Tumor Histologies)
Started	30	4	29
Completed	0	0	0
Not completed	30	4	29
Withdrawal of Consent	2	2	2
Adverse Event	1	-	-
Death	8	1	17
Radiological Disease Progression	1	-	-
Reason not Specified	9	-	6
Sponsor/EthicsCommittee Decided to Terminate Study	9	1	4

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1: Debio 1347 (Biliary Tract Cancer)
Reporting group description:	
Subjects with biliary tract cancer were included in this cohort to receive Debio 1347 80 milligrams (mg) tablets, orally, once daily (QD), from Day 1 to Day 28 in 28-day cycles until the occurrence of disease progression or unacceptable toxicity (up to a median of 20 weeks).	
Reporting group title	Cohort 2: Debio 1347 (Urothelial Cancer)
Reporting group description:	
Subjects with urothelial cancer were included in this cohort to receive Debio 1347 80 mg tablets, orally, QD, from Day 1 to Day 28 in 28-day cycles until the occurrence of disease progression or unacceptable toxicity (up to a median of 5.86 weeks).	
Reporting group title	Cohort 3: Debio 1347 (All Other Solid Tumor Histologies)
Reporting group description:	
Subjects with all other solid tumor histologies were included in this cohort to receive Debio 1347 80 mg tablets, orally, QD, from Day 1 to Day 28 in 28-day cycles until the occurrence of disease progression or unacceptable toxicity (up to a median of 8.14 weeks).	

Reporting group values	Cohort 1: Debio 1347 (Biliary Tract Cancer)	Cohort 2: Debio 1347 (Urothelial Cancer)	Cohort 3: Debio 1347 (All Other Solid Tumor Histologies)
Number of subjects	30	4	29
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	59.1	55.3	60.0
standard deviation	± 12.21	± 15.22	± 12.58
Gender categorical Units: Subjects			
Female	16	2	16
Male	14	2	13
Race Units: Subjects			
White	20	3	22
Black or African American	5	0	0
Asian	3	1	2
Not Willing to Provide	1	0	3
Other	1	0	2

Ethnicity			
Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	29	4	28

Reporting group values	Total		
Number of subjects	63		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	34		
Male	29		
Race			
Units: Subjects			
White	45		
Black or African American	5		
Asian	6		
Not Willing to Provide	4		
Other	3		
Ethnicity			
Units: Subjects			
Hispanic or Latino	2		
Not Hispanic or Latino	61		

End points

End points reporting groups

Reporting group title	Cohort 1: Debio 1347 (Biliary Tract Cancer)
Reporting group description: Subjects with biliary tract cancer were included in this cohort to receive Debio 1347 80 milligrams (mg) tablets, orally, once daily (QD), from Day 1 to Day 28 in 28-day cycles until the occurrence of disease progression or unacceptable toxicity (up to a median of 20 weeks).	
Reporting group title	Cohort 2: Debio 1347 (Urothelial Cancer)
Reporting group description: Subjects with urothelial cancer were included in this cohort to receive Debio 1347 80 mg tablets, orally, QD, from Day 1 to Day 28 in 28-day cycles until the occurrence of disease progression or unacceptable toxicity (up to a median of 5.86 weeks).	
Reporting group title	Cohort 3: Debio 1347 (All Other Solid Tumor Histologies)
Reporting group description: Subjects with all other solid tumor histologies were included in this cohort to receive Debio 1347 80 mg tablets, orally, QD, from Day 1 to Day 28 in 28-day cycles until the occurrence of disease progression or unacceptable toxicity (up to a median of 8.14 weeks).	

Primary: Objective Response Rate (ORR) as Centrally Measured by Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) Criteria

End point title	Objective Response Rate (ORR) as Centrally Measured by Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) Criteria ^[1]
End point description: ORR was defined as the percentage of subjects with a best overall response (BOR) of partial or complete response (PR or CR). BOR was defined as the best confirmed response observed from first administration of study drug until disease progression. CR was defined as disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. PR was defined as $\geq 30\%$ decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. The Intent-to-treat (ITT) Population consisted of all subjects who received study drug. Number of subjects analysed is the number of subjects with measurable disease and tumor assessment at Baseline.	
End point type	Primary
End point timeframe: Up to disease progression or end of study (up to approximately 3 years)	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Only descriptive statistics was planned to be reported for this endpoint.	

End point values	Cohort 1: Debio 1347 (Biliary Tract Cancer)	Cohort 2: Debio 1347 (Urothelial Cancer)	Cohort 3: Debio 1347 (All Other Solid Tumor Histologies)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	3	25	
Units: percentage of subjects				
number (confidence interval 90%)	6.7 (1.2 to 19.5)	0.0 (0.0 to 63.2)	4.0 (0.2 to 17.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)
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End point description:

DOR was defined as the time from the date of the initial PR or CR to date of the first documented progression or death due to any cause. CR was defined as disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. PR was defined as $\geq 30\%$ decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. The ITT population consisted of all subjects who received study drug. Only subjects with best overall response of CR or PR were analysed for this endpoint. '9999' signifies that median, lower and upper limit of 95% confidence interval (CI) were not estimable due to low number of subjects with event.

End point type	Secondary
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End point timeframe:

Up to disease progression or end of study (up to approximately 3 years)

End point values	Cohort 1: Debio 1347 (Biliary Tract Cancer)	Cohort 2: Debio 1347 (Urothelial Cancer)	Cohort 3: Debio 1347 (All Other Solid Tumor Histologies)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[2]	0 ^[3]	1	
Units: months				
median (confidence interval 95%)	(to)	(to)	5.55 (-9999 to 9999)	

Notes:

[2] - Due to limitation of responders and shortened observation time, interpretable data was not collected.

[3] - Due to limitation of responders and shortened observation time, interpretable data was not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)
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End point description:

DCR was defined as the percentage of subjects with a BOR of confirmed CR, confirmed PR or stable disease (SD) ≥ 6 weeks. BOR was defined as the best confirmed response observed from first administration of study drug until disease progression. CR was defined as disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. PR was defined as $\geq 30\%$ decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. SD was defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD), taking as reference the smallest sum diameters while on study. PD was defined as $\geq 20\%$ increase in the sum of diameters of target lesions, taking as reference the smallest sum on study. ITT population consisted of all subjects who received study drug.

End point type	Secondary
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End point timeframe:

Up to disease progression or end of study (up to approximately 3 years)

End point values	Cohort 1: Debio 1347 (Biliary Tract Cancer)	Cohort 2: Debio 1347 (Urothelial Cancer)	Cohort 3: Debio 1347 (All Other Solid Tumor Histologies)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	4	29	
Units: percentage of subjects				
number (confidence interval 95%)	63.3 (43.9 to 80.1)	0.0 (0.0 to 60.2)	34.5 (17.9 to 54.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)
End point description:	
PFS was defined as the time from the start date of treatment to date of the first documented progression or death due to any cause. ITT population consisted of all subjects who received study drug. '9999' signifies that the upper limit of 95% CI was not estimable due to low number of subjects with event.	
End point type	Secondary
End point timeframe:	
Up to disease progression or end of study (up to approximately 3 years)	

End point values	Cohort 1: Debio 1347 (Biliary Tract Cancer)	Cohort 2: Debio 1347 (Urothelial Cancer)	Cohort 3: Debio 1347 (All Other Solid Tumor Histologies)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	4	29	
Units: months				
median (confidence interval 95%)	3.68 (3.55 to 10.58)	1.77 (0.95 to 9999)	1.84 (1.71 to 3.52)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
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End point description:

OS was defined as defined as the time from the start date of treatment to date of death due to any cause. ITT population consisted of all subjects who received study drug. '9999' signifies that median, lower and upper limit of 95% CI were not estimable due to low number of subjects with events.

