



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 | v2 (current) |
| This version publication date | 23 June 2024 |
| First version publication date | 19 January 2023 |
| Version creation reason | • Correction of full data set Minor changes required |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | Debio 1347-201 |
|-----------------------|----------------|

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 | Australia: 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 | Korea, Republic of: 2 |
| Country: Number of subjects enrolled | Norway: 1 |
| Country: Number of subjects enrolled | Russian Federation: 1 |
| Country: Number of subjects enrolled | Singapore: 2 |
| Country: Number of subjects enrolled | Spain: 5 |
| Country: Number of subjects enrolled | Taiwan: 1 |
| Country: Number of subjects enrolled | United Kingdom: 1 |
| Country: Number of subjects enrolled | United States: 39 |
| 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) |
|------------------|--|

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) |
|------------------|--|

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 |
|----------|--------------|

| | |
|--|------------|
| 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 1 year and 9 months) | |
| 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) |
|-----------------|----------------------------|

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 |
|----------------|-----------|

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) |
|-----------------|----------------------------|

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 |
|----------------|-----------|

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) |
|-----------------|-----------------------|

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 |
|----------------|-----------|

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) |
|-----------------|--|

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 |
|----------------|-----------|

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: Predose and post dose up to Cycle 2 Day 28 (each cycle length = 28 days) | |

| 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 |
|-----------------|---|

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

End point timeframe:

Predose and post dose up to Cycle 2 Day 28 (each cycle length = 28 days)

| 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)

End point description:

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 | 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 |
|-----------------|------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 22.0 |
|--------------------|------|

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 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 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).

| Serious adverse events | Cohort 1: Debio 1347 (Biliary Tract Cancer) | Cohort 3: Debio 1347 (All Other Solid Tumor Histologies) | Cohort 2: Debio 1347 (Urothelial Cancer) |
|---|---|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 14 / 30 (46.67%) | 7 / 29 (24.14%) | 2 / 4 (50.00%) |
| number of deaths (all causes) | 9 | 17 | 1 |
| number of deaths resulting from adverse events | 0 | 1 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Malignant melanoma | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 29 (0.00%) | 0 / 4 (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%) | 1 / 29 (3.45%) | 0 / 4 (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 |

| | | | |
|--|----------------|----------------|---------------|
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 29 (0.00%) | 0 / 4 (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 / 29 (0.00%) | 0 / 4 (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 / 29 (0.00%) | 0 / 4 (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%) | 1 / 29 (3.45%) | 0 / 4 (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 |
| Investigations | | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 29 (0.00%) | 0 / 4 (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 / 29 (0.00%) | 0 / 4 (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%) | 1 / 29 (3.45%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |

| | | | |
|---|----------------|----------------|---------------|
| Nervous system disorders | | | |
| Syncope | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 29 (3.45%) | 0 / 4 (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 |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 29 (0.00%) | 0 / 4 (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%) | 1 / 29 (3.45%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 29 (0.00%) | 0 / 4 (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 / 29 (0.00%) | 0 / 4 (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%) | 1 / 29 (3.45%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 29 (0.00%) | 0 / 4 (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 / 29 (0.00%) | 0 / 4 (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 / 29 (0.00%) | 0 / 4 (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%) | 1 / 29 (3.45%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract obstruction | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 29 (3.45%) | 0 / 4 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 29 (3.45%) | 0 / 4 (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 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 29 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 1 / 29 (3.45%) | 1 / 4 (25.00%) |
| 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 / 29 (0.00%) | 0 / 4 (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 / 29 (0.00%) | 0 / 4 (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%) | 1 / 29 (3.45%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 29 (0.00%) | 0 / 4 (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 / 29 (0.00%) | 0 / 4 (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%) | 0 / 29 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 29 (0.00%) | 0 / 4 (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 / 29 (0.00%) | 0 / 4 (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 3: Debio 1347 (All Other Solid Tumor Histologies) | Cohort 2: Debio 1347 (Urothelial Cancer) |
|---|--|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 30 / 30 (100.00%) | 28 / 29 (96.55%) | 4 / 4 (100.00%) |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 9 / 30 (30.00%) | 10 / 29 (34.48%) | 1 / 4 (25.00%) |
| occurrences (all) | 10 | 10 | 1 |
| Pyrexia | | | |
| subjects affected / exposed | 6 / 30 (20.00%) | 1 / 29 (3.45%) | 0 / 4 (0.00%) |
| occurrences (all) | 7 | 1 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | 3 / 29 (10.34%) | 0 / 4 (0.00%) |
| occurrences (all) | 4 | 3 | 0 |
| Asthenia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 1 / 29 (3.45%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Pain | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 1 / 29 (3.45%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 29 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 29 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 4 / 30 (13.33%) | 4 / 29 (13.79%) | 0 / 4 (0.00%) |
| occurrences (all) | 4 | 4 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 4 / 30 (13.33%) | 4 / 29 (13.79%) | 0 / 4 (0.00%) |
| occurrences (all) | 4 | 6 | 0 |
| Oropharyngeal pain | | | |

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

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

| | | | |
|---|------------------------|------------------------|---------------------|
| Paraesthesia subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 29 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 3 / 30 (10.00%) 5 | 9 / 29 (31.03%) 11 | 0 / 4 (0.00%) 0 |
| Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | 0 / 29 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Eye disorders Dry eye subjects affected / exposed occurrences (all) | 3 / 30 (10.00%) 3 | 7 / 29 (24.14%) 7 | 1 / 4 (25.00%) 1 |
| Vision blurred subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | 3 / 29 (10.34%) 3 | 0 / 4 (0.00%) 0 |
| Lacrimation increased subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | 0 / 29 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| Photophobia subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 29 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) | 9 / 30 (30.00%) 11 | 11 / 29 (37.93%) 12 | 0 / 4 (0.00%) 0 |
| Stomatitis subjects affected / exposed occurrences (all) | 9 / 30 (30.00%) 17 | 9 / 29 (31.03%) 9 | 2 / 4 (50.00%) 2 |
| Diarrhoea subjects affected / exposed occurrences (all) | 8 / 30 (26.67%) 9 | 10 / 29 (34.48%) 12 | 0 / 4 (0.00%) 0 |
| Dry mouth subjects affected / exposed occurrences (all) | 11 / 30 (36.67%) 11 | 6 / 29 (20.69%) 6 | 1 / 4 (25.00%) 1 |

| | | | |
|---|------------------|-----------------|----------------|
| Nausea | | | |
| subjects affected / exposed | 10 / 30 (33.33%) | 8 / 29 (27.59%) | 0 / 4 (0.00%) |
| occurrences (all) | 10 | 9 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 7 / 30 (23.33%) | 7 / 29 (24.14%) | 1 / 4 (25.00%) |
| occurrences (all) | 9 | 9 | 1 |
| Abdominal pain | | | |
| subjects affected / exposed | 6 / 30 (20.00%) | 4 / 29 (13.79%) | 0 / 4 (0.00%) |
| occurrences (all) | 7 | 4 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 29 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 2 | 0 | 1 |
| Haemorrhoids | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 1 / 29 (3.45%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Oral pain | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 2 / 29 (6.90%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 2 / 29 (6.90%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Hepatobiliary disorders | | | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 5 / 29 (17.24%) | 0 / 4 (0.00%) |
| occurrences (all) | 9 | 8 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 14 / 30 (46.67%) | 9 / 29 (31.03%) | 1 / 4 (25.00%) |
| occurrences (all) | 14 | 10 | 1 |
| Dry skin | | | |
| subjects affected / exposed | 8 / 30 (26.67%) | 6 / 29 (20.69%) | 0 / 4 (0.00%) |
| occurrences (all) | 8 | 6 | 0 |
| Palmar-plantar erythrodysaesthesia syndrome | | | |
| subjects affected / exposed | 6 / 30 (20.00%) | 5 / 29 (17.24%) | 0 / 4 (0.00%) |
| occurrences (all) | 9 | 6 | 0 |
| Onychomadesis | | | |

| | | | |
|--|----------------------|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 3 / 30 (10.00%) 3 | 3 / 29 (10.34%) 3 | 0 / 4 (0.00%) 0 |
| Rash | | | |
| subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | 2 / 29 (6.90%) 2 | 1 / 4 (25.00%) 1 |
| Skin ulcer | | | |
| subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | 2 / 29 (6.90%) 2 | 1 / 4 (25.00%) 1 |
| Nail discolouration | | | |
| subjects affected / exposed occurrences (all) | 3 / 30 (10.00%) 3 | 0 / 29 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Nail disorder | | | |
| subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | 1 / 29 (3.45%) 1 | 0 / 4 (0.00%) 0 |
| Pruritus | | | |
| subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | 0 / 29 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| Rash maculo-papular | | | |
| subjects affected / exposed occurrences (all) | 3 / 30 (10.00%) 3 | 0 / 29 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Onycholysis | | | |
| subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | 0 / 29 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Pain of skin | | | |
| subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 4 | 0 / 29 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | 1 / 29 (3.45%) 1 | 1 / 4 (25.00%) 1 |
| Chronic kidney disease | | | |
| subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | 0 / 29 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|----------------------|----------------------|---------------------|
| Pain in extremity subjects affected / exposed occurrences (all) | 4 / 30 (13.33%) 6 | 2 / 29 (6.90%) 2 | 0 / 4 (0.00%) 0 |
| Arthralgia subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | 2 / 29 (6.90%) 2 | 0 / 4 (0.00%) 0 |
| Back pain subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | 2 / 29 (6.90%) 3 | 0 / 4 (0.00%) 0 |
| Flank pain subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 3 / 29 (10.34%) 3 | 0 / 4 (0.00%) 0 |
| Muscle spasms subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | 0 / 29 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| Musculoskeletal pain subjects affected / exposed occurrences (all) | 3 / 30 (10.00%) 3 | 0 / 29 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Myalgia subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 2 / 29 (6.90%) 2 | 0 / 4 (0.00%) 0 |
| Infections and infestations | | | |
| Paronychia subjects affected / exposed occurrences (all) | 6 / 30 (20.00%) 6 | 4 / 29 (13.79%) 4 | 0 / 4 (0.00%) 0 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 3 / 30 (10.00%) 5 | 3 / 29 (10.34%) 6 | 0 / 4 (0.00%) 0 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | 2 / 29 (6.90%) 2 | 0 / 4 (0.00%) 0 |
| Conjunctivitis subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | 0 / 29 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Metabolism and nutrition disorders | | | |

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

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: