



Clinical trial results:

A multicenter pilot phase II study for the preliminary evaluation of feasibility, activity and safety of the administration of Bendamustine and Ofatumumab in combination in marginal zone B-cell lymphomas (MZL)

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2011-003495-36 |
| Trial protocol | IT |
| Global end of trial date | 26 September 2016 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 15 October 2017 |
| First version publication date | 15 October 2017 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | S10BEOF01 |
|-----------------------|-----------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Clinical Organization for Strategies and Solutions S.r.l. - CLIOSS S.r.l. |
| Sponsor organisation address | Viale Pasteur 10, Nerviano (Mi), Italy, 20014 |
| Public contact | Direzione Scientifica, CLIOSS Srl, 0039 0331581482, cristina.davite@clioss.com |
| Scientific contact | Direzione Scientifica, CLIOSS Srl, 0039 0331581482, cristina.davite@clioss.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 | 03 May 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 26 September 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 26 September 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy (Overall Remission Rate) of ofatumumab and bendamustine in relapsed or refractory marginal zone B-cell lymphomas

Protection of trial subjects:

Study Protocol foresees that therapies considered necessary for the patient's well being might be given at the discretion of the Investigator, i.e. chronic treatments for concomitant medical conditions, as well as agents required for life-threatening medical problems.

Background therapy:

Study Protocol foresees that pre-medication with paracetamol, antihistamine and glucocorticoids had to be performed before each ofatumumab infusion.

Evidence for comparator:

NA

| | |
|---|---------------|
| Actual start date of recruitment | 13 March 2012 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|----------------|
| Country: Number of subjects enrolled | Switzerland: 8 |
| Country: Number of subjects enrolled | Italy: 8 |
| Worldwide total number of subjects | 16 |
| EEA total number of subjects | 8 |

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) | 9 |

| | |
|---------------------|---|
| From 65 to 84 years | 7 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Recruitment lasted from 28 March 2012 to 03 April 2014.

Pre-assignment

Screening details:

All 16 patients were eligible and treated with bendamustine and ofatumumab.

Period 1

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

Arms

| | |
|------------------|-------|
| Arm title | Arm 1 |
|------------------|-------|

Arm description:

All patients treated with ofatumumab and bendamustine

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | OFATUMUMAB |
| Investigational medicinal product code | GSK1841157 |
| Other name | NA |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Patients were treated with Ofatumumab iv 1000 mg on day 1 every 28 days for 6 cycles. The initial rate of the first infusion of 1000 mg ofatumumab (1 mg/mL) had to be 12 mL/h. If no infusion reactions occurred the infusion rate had to be increased every 30 minutes, to a maximum of 400 mL/h. If an infusion reaction developed, the infusion had to be temporarily slowed or interrupted. If the previous infusion were completed without grade ≥ 3 infusion-associated AEs, the subsequent infusion of the 1000 mg ofatumumab (1 mg/mL) could start at a rate of 25 mL/h and had to be doubled every 30 minutes up to a maximum of 400 mL/h.

| | |
|--|--|
| Investigational medicinal product name | BENDAMUSTINE HYDROCHLORIDE |
| Investigational medicinal product code | NA |
| Other name | NA |
| Pharmaceutical forms | Powder and solvent for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Bendamustine 90 mg/m² was administered on days 1 and 2 by iv infusion over 30-60 minutes. I

| Number of subjects in period 1 | Arm 1 |
|--------------------------------|-------|
| Started | 16 |
| Completed | 11 |
| Not completed | 5 |
| Start new therapy | 3 |
| Death | 1 |
| Lost to follow-up | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-------|
| Reporting group title | Arm 1 |
|-----------------------|-------|

Reporting group description:

All patients treated with ofatumumab and bendamustine

| Reporting group values | Arm 1 | Total | |
|---|----------|-------|--|
| Number of subjects | 16 | 16 | |
| Age categorical | | | |
| Alla treated patients | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 9 | 9 | |
| From 65-84 years | 7 | 7 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| All treated patients | | | |
| Units: years | | | |
| median | 63.5 | | |
| full range (min-max) | 46 to 78 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 7 | 7 | |
| Male | 9 | 9 | |
| Race | | | |
| Units: Subjects | | | |
| Caucasian | 16 | 16 | |
| Performance Status (ECOG) | | | |
| Units: Subjects | | | |
| Zero | 15 | 15 | |
| One | 1 | 1 | |
| Tumor Stage at Study Entry | | | |
| Units: Subjects | | | |
| Stage I | 1 | 1 | |
| Stage II | 2 | 2 | |
| Stage III | 1 | 1 | |
| Stage IV | 12 | 12 | |
| Primary Tumor Site | | | |
| One patient enrolled with the diagnosis of mediastinic marginal zone B-cell lymphoma at stage IV was actually suffering from neuroendocrin tumor. | | | |
| Units: Subjects | | | |
| Dist. Oesophagus, L. Orbit | 1 | 1 | |

| | | | |
|---------------------------|----|----|--|
| Gastric | 2 | 2 | |
| Gastric Fundus | 1 | 1 | |
| Left Orbit | 1 | 1 | |
| Lung | 2 | 2 | |
| Lymphonodes | 1 | 1 | |
| Mediastinum | 1 | 1 | |
| Right Thigh Radix | 1 | 1 | |
| Spleen | 5 | 5 | |
| Stomach | 1 | 1 | |
| Prior Antitumor Therapies | | | |
| Units: Subjects | | | |
| 1-3 | 11 | 11 | |
| 4-6 | 3 | 3 | |
| 7-9 | 2 | 2 | |
| Type of Prior Therapies | | | |
| Units: Subjects | | | |
| Systemic | 7 | 7 | |
| Sistemic + Surgery | 9 | 9 | |