End point type	Secondary
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End point timeframe:

Until death or loss to follow-up or end of study (up to approximately 3 years)

End point values	Cohort 1: Debio 1347 (Biliary Tract Cancer)	Cohort 2: Debio 1347 (Urothelial Cancer)	Cohort 3: Debio 1347 (All Other Solid Tumor Histologies)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	4	29	
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)	7.13 (4.30 to 11.37)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Treatment-Emergent Adverse Events (TEAEs) Assessed by National Cancer Institute Common Terminology Criteria (NCI CTCAE) v5.0 and Serious Adverse Events (SAEs)

End point title	Percentage of Subjects With Treatment-Emergent Adverse Events (TEAEs) Assessed by National Cancer Institute Common Terminology Criteria (NCI CTCAE) v5.0 and Serious Adverse Events (SAEs)
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End point description:

An AE is any untoward medical occurrence in a subject or clinical trial subject administered a medicinal product and which does not necessarily have a causal relationship with this treatment. A TEAE is defined as an AE that either starts or worsens in severity on or after the first administration of the study drug and within 30 days of the last administration of the study drug. An SAE is any untoward medical occurrence that at any dose results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect or is medically significant. Safety Population consisted of all subjects who received study drug.

End point type	Secondary
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End point timeframe:

From first dose of study drug up to 30 days post last dose (Up to approximately 3 years)

End point values	Cohort 1: Debio 1347 (Biliary Tract Cancer)	Cohort 2: Debio 1347 (Urothelial Cancer)	Cohort 3: Debio 1347 (All Other Solid Tumor Histologies)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	4	29	
Units: percentage of subjects				
number (not applicable)				
TEAEs	100.0	100.0	96.6	
Serious TEAEs	46.7	50.0	24.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Concentration at Steady State (C_{trough,ss}) of Debio 1347 in Plasma

End point title	Trough Concentration at Steady State (C _{trough,ss}) of Debio 1347 in Plasma
End point description: Geometric coefficient of variation (CV) reported in this endpoint is geometric CV%. The Pharmacokinetic (PK) Population included subjects who received one or more doses of Debio 1347 and have at least one PK concentration result available. Number of subjects analysed is the number of subjects with data available for analyses.	
End point type	Secondary
End point timeframe: Pre-dose on Days 14 and 28, and 1, 3, 7 hours post-dose on Day 28 of Cycle 1; pre-dose on Days 14 and 28, and 3 hours post-dose on Day 28 of Cycle 2	

End point values	Cohort 1: Debio 1347 (Biliary Tract Cancer)	Cohort 2: Debio 1347 (Urothelial Cancer)	Cohort 3: Debio 1347 (All Other Solid Tumor Histologies)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	3	26	
Units: nanogram per millilitre (ng/mL)				
geometric mean (geometric coefficient of variation)	619.6 (± 100.0)	306.8 (± 43.4)	463.2 (± 127.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve Over the Dosing Interval at Steady State (AUC_{tau,ss}) of Debio 1347 in Plasma

End point title	Area Under the Plasma Concentration-Time Curve Over the Dosing Interval at Steady State (AUC _{tau,ss}) of Debio 1347 in
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End point description:

Geometric CV reported in this endpoint is geometric CV%. PK Population included subjects who received one or more doses of Debio 1347 and have at least one PK concentration result available. Number of subjects analysed is the number of subjects with data available for analyses.

End point type	Secondary
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End point timeframe:

Pre-dose on Days 14 and 28, and 1, 3, 7 hours post-dose on Day 28 of Cycle 1; pre-dose on Days 14 and 28, and 3 hours post-dose on Day 28 of Cycle 2

End point values	Cohort 1: Debio 1347 (Biliary Tract Cancer)	Cohort 2: Debio 1347 (Urothelial Cancer)	Cohort 3: Debio 1347 (All Other Solid Tumor Histologies)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	3	26	
Units: hour*nanogram (h*ng)/mL				
geometric mean (geometric coefficient of variation)	23326.7 (± 70.4)	13999.0 (± 39.1)	18192.1 (± 86.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation of Debio 1347 Plasma Concentration (C) and QT Interval Corrected for Heart Rate Using Fridericia's Formula (QTcF)

End point title	Correlation of Debio 1347 Plasma Concentration (C) and QT Interval Corrected for Heart Rate Using Fridericia's Formula (QTcF)
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End point description:

End point type	Secondary
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End point timeframe:

Pre-dose on Days 14 and 28, and 1, 3, 7 hours post-dose on Day 28 of Cycle 1; pre-dose on Days 14 and 28, and 3 hours post-dose on Day 28 of Cycle 2

End point values	Cohort 1: Debio 1347 (Biliary Tract Cancer)	Cohort 2: Debio 1347 (Urothelial Cancer)	Cohort 3: Debio 1347 (All Other Solid Tumor Histologies)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[4]	0 ^[5]	0 ^[6]	
Units: correlation coefficient (r)				
geometric mean (confidence interval 90%)	(to)	(to)	(to)	

Notes:

[4] - Analysis of Debio 1347 C-QTcF relationship was not deemed necessary and was not conducted.

[5] - Analysis of Debio 1347 C-QTcF relationship was not deemed necessary and was not conducted.

[6] - Analysis of Debio 1347 C-QTcF relationship was not deemed necessary and was not conducted.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to 30 days post last dose (up to approximately 3 years)

Adverse event reporting additional description:

Safety Population consisted of all subjects who received study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.0
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Reporting groups

Reporting group title	Cohort 1: Debio 1347 (Biliary Tract Cancer)
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Reporting group description:

Subjects with biliary tract cancer were included in this cohort to receive Debio 1347 80 milligrams (mg) tablets, orally, once daily (QD), from Day 1 to Day 28 in 28-day cycles until the occurrence of disease progression or unacceptable toxicity (up to a median of 20 weeks).

Reporting group title	Cohort 2: Debio 1347 (Urothelial Cancer)
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Reporting group description:

Subjects with urothelial cancer were included in this cohort to receive Debio 1347 80 mg tablets, orally, QD, from Day 1 to Day 28 in 28-day cycles until the occurrence of disease progression or unacceptable toxicity (up to a median of 5.86 weeks).

Reporting group title	Cohort 3: Debio 1347 (All Other Solid Tumor Histologies)
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Reporting group description:

Subjects with all other solid tumor histologies were included in this cohort to receive Debio 1347 80 mg tablets, orally, QD, from Day 1 to Day 28 in 28-day cycles until the occurrence of disease progression or unacceptable toxicity (up to a median of 8.14 weeks).

Serious adverse events	Cohort 1: Debio 1347 (Biliary Tract Cancer)	Cohort 2: Debio 1347 (Urothelial Cancer)	Cohort 3: Debio 1347 (All Other Solid Tumor Histologies)
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 30 (46.67%)	2 / 4 (50.00%)	7 / 29 (24.14%)
number of deaths (all causes)	9	1	17
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			

subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Laryngeal haemorrhage			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Cardiac arrest			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			

subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 30 (10.00%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			

subjects affected / exposed	1 / 30 (3.33%)	1 / 4 (25.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary sepsis			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary tract infection			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			

subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Cohort 1: Debio 1347 (Biliary Tract Cancer)	Cohort 2: Debio 1347 (Urothelial Cancer)	Cohort 3: Debio 1347 (All Other Solid Tumor Histologies)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 30 (100.00%)	4 / 4 (100.00%)	28 / 29 (96.55%)
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	9 / 30 (30.00%)	1 / 4 (25.00%)	10 / 29 (34.48%)
occurrences (all)	10	1	10
Pyrexia			
subjects affected / exposed	6 / 30 (20.00%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences (all)	7	0	1
Oedema peripheral			
subjects affected / exposed	3 / 30 (10.00%)	0 / 4 (0.00%)	3 / 29 (10.34%)
occurrences (all)	4	0	3
Asthenia			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences (all)	2	0	1
Pain			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences (all)	2	0	1
Influenza like illness			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences (all)	2	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			

Dyspnoea			
subjects affected / exposed	4 / 30 (13.33%)	0 / 4 (0.00%)	4 / 29 (13.79%)
occurrences (all)	4	0	4
Epistaxis			
subjects affected / exposed	4 / 30 (13.33%)	0 / 4 (0.00%)	4 / 29 (13.79%)
occurrences (all)	4	0	6
Oropharyngeal pain			
subjects affected / exposed	4 / 30 (13.33%)	0 / 4 (0.00%)	4 / 29 (13.79%)
occurrences (all)	4	0	4
Cough			
subjects affected / exposed	3 / 30 (10.00%)	1 / 4 (25.00%)	3 / 29 (10.34%)
occurrences (all)	3	1	3
Nasal dryness			
subjects affected / exposed	1 / 30 (3.33%)	2 / 4 (50.00%)	2 / 29 (6.90%)
occurrences (all)	1	2	2
Haemoptysis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	3 / 29 (10.34%)
occurrences (all)	0	0	3
Productive cough			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	2 / 29 (6.90%)
occurrences (all)	1	0	2
Rhinorrhoea			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	4 / 29 (13.79%)
occurrences (all)	2	0	4
Depression			
subjects affected / exposed	1 / 30 (3.33%)	1 / 4 (25.00%)	0 / 29 (0.00%)
occurrences (all)	1	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 30 (13.33%)	1 / 4 (25.00%)	4 / 29 (13.79%)
occurrences (all)	5	1	4
Weight decreased			

subjects affected / exposed	4 / 30 (13.33%)	1 / 4 (25.00%)	2 / 29 (6.90%)
occurrences (all)	6	1	2
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 30 (10.00%)	1 / 4 (25.00%)	2 / 29 (6.90%)
occurrences (all)	4	2	2
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 30 (10.00%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences (all)	5	0	1
Neutrophil count decreased			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	3 / 29 (10.34%)
occurrences (all)	0	1	3
Platelet count decreased			
subjects affected / exposed	3 / 30 (10.00%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences (all)	5	0	1
White blood cell count decreased			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	3 / 29 (10.34%)
occurrences (all)	0	1	5
Blood bilirubin increased			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences (all)	4	0	1
Blood creatinine increased			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	2 / 29 (6.90%)
occurrences (all)	1	0	3
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	7 / 30 (23.33%)	1 / 4 (25.00%)	9 / 29 (31.03%)
occurrences (all)	7	1	9
Dizziness			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	2 / 29 (6.90%)
occurrences (all)	2	0	2
Headache			
subjects affected / exposed	3 / 30 (10.00%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences (all)	3	0	1
Peripheral sensory neuropathy			

subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 3	0 / 4 (0.00%) 0	1 / 29 (3.45%) 1
Lethargy subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	1 / 4 (25.00%) 1	1 / 29 (3.45%) 1
Taste disorder subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 4 (0.00%) 0	2 / 29 (6.90%) 2
Paraesthesia subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	1 / 4 (25.00%) 1	0 / 29 (0.00%) 0
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 5	0 / 4 (0.00%) 0	9 / 29 (31.03%) 11
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2	0 / 4 (0.00%) 0	0 / 29 (0.00%) 0
Eye disorders Dry eye subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 3	1 / 4 (25.00%) 1	7 / 29 (24.14%) 7
Vision blurred subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1	0 / 4 (0.00%) 0	3 / 29 (10.34%) 3
Lacrimation increased subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1	1 / 4 (25.00%) 1	0 / 29 (0.00%) 0
Photophobia subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	1 / 4 (25.00%) 1	0 / 29 (0.00%) 0
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all)	9 / 30 (30.00%) 11	0 / 4 (0.00%) 0	11 / 29 (37.93%) 12
Stomatitis			

subjects affected / exposed	9 / 30 (30.00%)	2 / 4 (50.00%)	9 / 29 (31.03%)
occurrences (all)	17	2	9
Diarrhoea			
subjects affected / exposed	8 / 30 (26.67%)	0 / 4 (0.00%)	10 / 29 (34.48%)
occurrences (all)	9	0	12
Dry mouth			
subjects affected / exposed	11 / 30 (36.67%)	1 / 4 (25.00%)	6 / 29 (20.69%)
occurrences (all)	11	1	6
Nausea			
subjects affected / exposed	10 / 30 (33.33%)	0 / 4 (0.00%)	8 / 29 (27.59%)
occurrences (all)	10	0	9
Vomiting			
subjects affected / exposed	7 / 30 (23.33%)	1 / 4 (25.00%)	7 / 29 (24.14%)
occurrences (all)	9	1	9
Abdominal pain			
subjects affected / exposed	6 / 30 (20.00%)	0 / 4 (0.00%)	4 / 29 (13.79%)
occurrences (all)	7	0	4
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 30 (6.67%)	1 / 4 (25.00%)	0 / 29 (0.00%)
occurrences (all)	2	1	0
Haemorrhoids			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences (all)	2	0	1
Oral pain			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	2 / 29 (6.90%)
occurrences (all)	1	0	2
Abdominal distension			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	5 / 29 (17.24%)
occurrences (all)	9	0	8
Skin and subcutaneous tissue disorders			
Alopecia			

subjects affected / exposed	14 / 30 (46.67%)	1 / 4 (25.00%)	9 / 29 (31.03%)
occurrences (all)	14	1	10
Dry skin			
subjects affected / exposed	8 / 30 (26.67%)	0 / 4 (0.00%)	6 / 29 (20.69%)
occurrences (all)	8	0	6
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	6 / 30 (20.00%)	0 / 4 (0.00%)	5 / 29 (17.24%)
occurrences (all)	9	0	6
Onychomadesis			
subjects affected / exposed	3 / 30 (10.00%)	0 / 4 (0.00%)	3 / 29 (10.34%)
occurrences (all)	3	0	3
Rash			
subjects affected / exposed	1 / 30 (3.33%)	1 / 4 (25.00%)	2 / 29 (6.90%)
occurrences (all)	1	1	2
Skin ulcer			
subjects affected / exposed	1 / 30 (3.33%)	1 / 4 (25.00%)	2 / 29 (6.90%)
occurrences (all)	1	1	2
Nail discolouration			
subjects affected / exposed	3 / 30 (10.00%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences (all)	3	0	0
Nail disorder			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences (all)	2	0	1
Pruritus			
subjects affected / exposed	2 / 30 (6.67%)	1 / 4 (25.00%)	0 / 29 (0.00%)
occurrences (all)	2	1	0
Rash maculo-papular			
subjects affected / exposed	3 / 30 (10.00%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences (all)	3	0	0
Onycholysis			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences (all)	2	0	0
Pain of skin			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences (all)	4	0	0

Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 30 (3.33%)	1 / 4 (25.00%)	1 / 29 (3.45%)
occurrences (all)	1	1	1
Chronic kidney disease			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	4 / 30 (13.33%)	0 / 4 (0.00%)	2 / 29 (6.90%)
occurrences (all)	6	0	2
Arthralgia			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	2 / 29 (6.90%)
occurrences (all)	2	0	2
Back pain			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	2 / 29 (6.90%)
occurrences (all)	1	0	3
Flank pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	3 / 29 (10.34%)
occurrences (all)	0	0	3
Muscle spasms			
subjects affected / exposed	2 / 30 (6.67%)	1 / 4 (25.00%)	0 / 29 (0.00%)
occurrences (all)	2	1	0
Musculoskeletal pain			
subjects affected / exposed	3 / 30 (10.00%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences (all)	3	0	0
Myalgia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Infections and infestations			
Paronychia			
subjects affected / exposed	6 / 30 (20.00%)	0 / 4 (0.00%)	4 / 29 (13.79%)
occurrences (all)	6	0	4
Urinary tract infection			
subjects affected / exposed	3 / 30 (10.00%)	0 / 4 (0.00%)	3 / 29 (10.34%)
occurrences (all)	5	0	6

Nasopharyngitis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	2 / 29 (6.90%)
occurrences (all)	1	0	2
Conjunctivitis			
subjects affected / exposed	2 / 30 (6.67%)	0 / 4 (0.00%)	0 / 29 (0.00%)
occurrences (all)	2	0	0
Metabolism and nutrition disorders			
Hyperphosphataemia			
subjects affected / exposed	24 / 30 (80.00%)	2 / 4 (50.00%)	22 / 29 (75.86%)
occurrences (all)	40	2	31
Decreased appetite			
subjects affected / exposed	5 / 30 (16.67%)	1 / 4 (25.00%)	9 / 29 (31.03%)
occurrences (all)	7	1	9
Hypomagnesaemia			
subjects affected / exposed	4 / 30 (13.33%)	0 / 4 (0.00%)	6 / 29 (20.69%)
occurrences (all)	5	0	7
Hypophosphataemia			
subjects affected / exposed	3 / 30 (10.00%)	1 / 4 (25.00%)	3 / 29 (10.34%)
occurrences (all)	3	1	3
Hypercalcaemia			
subjects affected / exposed	3 / 30 (10.00%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences (all)	3	0	6
Hyponatraemia			
subjects affected / exposed	3 / 30 (10.00%)	0 / 4 (0.00%)	1 / 29 (3.45%)
occurrences (all)	3	0	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 4 (25.00%)	2 / 29 (6.90%)
occurrences (all)	0	1	3
Hypokalaemia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 4 (0.00%)	2 / 29 (6.90%)
occurrences (all)	1	0	2
Dehydration			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Hyperkalaemia			

subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	3
Hypocalcaemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 4 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 December 2018	The following changes were implemented with Amendment 1: 1. The Risk-benefit Assessment was added and minor updates were made. 2. Inclusion criteria was updated to reflect that subjects should refrain from donating egg(s) or sperm during clinical trials with Debio 1347 and for a suitable period post-investigational medicinal product (IMP) use. 3. Updated inclusion criteria regarding the maximum total bilirubin level allowed since subjects with cholangiocarcinoma were to be enrolled. 4. Inclusion criteria updated to clearly state that the subjects must have exhausted all lines of standard therapy, unless, for some reason, they are ineligible to it. 5. Inclusion criteria updated to clarify sexual abstinence is only a highly effective method when it is the usual and preferred lifestyle of the subject. 6. Exclusion criterion updated to clarify the chemotherapy or radiotherapy or small molecule anti-cancer agents exclusion criteria. Clarification that Debio 1347 has no potential genotoxicity. 7. Added that the use of proton pump inhibitors has been prohibited. 8. Updated post-study safety reporting language. 9. Added requirement for pregnancy testing in female subjects for 6 months post End of treatment. 10. Added a description of the End-of-study and End of treatment Criteria.
16 July 2020	The protocol was amended as per Amendment 2 to reflect the changes due to the permanent halt to the enrolment in the study and for all subjects who remained on treatment with Debio 1347 after the implementation of Protocol Amendment 2, the assessments and procedures defined in the study protocol were no longer to be in force and were to be replaced by standard institutional care practice. Subjects were to be followed regularly (at least every 2 months) to assess the potential occurrence of safety event and conduct safety laboratory analysis. Only safety data were to be collected in the electronic case report form (eCRF).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
17 June 2020	Due to lower efficacy of Debio 1347 observed during initial statistical review of pooled data, the Sponsor decided to permanently halt the enrolment in the study after consultation with the data monitoring committee (DMC).	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to the premature termination of subject recruitment and shortened follow up, the primary efficacy analysis was likely underpowered in the final analysis, leading to greater statistical uncertainty in results.

Notes: