



Clinical trial results:

A Phase II multicenter study comparing the efficacy of the oral angionenesis inhibitor nintedanib with the intravenous cytotoxic compound ifosfamide for treatment of patients with advanced metastatic soft tissue sarcoma after failure of systemic non-oxazaphosphorine-based first line chemotherapy for inoperable disease "ANITA"

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2016-002093-12 |
| Trial protocol | BE GB PL NL ES LT |
| Global end of trial date | 13 May 2021 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 19 May 2022 |
| First version publication date | 19 May 2022 |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | 1506-STBSG |
|-----------------------|------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02808247 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | EORTC |
| Sponsor organisation address | Avenue E Mounier 83/11, Brussels, Belgium, 1200 |
| Public contact | Clinical Operations Department, European Organisation for the Research and, 0032 27741345, regulatory@eortc.org |
| Scientific contact | Clinical Operations Department, European Organisation for the Research and, 0032 27741345, regulatory@eortc.org |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 18 November 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 18 November 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 13 May 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial is to evaluate whether nintedanib given as second-line therapy for advanced, inoperable and/or metastatic STS prolongs progression-free survival when compared with ifosfamide.

Protection of trial subjects:

The responsible investigator ensure that this study was conducted in agreement with either the Declaration of Helsinki (available on the World Medical Association web site (<http://www.wma.net>)) and/or the laws and regulations of the country, whichever provides the greatest protection of the patient. The protocol had been written, and the study was conducted according to the ICH Harmonized Tripartite Guideline on Good Clinical Practice (ICH-GCP, available online at https://www.ema.europa.eu/documents/scientific-guideline/ich-e6-r1-guideline-goodclinicalpractice_en.pdf). The protocol was approved by the competent ethics committee(s) as required

Background therapy:

Ifosfamide 3 g/m² intravenously on days 1, 2 and 3 every 21 days for up to a maximum of 6 cycles.

Evidence for comparator:

Investigational arm: Nintedanib 200 mg twice daily orally.

| | |
|---|--------------|
| Actual start date of recruitment | 26 July 2017 |
| 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 | Netherlands: 10 |
| Country: Number of subjects enrolled | Poland: 6 |
| Country: Number of subjects enrolled | Spain: 15 |
| Country: Number of subjects enrolled | United Kingdom: 11 |
| Country: Number of subjects enrolled | Belgium: 17 |
| Country: Number of subjects enrolled | France: 17 |
| Country: Number of subjects enrolled | Lithuania: 2 |
| Country: Number of subjects enrolled | Switzerland: 2 |
| Worldwide total number of subjects | 80 |
| EEA total number of subjects | 67 |

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) | 53 |
| From 65 to 84 years | 27 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

A total of 80 patients were randomized (40 pts per arm) between July 26, 2017 and November 21, 2019 by 18 institutions in 8 countries.

Pre-assignment

Screening details:

- Histologically proven advanced, inoperable (medical or surgical) and/or metastatic malignant STS of intermediate or high grade,
- One line of previous systemic chemotherapy for advanced, inoperable and/or metastatic malignant STS.
- No active brain metastases

Period 1

| | |
|------------------------------|---------------------------|
| Period 1 title | Enrolled (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Blinding implementation details:

NA

Arms

| | |
|------------------------------|------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Ifosfamide |

Arm description:

Ifosfamide 3 g/m² intravenously on days 1, 2 and 3 every 21 days for up to a maximum of 6 cycles.

| | |
|--|---|
| Arm type | Active comparator |
| Investigational medicinal product name | ifosfamide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for concentrate for solution for infusion, Powder for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Ifosfamide 3 g/m² intravenously on days 1, 2 and 3 every 21 days for up to a maximum of 6 cycles.

| | |
|------------------|------------|
| Arm title | Nintedanib |
|------------------|------------|

Arm description:

Nintedanib 200 mg twice daily orally.

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

Dosage and administration details:

Nintedanib 200 mg twice daily orally.

| Number of subjects in period 1 | Ifosfamide | Nintedanib |
|---------------------------------------|------------|------------|
| Started | 40 | 40 |
| Completed | 38 | 39 |
| Not completed | 2 | 1 |
| Consent withdrawn by subject | 2 | - |
| Lack of efficacy | - | 1 |

Baseline characteristics

Reporting groups

| | |
|---|------------|
| Reporting group title | Ifosfamide |
| Reporting group description: | |
| Ifosfamide 3 g/m2 intravenously on days 1, 2 and 3 every 21 days for up to a maximum of 6 cycles. | |
| Reporting group title | Nintedanib |
| Reporting group description: | |
| Nintedanib 200 mg twice daily orally. | |

| Reporting group values | Ifosfamide | Nintedanib | Total |
|--|------------|------------|-------|
| Number of subjects | 40 | 40 | 80 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 27 | 26 | 53 |
| From 65-84 years | 13 | 14 | 27 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 23 | 20 | 43 |
| Male | 17 | 20 | 37 |
| Performance status | | | |
| WHO performance status | | | |
| Units: Subjects | | | |
| Cat 0 | 22 | 20 | 42 |
| Cat 1 | 14 | 19 | 33 |
| Cat 2 | 3 | 1 | 4 |
| Missing | 1 | 0 | 1 |
| Tumor Type | | | |
| Units: Subjects | | | |
| Liposarcoma | 11 | 11 | 22 |
| Fibroblastic sarcoma | 4 | 5 | 9 |
| Leiomyosarcoma | 17 | 14 | 31 |
| Vascular Tumours | 2 | 1 | 3 |
| Tumors of uncertain differentiation | 1 | 2 | 3 |
| MPNST | 2 | 3 | 5 |
| Undifferentiated / unclassified sarcoma | 3 | 3 | 6 |
| Other | 0 | 1 | 1 |
| Tumor grade | | | |
| Units: Subjects | | | |
| Low | 1 | 0 | 1 |

| | | | |
|------------------------------|-------------|-------------|----|
| Intermediate | 13 | 19 | 32 |
| High | 23 | 20 | 43 |
| Not assessable | 3 | 1 | 4 |
| Tumor size | | | |
| Units: mm | | | |
| median | 72.5 | 94 | |
| inter-quartile range (Q1-Q3) | 45 to 137.5 | 65 to 142.5 | - |

End points

End points reporting groups

| | |
|---|------------|
| Reporting group title | Ifosfamide |
| Reporting group description: | |
| Ifosfamide 3 g/m ² intravenously on days 1, 2 and 3 every 21 days for up to a maximum of 6 cycles. | |
| Reporting group title | Nintedanib |
| Reporting group description: | |
| Nintedanib 200 mg twice daily orally. | |

Primary: Progression free survival

| | |
|---|---------------------------|
| End point title | Progression free survival |
| End point description: | |
| Progression-free survival will be measured from the date of randomization until the date of first documented progression or death, whichever occurs first. Patients who are alive without evidence of progression at their last radiological assessment will be censored at that date. As per the clinical evaluation schedule, radiological follow-up was to be discontinued after starting a new treatment in the absence of progression. When this occurs, follow-up was censored at the date of starting new treatment. Note that death after starting new treatment is still considered an event for this endpoint. | |
| End point type | Primary |
| End point timeframe: | |
| Progression-free survival will be measured from the date of randomization until the date of first documented progression or death, whichever occurs first. | |

| End point values | Ifosfamide | Nintedanib | | |
|----------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 40 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 4.4 (2.9 to 6.7) | 2.5 (1.5 to 3.4) | | |

| | |
|----------------------------|--|
| Attachments (see zip file) | Progression free survival/1506_PFS.pdf |
|----------------------------|--|

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Primary analysis of progression free survival |
| Comparison groups | Nintedanib v Ifosfamide |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.07 ^[1] |
| Method | Regression, Cox |
| Parameter estimate | Cox proportional hazard |
| Point estimate | 1.56 |

| | |
|---------------------|-------------|
| Confidence interval | |
| level | Other: 80 % |
| sides | 2-sided |
| lower limit | 1.14 |
| upper limit | 2.13 |

Notes:

[1] - From a Cox proportional hazards adjusted for stratification factors tumor grade and histology

Secondary: Progression free rate at 12 weeks

| | |
|-----------------|-----------------------------------|
| End point title | Progression free rate at 12 weeks |
|-----------------|-----------------------------------|

End point description:

Patients achieving RECIST 1.1 CR, PR or SD at the 12 week disease assessment will be considered a success for this endpoint. All other conditions, e.g. no available imaging, RECIST 1.1 progression prior to or at week 12, non-evaluable assessments, switching to new anti-tumor treatment in the absence of documented progression, or early death will be counted as a failure.

Note that when an assessment was performed later than the foreseen time window of 12 weeks, but before and after was documented as a stable disease (or response), then the 12 week assessment was not considered a failure for this analysis.

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

End point timeframe:

Patients achieving RECIST 1.1 CR, PR or SD at the 12 week disease assessment will be considered a success for this endpoint.

| End point values | Ifosfamide | Nintedanib | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 40 | | |
| Units: subjects | | | | |
| No | 22 | 26 | | |
| Yes | 18 | 14 | | |

Statistical analyses

| | |
|----------------------------|------------------|
| Statistical analysis title | Interim analysis |
|----------------------------|------------------|

Statistical analysis description:

Decision rule: If less than 19 out of these 36 patients on nintedanib are progression-free at the 12 week assessment, the trial will stop early. Otherwise, the trial will continue as planned.

Note that if more than 17 failures are observed in the nintedanib arm, the trial should be stopped.

| | |
|---|--------------------------------------|
| Comparison groups | Nintedanib v Ifosfamide |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[2] |
| P-value | > 0.1 ^[3] |
| Method | Decision rule based on A'Hern design |
| Parameter estimate | Binomial estimate and exact 80% CI |
| Point estimate | 0.35 |

| | |
|---------------------|-------------|
| Confidence interval | |
| level | Other: 80 % |
| sides | 2-sided |
| lower limit | 0.249 |
| upper limit | 0.463 |

Notes:

[2] - This interim look originates from a single arm, single stage A'Hern design with type I and II error fixed at $\alpha = 0.1$ and $\beta = 0.15$, testing the null hypothesis $H_0: P \leq 40\%$ versus $H_A: P > 40\%$. The decision rule is computed under the alternative hypothesis that $P = 60\%$. The analysis is done in the Nintedanib arm only.

[3] - Decision rule: If less than 19 out of the first 36 patients on nintedanib are progression-free at the 12 week assessment, the trial will stop early. Otherwise, the trial will continue as planned. Therefore this trial was closed for futility

Secondary: Overall survival

| | |
|-----------------|------------------|
| End point title | Overall survival |
|-----------------|------------------|

End point description:

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

End point timeframe:

Overall survival (OS) was computed from the date of start of treatment to the date of death (due to any cause). Patients alive at the time of analysis will be censored at the date of last follow-up.

| End point values | Ifosfamide | Nintedanib | | |
|----------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 40 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 24.1 (10.9 to 100) | 13.7 (9.4 to 23.4) | | |

| | |
|----------------------------|-------------|
| Attachments (see zip file) | 1506_OS.pdf |
|----------------------------|-------------|

Statistical analyses

| | |
|---|-------------------------|
| Statistical analysis title | Overall survival |
| Comparison groups | Ifosfamide v Nintedanib |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.111 ^[4] |
| Method | Regression, Cox |
| Parameter estimate | Cox proportional hazard |
| Point estimate | 1.65 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.89 |
| upper limit | 3.06 |

Notes:

[4] - Cox Proportional hazards model adjusted for stratification factors tumor grade and histology

Secondary: Best response

| | |
|-----------------|---------------|
| End point title | Best response |
|-----------------|---------------|

End point description:

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

End point timeframe:

Best response observed on treatment

| End point values | Ifosfamide | Nintedanib | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 40 | | |
| Units: subjects | | | | |
| Partial response | 2 | 2 | | |
| Stable disease | 23 | 18 | | |
| Progressive disease | 10 | 19 | | |
| Early death | 2 | 0 | | |
| Not evaluable | 3 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time on nintedanib treatment

| | |
|-----------------|---|
| End point title | Time on nintedanib treatment ^[5] |
|-----------------|---|

End point description:

computed from the date of start of treatment to the date of discontinuation of treatment for any reason, including disease progression, treatment toxicity, and death. Patients alive and still on protocol treatment at the time of the analysis will be censored at the date of last known treatment administration.

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

End point timeframe:

computed from the date of start of treatment to the date of discontinuation of treatment for any reason, including disease progression, treatment toxicity, and death.

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The endpoint is only valid in one arm, i.e. in the arm of patients who received nintedanib treatment

| | | | | |
|----------------------------------|------------------|--|--|--|
| End point values | Nintedanib | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 40 | | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 2.5 (1.4 to 3.4) | | | |

| | |
|-----------------------------------|----------------|
| Attachments (see zip file) | 1506_ntrt.jpeg |
|-----------------------------------|----------------|

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events, laboratory and physical abnormalities were collected till 90 days after the end of treatment. For SAEs: all SAEs till 30 days after end of treatment; afterwards, only related SA

Adverse event reporting additional description:

AEs are evaluated using CTC grading, SAEs using MedDra. Non-SAEs has not been collected specifically, all AEs will be reported in non-SAE section.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Ifosfamide |
|-----------------------|------------|

Reporting group description:

Ifosfamide

| | |
|-----------------------|------------|
| Reporting group title | Nintedanib |
|-----------------------|------------|

Reporting group description:

Nintedanib

| Serious adverse events | Ifosfamide | Nintedanib | |
|---|------------------|-----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 16 / 38 (42.11%) | 8 / 39 (20.51%) | |
| number of deaths (all causes) | 18 | 24 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TRANSAMINASES INCREASED | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| ENCEPHALOPATHY | | | |
| alternative dictionary used: | | | |

| | | | |
|---|-----------------|----------------|--|
| MedDRA 24.1 | | | |
| subjects affected / exposed | 4 / 38 (10.53%) | 0 / 39 (0.00%) | |
| occurrences causally related to treatment / all | 4 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ISCHAEMIC STROKE | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SYNCOPE | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 1 / 39 (2.56%) | |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FEBRILE NEUTROPENIA | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 4 / 38 (10.53%) | 0 / 39 (0.00%) | |
| occurrences causally related to treatment / all | 5 / 5 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PANCYTOPENIA | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| THROMBOCYTOPENIA | | | |
| alternative dictionary used: MedDRA 24.1 | | | |

| | | | |
|--|----------------|----------------|--|
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| CHEST PAIN | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SUDDEN DEATH | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DIARRHOEA | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 2 / 39 (5.13%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INTESTINAL OBSTRUCTION | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VOMITING | | | |
| alternative dictionary used: MedDRA 24.1 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 38 (2.63%) | 1 / 39 (2.56%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| BILE DUCT STENOSIS | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| PULMONARY EMBOLISM | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Renal and urinary disorders | | | |
| ACUTE KIDNEY INJURY | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 3 / 38 (7.89%) | 0 / 39 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| ANAL ABSCESS | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BILIARY TRACT INFECTION | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LOCALISED INFECTION | | | |
| alternative dictionary used: MedDRA 24.1 | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PERITONITIS | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMONIA | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RESPIRATORY TRACT INFECTION | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SEPSIS | | | |
| alternative dictionary used: MedDRA 24.1 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Ifosfamide | Nintedanib | |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 33 / 38 (86.84%) | 35 / 39 (89.74%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| TUMOR PAIN | | | |
| alternative dictionary used: CTCAE 4.0 | | | |

| | | | |
|--|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 1 / 39 (2.56%) 1 | |
| Vascular disorders | | | |
| HYPERTENSION | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 7 / 38 (18.42%) | 15 / 39 (38.46%) | |
| occurrences (all) | 12 | 35 | |
| HYPOTENSION | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| LYMPHEDEMA | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| PHLEBITIS | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| THROMBOEMBOLIC EVENT | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 4 / 38 (10.53%) | 2 / 39 (5.13%) | |
| occurrences (all) | 4 | 3 | |
| General disorders and administration site conditions | | | |
| FATIGUE | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 22 / 38 (57.89%) | 18 / 39 (46.15%) | |
| occurrences (all) | 41 | 30 | |
| FEVER | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 4 / 38 (10.53%) | 3 / 39 (7.69%) | |
| occurrences (all) | 4 | 3 | |
| FLU LIKE SYMPTOMS | | | |
| alternative dictionary used: CTCAE 4.0 | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 38 (2.63%) | 2 / 39 (5.13%) | |
| occurrences (all) | 1 | 2 | |
| LOCALIZED EDEMA | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |
| MALAISE | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| NON-CARDIAC CHEST PAIN | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 4 / 38 (10.53%) | 4 / 39 (10.26%) | |
| occurrences (all) | 5 | 5 | |
| PAIN | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 2 / 39 (5.13%) | |
| occurrences (all) | 0 | 2 | |
| SUDDEN DEATH NOS | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| BRONCHIAL INFECTION | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |
| COUGH | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 2 / 39 (5.13%) | |
| occurrences (all) | 2 | 4 | |
| DYSPNEA | | | |
| alternative dictionary used: CTCAE 4.0 | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 4 / 38 (10.53%) | 4 / 39 (10.26%) | |
| occurrences (all) | 5 | 6 | |
| HICCUPS | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| HOARSENESS | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| RESPIRATORY, THORACIC-OTHER-HAEMOPTYSIS | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| UPPER RESPIRATORY INFECTION | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| VOICE ALTERATION | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |
| Psychiatric disorders | | | |
| DEPRESSION | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |
| INSOMNIA | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| PSYCHIATRIC DISORDERS - OTHER: PSYCHOLOGIC DISTRES | | | |
| alternative dictionary used: CTCAE 4.0 | | | |

| | | | |
|---|---|---|--|
| subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 1 / 39 (2.56%) 1 | |
| Investigations ELECTROCARDIOGRAM QT CORRECTED INTERVAL PROLONGED alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) WEIGHT LOSS alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 6 / 38 (15.79%) 7 | 1 / 39 (2.56%) 1 6 / 39 (15.38%) 8 | |
| Cardiac disorders ATRIAL FIBRILLATION alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) MYOCARDIAL INFARCTION alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) PALPITATIONS alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) | 1 / 38 (2.63%) 1 1 / 38 (2.63%) 1 0 / 38 (0.00%) 0 | 0 / 39 (0.00%) 0 0 / 39 (0.00%) 0 1 / 39 (2.56%) 1 | |
| Nervous system disorders DEPRESSION alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) DIZZINESS alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) DYSGEUSIA alternative dictionary used: CTCAE 4.0 | 0 / 38 (0.00%) 0 0 / 38 (0.00%) 0 | 1 / 39 (2.56%) 1 1 / 39 (2.56%) 1 | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 38 (2.63%) | 6 / 39 (15.38%) | |
| occurrences (all) | 1 | 6 | |
| ENCEPHALOPATHY | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 9 / 38 (23.68%) | 0 / 39 (0.00%) | |
| occurrences (all) | 15 | 0 | |
| HEADACHE | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| HICCUPS | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| PARESTHESIA | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| PERIPHERAL MOTOR NEUROPATHY | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |
| PERIPHERAL SENSORY NEUROPATHY | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| SYNCOPE | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 39 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Blood and lymphatic system disorders | | | |
| ANEMIA | | | |
| alternative dictionary used: CTCAE 4.0 | | | |

| | | | |
|--|--|---|--|
| subjects affected / exposed occurrences (all) BLOOD&LYMPHATIC SYSTEM DISORDERS:MEDULLAR TOXICITY alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) FEBRILE NEUTROPENIA alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) INFECTIONS AND INFESTATIONS- OTHER: BLOOD INFECTION alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) PANCYTOPENIA alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) | 8 / 38 (21.05%) 19 1 / 38 (2.63%) 1 5 / 38 (13.16%) 7 0 / 38 (0.00%) 0 1 / 38 (2.63%) 1 | 1 / 39 (2.56%) 3 0 / 39 (0.00%) 0 0 / 39 (0.00%) 0 1 / 39 (2.56%) 1 0 / 39 (0.00%) 0 | |
| Eye disorders BLURRED VISION alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) CONJUNCTIVITIS alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 0 / 38 (0.00%) 0 | 1 / 39 (2.56%) 1 1 / 39 (2.56%) 1 | |
| Gastrointestinal disorders ABDOMINAL PAIN alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) ANAL HEMORRHAGE alternative dictionary used: CTCAE 4.0 | 4 / 38 (10.53%) 7 | 4 / 39 (10.26%) 6 | |

| | | |
|--|------------------|------------------|
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) |
| occurrences (all) | 0 | 1 |
| BLOATING | | |
| alternative dictionary used: CTCAE 4.0 | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 1 / 39 (2.56%) |
| occurrences (all) | 1 | 1 |
| CONSTIPATION | | |
| alternative dictionary used: CTCAE 4.0 | | |
| subjects affected / exposed | 11 / 38 (28.95%) | 4 / 39 (10.26%) |
| occurrences (all) | 18 | 7 |
| DIARRHEA | | |
| alternative dictionary used: CTCAE 4.0 | | |
| subjects affected / exposed | 6 / 38 (15.79%) | 14 / 39 (35.90%) |
| occurrences (all) | 9 | 31 |
| DRY MOUTH | | |
| alternative dictionary used: CTCAE 4.0 | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) |
| occurrences (all) | 0 | 1 |
| ESOPHAGEAL PAIN | | |
| alternative dictionary used: CTCAE 4.0 | | |
| subjects affected / exposed | 4 / 38 (10.53%) | 1 / 39 (2.56%) |
| occurrences (all) | 4 | 1 |
| FLATULENCE | | |
| alternative dictionary used: CTCAE 4.0 | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 2 / 39 (5.13%) |
| occurrences (all) | 0 | 3 |
| GASTROESOPHAGEAL REFLUX DISEASE | | |
| alternative dictionary used: CTCAE 4.0 | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) |
| occurrences (all) | 0 | 1 |
| MUCOSITIS ORAL | | |
| alternative dictionary used: CTCAE 4.0 | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 3 / 39 (7.69%) |
| occurrences (all) | 2 | 3 |

| | | | |
|--|------------------------|------------------------|--|
| NAUSEA alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) | 17 / 38 (44.74%) 38 | 10 / 39 (25.64%) 13 | |
| SMALL INTESTINAL OBSTRUCTION alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) | 1 / 38 (2.63%) 2 | 0 / 39 (0.00%) 0 | |
| SMALL INTESTINAL PERFORATION alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 2 / 39 (5.13%) 2 | |
| VOMITING alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) | 11 / 38 (28.95%) 19 | 7 / 39 (17.95%) 12 | |
| Hepatobiliary disorders BILE DUCT STENOSIS alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 1 / 39 (2.56%) 1 | |
| HEPATIC INFECTION alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) | 1 / 38 (2.63%) 1 | 0 / 39 (0.00%) 0 | |
| PORTAL HYPERTENSION alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 1 / 39 (2.56%) 1 | |
| Skin and subcutaneous tissue disorders ALOPECIA alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) | 5 / 38 (13.16%) 6 | 0 / 39 (0.00%) 0 | |
| DRY SKIN | | | |

| | | | |
|---|----------------------|---------------------|--|
| alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 2 / 39 (5.13%) 2 | |
| PRURITUS alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 1 / 39 (2.56%) 1 | |
| Renal and urinary disorders ACUTE KIDNEY INJURY alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) | 5 / 38 (13.16%) 6 | 0 / 39 (0.00%) 0 | |
| RENAL&URINARY DISORDERS-OTHER: RENAL TUBULOPATHY alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) | 1 / 38 (2.63%) 1 | 0 / 39 (0.00%) 0 | |
| URINARY FREQUENCY alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) | 1 / 38 (2.63%) 1 | 0 / 39 (0.00%) 0 | |
| URINARY TRACT PAIN alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) | 1 / 38 (2.63%) 1 | 0 / 39 (0.00%) 0 | |
| Musculoskeletal and connective tissue disorders ARTHRALGIA alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) | 1 / 38 (2.63%) 1 | 1 / 39 (2.56%) 1 | |
| BACK PAIN alternative dictionary used: CTCAE 4.0 subjects affected / exposed occurrences (all) | 1 / 38 (2.63%) 1 | 2 / 39 (5.13%) 3 | |
| BONE PAIN | | | |

| | | | |
|--|----------------|----------------|--|
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| BUTTOCK PAIN | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |
| CHEST WALL PAIN | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |
| GENERALIZED MUSCLE WEAKNESS | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 1 / 39 (2.56%) | |
| occurrences (all) | 1 | 1 | |
| MUSCULOSKELETAL &CONNECTIVE TIS.DIS.RCALF SWELLING | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |
| MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDER | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |
| MUSCULOSKELETAL&CONNECTIVE TISSUE DISORDER | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |
| MUSCULOSKELETAL&CONNECTIVE TISSUE DISORDER-GROIN P | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |
| MYALGIA | | | |
| alternative dictionary used: CTCAE | | | |

| | | | |
|--|-----------------|-----------------|--|
| 4.0 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |
| PAIN IN EXTREMITY | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 4 / 38 (10.53%) | 6 / 39 (15.38%) | |
| occurrences (all) | 4 | 7 | |
| Infections and infestations | | | |
| BILIARY TRACT INFECTION | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| BRONCHIAL INFECTION | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |
| INFECTIONS AND INFESTATIONS - PLASTRON RIGHT FOSSA | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| INFECTIONS AND INFESTATIONS-OTHER: SIGMOIDITIS | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |
| INFECTIONS AND INFESTATIONS-OTHER:HERPES LABIALIS | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |
| LIP INFECTION | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| LUNG INFECTION | | | |
| alternative dictionary used: CTCAE | | | |

| | | | |
|--|----------------|----------------|--|
| 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| MUCOSAL INFECTION | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |
| PERITONITIS | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |
| SEPSIS | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| UPPER RESPIRATORY INFECTION | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 1 / 39 (2.56%) | |
| occurrences (all) | 2 | 1 | |
| URINARY TRACT INFECTION | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 1 / 39 (2.56%) | |
| occurrences (all) | 2 | 1 | |
| WOUND INFECTION | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |
| Metabolism and nutrition disorders | | | |
| ACIDOSIS | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| ANOREXIA | | | |
| alternative dictionary used: CTCAE 4.0 | | | |

| | | | |
|--|------------------|-----------------|--|
| subjects affected / exposed | 14 / 38 (36.84%) | 7 / 39 (17.95%) | |
| occurrences (all) | 19 | 11 | |
| HYPERGLYCEMIA | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| HYPOGLYCEMIA | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| HYPOKALEMIA | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 39 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| HYPOPHOSPHATEMIA | | | |
| alternative dictionary used: CTCAE 4.0 | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 39 (0.00%) | |
| occurrences (all) | 5 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

| |
|--|
| As the study was closed for futility, there is limited follow-up data for QoL, HE and long term endpoints such as overall survival |
|--|

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/34062484>