End points

End points reporting groups

| | |
|---|--------------------|
| Reporting group title | Arm 1 |
| Reporting group description: All patients treated with ofatumumab and bendamustine | |
| Subject analysis set title | Evaluable patients |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Efficacy Evaluable (EE) population defined as all treated patients, with no major deviations from the eligibility criteria affecting efficacy evaluation, for whom the tumor response could be evaluated at least once while on treatment. These patients should have received at least 2 cycles after treatment starts, unless disease progression occurred at cycle 1. | |

Primary: Overall Response Rate (ORR)

| | |
|--|--|
| End point title | Overall Response Rate (ORR) ^[1] |
| End point description: Overall Remission Rate (ORR) was defined as the percentage of patients with a CR or PR as per Cheson criteria (2007) . For patients with splenic MZL response was defined according to Matutes et al. (2008) and for patients with gastric lymphomas histological response was evaluated according to GELA scoring system (Copie-Bergman et al 2003). A patient with unknown or missing response was to be treated as a non-responder, i.e., the patient was to be included in the denominator when calculating the percentage. Exact methods for calculated confidence intervals were to be utilized. | |
| End point type | Primary |
| End point timeframe: CT-scan at the end of cycle 2 and at FU1 (4 months), FU2 (8 months) and FU3 (24 months) after the end of treatment. | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: An ORR of at least 90% was obtained, as expected. The p-value given by the exact binomial test ($<.001$) lead the rejection of the null hypothesis ($p=0.55$) in favour of the alternative one ($p=0.90$).

| End point values | Evaluable patients | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 14 | | | |
| Units: percentage | | | | |
| number (not applicable) | | | | |
| CR + PR | 92.9 | | | |
| SD | 7.1 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

| | |
|---|---------------------------------|
| End point title | Progression Free Survival (PFS) |
| End point description: Progression Free Survival was defined as the time from the first treatment administration to documentation of disease progression, start of a new antitumor therapy or death (for any cause). | |

Patients not known to have progressed or started a new antitumor therapy or died (for any cause) were to be censored for PFS at the time of last tumor assessment.

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

End point timeframe:

Two years after the end of the treatment.

| End point values | Evaluable patients | | | |
|----------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | | | | |
| Units: months | | | | |
| median (confidence interval 95%) | | | | |
| Progression Free Survival | 33 (21.9 to 999999) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

| | |
|-----------------|----------------------|
| End point title | Duration of Response |
|-----------------|----------------------|

End point description:

Duration of Response was defined, for the subset of patients with a CR or PR, as the time from when criteria for response were first met until first documented relapse or progression or death due to any cause. If sample size permitted, duration of response had to be summarized descriptively using Kaplan-Meier medians and quartiles. Only the subset of patients who showed a CR or PR were to be included in this summary.

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

End point timeframe:

Time to relapse.

| End point values | Evaluable patients | | | |
|----------------------------------|-----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 13 ^[2] | | | |
| Units: months | | | | |
| median (confidence interval 95%) | | | | |
| Duration of Response | 30.4 (15.5 to 999999) | | | |

Notes:

[2] - Only patients showing CR and PR

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

During all study period and followed until 28 days following the last dose of investigational product.

Adverse event reporting additional description:

Drug-related and serious adverse events ongoing at the end of this observation period had to be recorded until they were resolved or the investigator assessed them as chronic or the subject was lost to follow-up or started a new anti-cancer treatment, whichever occurred earlier.

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

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 20 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|-------|
| Reporting group title | Arm 1 |
|-----------------------|-------|

Reporting group description:

All patients treated with ofatumumab and bendamustine

| Serious adverse events | Arm 1 | | |
|---|-----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 16 (25.00%) | | |
| number of deaths (all causes) | 2 | | |
| number of deaths resulting from adverse events | 0 | | |
| Investigations | | | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Troponin I increased | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Myocardial infarction | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Renal failure acute | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Fistula | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Anal abscess | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Septic shock | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Arm 1 | | |
|---|-------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 16 / 16 (100.00%) | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Phlebitis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Thrombophlebitis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 8 / 16 (50.00%) | | |
| occurrences (all) | 15 | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 8 / 16 (50.00%) | | |
| occurrences (all) | 12 | | |
| Asthenia | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 2 / 16 (12.50%) | | |
| occurrences (all) | 3 | | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | | |
| occurrences (all) | 2 | | |
| Face oedema | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 3 | | |
| Infusion site extravasation | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Infusion site pain | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Localised oedema | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Pain | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | | |
| occurrences (all) | 3 | | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Pneumonitis | | | |

| | | | |
|--|------------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | | |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | | |
| