



Clinical trial results:

A multicenter, multinational, randomized, controlled, assessor blinded study, performed in subjects with thermal burns, to evaluate the efficacy and safety of NexoBrid compared to Gel Vehicle and compared to Standard of Care

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2014-001672-55 |
| Trial protocol | DE CZ RO LV IT |
| Global end of trial date | 20 August 2020 |

Results information

| | |
|-----------------------------------|--|
| Result version number | v1 (current) |
| This version publication date | 13 November 2021 |
| First version publication date | 13 November 2021 |
| Summary attachment (see zip file) | CSR 12 month (MW2010-03-02_CSR_20200524.pdf) CSR 24 month (NexoBrid_24M_CSR_Addendum.pdf) |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | MW2010-03-02 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02148705 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | MediWound Ltd |
| Sponsor organisation address | 42 Hayarkon Street, Yavne, Israel, 8122745 |
| Public contact | Lior Rosenberg, MediWound Ltd, 972 779714100, liorr@mediwound.com |
| Scientific contact | Lior Rosenberg, MediWound Ltd, 972 779714100, liorr@mediwound.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 | 23 March 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 20 August 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 20 August 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Demonstration of safety and efficacy of NexoBrid® in removing burn eschar in hospitalized patients with deep partial thickness and full thickness thermal burn wounds.

Protection of trial subjects:

The study will be carried out in accordance with accepted international standards, which meet regulations relating to Good Clinical Practice (GCP). These standards are drawn from the following guidelines: ICH Guideline for Good Clinical Practice, 1 May 1996 amended September 1997 and Declaration of Helsinki (as amended in Seoul, October 2008), concerning medical research in humans. The investigator(s) will ensure that this study is conducted in full conformity with the principles of the "Declaration of Helsinki" and with the laws and regulations of the participating countries, whichever affords the greater protection to the individual. It is the responsibility of the investigator to obtain informed consent in written form (according to local legal requirements) from each subject participating in this study. All patients will be informed of the aims, methods, anticipated benefits, potential hazards and confidentiality of data. Candidates will also be told that they are free to refuse participation at any time.

Background therapy:

Patients will be treated in the same way in all study arms (NexoBrid, SOC or Gel vehicle) except for the eschar removal stage which will be performed as per the randomization study arm. Prior to initiation of eschar removal treatment subjects will be medicated with appropriate analgesia and undergo wound cleansing and dressing of all wounds with antibacterial solutions. Following wound cleansing and antibacterial treatments, subjects will undergo the eschar removal process as per treatment assignment (NexoBrid, SOC or Gel Vehicle, following randomization). Subsequent to complete eschar removal, all wounds will be assessed and treated in the same manner, in accordance with post-eschar removal wound care strategy. Post eschar removal, subjects will undergo daily vital signs and pain assessments, until hospital discharge (HD) and weekly assessments of wound progress, until wound closure.

Evidence for comparator:

Comparators: Standard of Care (SOC) and Gel Vehicle (Collagenase Santyl®):

Eschar removal is considered a critical initial stage of the comprehensive wound care process. Early (ie, within 1 to 2 days/before the onset of inflammation) and rapid debridement of eschar is essential to initiate body's own wound healing process, to allow clinical visual evaluation of burn severity and depth, preserve viable tissue, and prevent further complications.

The SOC for burn eschar removal relies primarily on surgical tangential excision to mechanically remove the eschar. According to 1 estimate, these nonselective methods are estimated to excise tissue that consists of 30% to 50% viable dermal tissue, thereby increasing the surface area needed for autografting along with increased risk of scar formation and functional compromise.

Alternatively, physicians can use a nonsurgical debridement, which includes collagenase ointment (Collagenase Santyl®), antimicrobial agents such as silver sulfadiazine (SSD), or various hydrogels which result in a lengthy sloughing period. Collagenase Santyl ointment is a licensed, nonsurgical debridement product that currently exists on the US market.

| | |
|---|-----------------|
| Actual start date of recruitment | 01 January 2015 |
| 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 | United States: 98 |
| Country: Number of subjects enrolled | Germany: 6 |
| Country: Number of subjects enrolled | Belgium: 10 |
| Country: Number of subjects enrolled | Czechia: 11 |
| Country: Number of subjects enrolled | Romania: 20 |
| Country: Number of subjects enrolled | Italy: 17 |
| Country: Number of subjects enrolled | Israel: 2 |
| Country: Number of subjects enrolled | Georgia: 11 |
| Worldwide total number of subjects | 175 |
| EEA total number of subjects | 64 |

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) | 159 |
| From 65 to 84 years | 16 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The patients included in this study were hospitalized burn victims with DPT (deep partial thickness) and FT (full thickness) thermal burns

Pre-assignment

Screening details:

Signing of Informed Consent, demographics, medical history, concomitant medication, physical examination, vital signs, pain assessment, burn etiology, clinical assessment of the burn, randomization

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Single blind |
| Roles blinded | Assessor ^[1] |

Blinding implementation details:

For patients who were randomized to one of the topical treatment arms, NexoBrid or Gel Vehicle, eschar removal assessment was performed by an assessor blinded to the treatment arm. The eschar removal assessment was performed by an individual who was not involved in the treatment of the patient or wound, as the treating physician could distinguish between treatments administered to each patient. For the purpose of standardization, if feasible, the same blinded assessor was assigned at each center

Arms

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

Arm description:

NexoBrid is presented as lyophilised Bromelain powder and gel vehicle for preparation of a gel for cutaneous use, including concentrate of proteolytic enzymes enriched in Bromelain as the active component. Following mixing of the powder with the gel vehicle, each gram of the prepared product contains 0.09 g partially purified Bromelain. Partially purified Bromelain is a mixture of enzymes extracted from the stem of *Ananas comosus* (pineapple plant).

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | NexoBrid |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and gel for gel |
| Routes of administration | Cutaneous use |

Dosage and administration details:

2 or 5 g of NexoBrid sterile powder was mixed in 20 or 50 g of sterile Gel Vehicle (ratio of 1:10), NexoBrid was applied to the burn wound at a dose of 2 g NexoBrid sterile powder mixed with 20 g sterile Gel Vehicle per 1% of TBSA (~ surface of an adult palm) for 4 hours (or 5 g NexoBrid sterile powder mixed with 50 g sterile Gel Vehicle per 2.5% of TBSA). The NexoBrid powder and the Gel Vehicle were mixed at the patient's bedside ≤15 minutes prior to use.

| | |
|------------------|------------------------|
| Arm title | SOC (Standard of Care) |
|------------------|------------------------|

Arm description:

Standard of care. Includes surgical and/or non surgical eschar removal procedures.

| | |
|--|-------------------------------------|
| Arm type | Standard of care |
| Investigational medicinal product name | Standard of care procedures |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Cream, Cutaneous solution, Ointment |
| Routes of administration | Cutaneous use, Topical use |

Dosage and administration details:

SOC arm will include surgical and/or non-surgical eschar removal procedures.

Surgical procedures will include tangential/ minor/ avulsion/ Versajet/ dermabrasion excisions. Non-surgical procedures will include the application of (collagenase ointment (e.g. Santyl), antimicrobial solutions (e.g. Dakin's Solution, Sulfa-Nystatin Solution), ointments/creams (e.g. Bacitracin, Polysporin, Silvadene) and/or Silver dressings (e.g. Mepilex Ag, Aquacel Ag, Acticoat).

The need of either non-surgical or surgical procedures will be determined by the burn specialists and can be repeated as needed until complete debridement.

| | |
|------------------|-------------|
| Arm title | Gel Vehicle |
|------------------|-------------|

Arm description:

Gel Vehicle will be applied on the burn skin.

| | |
|--|---------------|
| Arm type | Placebo |
| Investigational medicinal product name | Gel Vehicle |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Gel |
| Routes of administration | Cutaneous use |

Dosage and administration details:

Twenty (20) grams or 50 grams of sterile Gel Vehicle will be applied on the burn skin. Gel Vehicle is applied to the burn wound at a dose of 20 grams sterile Gel per 1% of TBSA (~ surface of an adult palm) or 50 grams per 2.5% TBSA for four hours.

Gel Vehicle may be applied for a second time to the same burn area, if eschar removal from the target wound after the first application is not complete but at least 50% of the eschar was removed during the first application. The Gel Vehicle may only be applied twice to the same burn wound area.

Gel Vehicle should not be applied to more than 15% TBSA ($\pm 3\%$ TBSA) in one session.

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: For patients who were randomized to 1 of the topical treatment arms, NexoBrid or Gel Vehicle, escharremoval assessment was performed by an assessor blinded to the treatment arm. The eschar removal assessment was performed by an individual who was not involved in the treatment of the patient or wound, as the treating physician could distinguish between treatments administered to each patient.

| Number of subjects in period 1 | NexoBrid | SOC (Standard of Care) | Gel Vehicle |
|--|----------|------------------------|-------------|
| Started | 75 | 75 | 25 |
| First stage | 67 | 63 | 23 |
| Second stage | 56 | 58 | 20 |
| Third stage | 43 | 36 | 10 |
| Completed | 43 | 36 | 10 |
| Not completed | 32 | 39 | 15 |
| Adverse event, serious fatal | 2 | - | - |
| Consent withdrawn by subject | 4 | 8 | - |
| Subject received no study drug treatment | - | 1 | - |
| Patient withdrew due to relocation | - | 1 | - |
| Pregnancy | - | 1 | - |
| Lost to follow-up | 24 | 27 | 13 |
| Patient in incarcerated | - | 1 | - |
| Jail | 1 | - | - |
| Left country | 1 | - | - |
| Site closure | - | - | 1 |

| | | | |
|-------------|---|---|---|
| Not treated | - | - | 1 |
|-------------|---|---|---|

Baseline characteristics

Reporting groups

| | |
|---|------------------------|
| Reporting group title | NexoBrid |
| Reporting group description: | |
| NexoBrid is presented as lyophilised Bromelain powder and gel vehicle for preparation of a gel for cutaneous use, including concentrate of proteolytic enzymes enriched in Bromelain as the active component. Following mixing of the powder with the gel vehicle, each gram of the prepared product contains 0.09 g partially purified Bromelain. Partially purified Bromelain is a mixture of enzymes extracted from the stem of <i>Ananas comosus</i> (pineapple plant). | |
| Reporting group title | SOC (Standard of Care) |
| Reporting group description: | |
| Standard of care. Includes surgical and/or non surgical eschar removal procedures. | |
| Reporting group title | Gel Vehicle |
| Reporting group description: | |
| Gel Vehicle will be applied on the burn skin. | |

| Reporting group values | NexoBrid | SOC (Standard of Care) | Gel Vehicle |
|--|----------|------------------------|-------------|
| Number of subjects | 75 | 75 | 25 |
| 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) | 69 | 69 | 21 |
| From 65-84 years | 6 | 6 | 4 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 26 | 16 | 10 |
| Male | 49 | 59 | 15 |

| Reporting group values | Total | | |
|--|-------|--|--|
| Number of subjects | 175 | | |
| 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) | 159 | | |
| From 65-84 years | 16 | | |

| | | | |
|-------------------|---|--|--|
| 85 years and over | 0 | | |
|-------------------|---|--|--|

| | | | |
|--------------------|-----|--|--|
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 52 | | |
| Male | 123 | | |

End points

End points reporting groups

| | |
|--|--|
| Reporting group title | NexoBrid |
| Reporting group description: NexoBrid is presented as lyophilised Bromelain powder and gel vehicle for preparation of a gel for cutaneous use, including concentrate of proteolytic enzymes enriched in Bromelain as the active component. Following mixing of the powder with the gel vehicle, each gram of the prepared product contains 0.09 g partially purified Bromelain. Partially purified Bromelain is a mixture of enzymes extracted from the stem of Ananas comosus (pineapple plant). | |
| Reporting group title | SOC (Standard of Care) |
| Reporting group description: Standard of care. Includes surgical and/or non surgical eschar removal procedures. | |
| Reporting group title | Gel Vehicle |
| Reporting group description: Gel Vehicle will be applied on the burn skin. | |
| Subject analysis set title | Full analysis set including only NexoBrid and Gel Vehicle treatment arms |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Subset of the FAS including only NexoBrid and Gel Vehicle treatment arms | |

Primary: Incidence of Complete Eschar Removal

| | |
|--|---|
| End point title | Incidence of Complete Eschar Removal ^[1] |
| End point description: The primary efficacy endpoint was analyzed using a subset of the FAS including only NexoBrid and Gel Vehicle treatment arms. The main analysis was based on the binary variable (yes/no): "has complete eschar removal been achieved in all TWs" and compared NexoBrid with the Gel Vehicle. | |
| End point type | Primary |
| End point timeframe: Stage 1: Acute Phase – baseline to 3 months after wound closure | |
| Notes: [1] - 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: Following the goal to seek an indication for NexoBrid that focuses on non surgical eschar removal, this primary endpoint will assess whether non-surgical eschar removal by NexoBrid allows effective removal of the offending eschar compared with its comparator. | |

| End point values | NexoBrid | Gel Vehicle | Full analysis set including only NexoBrid and Gel Vehicle treatment arms | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 75 | 25 | 100 | |
| Units: Patients | 75 | 25 | 100 | |

Statistical analyses

| | |
|--|------------------|
| Statistical analysis title | Primary Endpoint |
| Statistical analysis description: The primary efficacy endpoint was analyzed using a subset of the FAS including only NexoBrid and Gel Vehicle treatment arms. The main analysis was based on the binary variable (yes/no): "has complete | |

eschar removal been achieved in all TWs” and compared NexoBrid with the Gel Vehicle.

| | |
|---|----------------------------|
| Comparison groups | NexoBrid v Gel Vehicle |
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[2] |
| P-value | < 0.0001 |
| Method | Fisher exact |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 288.281 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 35.549 |
| upper limit | 13984.356 |

Notes:

[2] - Demonstrate the superiority of NexoBrid treatment over Gel Vehicle

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All stages: from study start to study termination

Adverse event reporting additional description:

Adverse event data is based on CRF data entry

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 21.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | SOC AE |
|-----------------------|--------|

Reporting group description:

The analysis of AEs was based on the Safety Analysis Set consisting of 68 patients treated with SOC

| | |
|-----------------------|----------------|
| Reporting group title | Gel Vehicle AE |
|-----------------------|----------------|

Reporting group description:

The analysis of AEs was based on the Safety Analysis Set consisting of 24 patients treated with Gel Vehicle

| | |
|-----------------------|-------------|
| Reporting group title | NexoBrid AE |
|-----------------------|-------------|

Reporting group description:

The analysis of AEs was based on the Safety Analysis Set consisting of 77 patients treated with NexoBrid.

| Serious adverse events | SOC AE | Gel Vehicle AE | NexoBrid AE |
|---|--|-----------------|------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 9 / 68 (13.24%) | 3 / 24 (12.50%) | 10 / 77 (12.99%) |
| number of deaths (all causes) | 0 | 0 | 2 |
| number of deaths resulting from adverse events | 0 | 0 | 2 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Glioblastoma | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (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 |
| Squamous cell carcinoma of the oral cavity | Additional description: Preferred Term | | |

| | | | |
|---|--|----------------|----------------|
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (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 |
| Vascular disorders | | | |
| Phlebitis superficial | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 1 / 24 (4.17%) | 0 / 77 (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 |
| Deep vein thrombosis | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (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 |
| Surgical and medical procedures | | | |
| Cholecystectomy | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (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 |
| Eventration repair | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Internal fixation of fracture | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Therapeutic procedure | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Failure to thrive | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|--|----------------|----------------|
| General disorders and administration site conditions | | | |
| Death | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Chest pain | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (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 |
| Infusion site thrombosis | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 1 / 24 (4.17%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory distress syndrome | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (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 |
| Acute respiratory failure | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Neonatal respiratory failure | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient tachypnoea of the newborn | Additional description: Preferred Term | | |

| | | | |
|---|--|----------------|----------------|
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Anxiety | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (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 |
| Suicide attempt | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Graft loss | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (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 |
| Thermal burn | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intentional overdose | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Atrial septal defect | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital tricuspid valve incompetence | Additional description: Preferred Term | | |

| | | | |
|---|--|----------------|----------------|
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngomalacia | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Patent ductus arteriosus | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Persistent foetal circulation | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular septal defect | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Trisomy 21 | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | Additional description: Preferred Term | | |
| Acute coronary syndrome | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (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 |
| Bifascicular block | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (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 |
| Nervous system disorders | | | |

| | | | |
|---|--|----------------|----------------|
| Cerebral ventricle dilatation subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| | 0 / 0 | 0 / 0 | 0 / 1 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) | 1 / 24 (4.17%) | 0 / 77 (0.00%) |
| | 0 / 0 | 0 / 1 | 0 / 0 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders Appendicitis noninfective subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| | 0 / 0 | 0 / 0 | 0 / 1 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Subileus subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| | 0 / 0 | 0 / 0 | 0 / 1 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| | 0 / 0 | 0 / 0 | 0 / 1 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations Cellulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| | 0 / 0 | 0 / 0 | 0 / 1 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (0.00%) |
| | 0 / 1 | 0 / 0 | 0 / 0 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | Additional description: Preferred Term | | |

| | | | |
|---|--|----------------|----------------|
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteomyelitis | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic shock | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (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 |
| Sepsis | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 2 / 77 (2.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound infection bacterial | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 3 / 77 (3.90%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | Additional description: Preferred Term | | |
| Diabetic metabolic decompensation | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (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: 0 %

| Non-serious adverse events | SOC AE | Gel Vehicle AE | NexoBrid AE |
|---|--|------------------|------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 41 / 68 (60.29%) | 15 / 24 (62.50%) | 49 / 77 (63.64%) |
| Vascular disorders | | | |
| Arterial thrombosis | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 1 / 24 (4.17%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Extremity necrosis | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Haemorrhage | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypertension | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 1 / 24 (4.17%) | 2 / 77 (2.60%) |
| occurrences (all) | 0 | 1 | 2 |
| Hypotension | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 2 / 77 (2.60%) |
| occurrences (all) | 1 | 0 | 2 |
| Phlebitis | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 1 | 0 | 1 |
| Phlebitis superficial | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 1 / 24 (4.17%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Varicose vein | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Surgical and medical procedures | | | |
| Colon operation | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Wound drainage | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| General disorders and administration site conditions | | | |

| | | | |
|--|--|---------------------|----------------------|
| Asthenia subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Cyst subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Hyperthermia subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Pain subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 2 / 68 (2.94%) 2 | 0 / 24 (0.00%) 0 | 6 / 77 (7.79%) 11 |
| Hypothermia subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 2 / 77 (2.60%) 2 |
| Pyrexia subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 6 / 68 (8.82%) 8 | 2 / 24 (8.33%) 3 | 6 / 77 (7.79%) 7 |
| Peripheral swelling subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Immune system disorders Allergy to arthropod sting subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Drug hypersensitivity subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 2 / 77 (2.60%) 2 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 1 | 1 / 24 (4.17%) 1 | 0 / 77 (0.00%) 0 |
| Dyspnoea subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) 0 | 1 / 24 (4.17%) 1 | 0 / 77 (0.00%) 0 |
| Increased viscosity of bronchial secretion | Additional description: Preferred Term | | |
| | | | |

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|-----------------------------|--|----------------|----------------|
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Laryngospasm | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 1 / 24 (4.17%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oropharyngeal pain | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 1 / 24 (4.17%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Pulmonary oedema | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 1 / 24 (4.17%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Psychiatric disorders | | | |
| Adjustment disorder | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Agitation | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 1 / 24 (4.17%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Alcoholism | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Drug dependence | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Anxiety | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 1 | 0 | 1 |
| Depression | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Insomnia | Additional description: Preferred Term | | |
| subjects affected / exposed | 4 / 68 (5.88%) | 1 / 24 (4.17%) | 4 / 77 (5.19%) |
| occurrences (all) | 4 | 1 | 4 |
| Emotional distress | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|--|--|---------------------|---------------------|
| Major depression subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Panic disorder subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Mental status changes subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Substance use disorder subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Post-traumatic stress disorder subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Sleep disorder subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Suicide attempt subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Investigations | | | |
| Bacterial test subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Blood pressure increased subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) 0 | 1 / 24 (4.17%) 1 | 1 / 77 (1.30%) 1 |
| Bacterial test positive subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Body temperature increased subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| C-reactive protein increased | Additional description: Preferred Term | | |

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|--|--|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 2 / 77 (2.60%) 2 |
| Haemoglobin decreased | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Hepatic enzyme increased | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Lymphocyte count decreased | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | 2 / 24 (8.33%) 2 | 1 / 77 (1.30%) 1 |
| Inflammatory marker increased | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| White blood cell count increased | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Contusion | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Cranio-cerebral injury | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Graft loss | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 2 / 68 (2.94%) 2 | 1 / 24 (4.17%) 1 | 3 / 77 (3.90%) 4 |
| Hand fracture | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Incisional hernia | Additional description: Preferred Term | | |

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|--------------------------------|--|----------------|----------------|
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Intentional overdose | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Limb injury | Additional description: Preferred Term | | |
| subjects affected / exposed | 2 / 68 (2.94%) | 1 / 24 (4.17%) | 0 / 77 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Muscle strain | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 1 | 0 | 1 |
| Paravenous drug administration | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Post procedural haemorrhage | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Post-traumatic pain | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 1 / 24 (4.17%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin abrasion | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 1 | 0 | 1 |
| Skin graft failure | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin laceration | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Subcutaneous haematoma | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 2 / 77 (2.60%) |
| occurrences (all) | 0 | 0 | 2 |
| Sunburn | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Wound complication | Additional description: Preferred Term | | |

| | | | |
|--|--|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 2 / 68 (2.94%) 3 | 0 / 24 (0.00%) 0 | 3 / 77 (3.90%) 3 |
| Thermal burn | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Cardiac disorders | | | |
| Sinus tachycardia | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 2 / 68 (2.94%) 2 | 1 / 24 (4.17%) 1 | 0 / 77 (0.00%) 0 |
| Tachycardia | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 5 / 77 (6.49%) 5 |
| Nervous system disorders | | | |
| Dizziness | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Cervical radiculopathy | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Headache | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 3 / 68 (4.41%) 3 | 3 / 24 (12.50%) 3 | 3 / 77 (3.90%) 7 |
| Seizure | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Blood and lymphatic system disorders | | | |
| Anaemia | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Leukocytosis | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 4 / 77 (5.19%) 4 |
| Thrombocytosis | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 2 / 68 (2.94%) 2 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Haemorrhagic anaemia | Additional description: Preferred Term | | |

| | | | |
|--|--|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 2 / 68 (2.94%) 2 | 0 / 24 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Ear and labyrinth disorders | | | |
| Tinnitus | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Ascites | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Constipation | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 7 / 68 (10.29%) 7 | 2 / 24 (8.33%) 2 | 4 / 77 (5.19%) 4 |
| Diarrhoea | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | 1 / 24 (4.17%) 1 | 0 / 77 (0.00%) 0 |
| Dyspepsia | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | 1 / 24 (4.17%) 1 | 0 / 77 (0.00%) 0 |
| Gastritis | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | 1 / 24 (4.17%) 1 | 0 / 77 (0.00%) 0 |
| Gastrooesophageal reflux disease | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Melaena | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Nausea | Additional description: Preferred Term | | |
| subjects affected / exposed occurrences (all) | 6 / 68 (8.82%) 6 | 4 / 24 (16.67%) 4 | 5 / 77 (6.49%) 5 |
| Tooth loss | Additional description: Preferred Term | | |

| | | | |
|--|--|----------------|----------------|
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vomiting | Additional description: Preferred Term | | |
| subjects affected / exposed | 3 / 68 (4.41%) | 1 / 24 (4.17%) | 5 / 77 (6.49%) |
| occurrences (all) | 4 | 1 | 5 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis contact | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Erythema | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 2 / 77 (2.60%) |
| occurrences (all) | 1 | 0 | 2 |
| Hypertrophic scar | Additional description: Preferred Term | | |
| subjects affected / exposed | 2 / 68 (2.94%) | 1 / 24 (4.17%) | 0 / 77 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Milia | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 1 / 24 (4.17%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 4 / 77 (5.19%) |
| occurrences (all) | 0 | 0 | 4 |
| Skin lesion | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin warm | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Renal and urinary disorders | | | |
| Acute kidney injury | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 1 | 0 | 1 |
| Urinary retention | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Renal failure | Additional description: Preferred Term | | |

| | | | |
|---|--|-----------------|----------------|
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | Additional description: Preferred Term | | |
| subjects affected / exposed | 2 / 68 (2.94%) | 0 / 24 (0.00%) | 2 / 77 (2.60%) |
| occurrences (all) | 4 | 0 | 2 |
| Arthritis | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Arthralgia | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Extremity contracture | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 1 / 24 (4.17%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Joint contracture | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Costochondritis | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Muscle spasms | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Joint range of motion decreased | Additional description: Preferred Term | | |
| subjects affected / exposed | 5 / 68 (7.35%) | 4 / 24 (16.67%) | 3 / 77 (3.90%) |
| occurrences (all) | 30 | 21 | 8 |
| Neck pain | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 1 | 0 | 1 |
| Myalgia | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Pain in extremity | Additional description: Preferred Term | | |

| | | | |
|----------------------------------|--|----------------|----------------|
| subjects affected / exposed | 0 / 68 (0.00%) | 1 / 24 (4.17%) | 3 / 77 (3.90%) |
| occurrences (all) | 0 | 1 | 3 |
| Osteoarthritis | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Spinal pain | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Temporomandibular joint syndrome | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Periarthritis | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Infections and infestations | | | |
| Bacterial infection | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abscess jaw | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Bronchitis | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Candida infection | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Cellulitis | Additional description: Preferred Term | | |
| subjects affected / exposed | 4 / 68 (5.88%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 4 | 0 | 1 |
| Ear infection | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Folliculitis | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 1 / 24 (4.17%) | 2 / 77 (2.60%) |
| occurrences (all) | 1 | 1 | 4 |

| | | | |
|--|--|---------------------|---------------------|
| Fungal skin infection subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Gastrointestinal viral infection subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Herpes zoster subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Hordeolum subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Influenza subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 4 | 1 / 24 (4.17%) 1 | 2 / 77 (2.60%) 2 |
| Otitis media subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 2 / 77 (2.60%) 2 |
| Pneumonia subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Rhinitis subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 1 | 1 / 24 (4.17%) 1 | 0 / 77 (0.00%) 0 |
| Sepsis subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Septic arthritis staphylococcal subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Sinusitis subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 3 / 68 (4.41%) 4 | 1 / 24 (4.17%) 1 | 1 / 77 (1.30%) 1 |

| | | | |
|--|--|---------------------|---------------------|
| Subcutaneous abscess subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Staphylococcal skin infection subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Tooth abscess subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Wound infection subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 3 / 77 (3.90%) 3 |
| Urinary tract infection subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 4 / 77 (5.19%) 5 |
| Wound infection bacterial subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 4 / 68 (5.88%) 4 | 0 / 24 (0.00%) 0 | 2 / 77 (2.60%) 3 |
| Wound infection staphylococcal subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Wound infection fungal subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 1 / 77 (1.30%) 1 |
| Bacterial disease carrier subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Metabolism and nutrition disorders | | | |
| Diabetes mellitus subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 1 / 68 (1.47%) 1 | 0 / 24 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Dehydration subjects affected / exposed occurrences (all) | Additional description: Preferred Term | | |
| | 0 / 68 (0.00%) 0 | 0 / 24 (0.00%) 0 | 2 / 77 (2.60%) 2 |
| Hyperkalaemia | Additional description: Preferred Term | | |
| | | | |

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|-----------------------------|--|----------------|----------------|
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypoalbuminaemia | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypocalcaemia | Additional description: Preferred Term | | |
| subjects affected / exposed | 1 / 68 (1.47%) | 0 / 24 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypokalaemia | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 1 / 24 (4.17%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 1 | 1 |
| Malnutrition | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |
| Vitamin D deficiency | Additional description: Preferred Term | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 0 / 24 (0.00%) | 1 / 77 (1.30%) |
| occurrences (all) | 0 | 0 | 1 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---------------------|
| 02 September 2014 | Protocol Version 7 |
| 22 February 2015 | Protocol Version 8 |
| 12 August 2015 | Protocol Version 9 |
| 23 June 2016 | Protocol Version 11 |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported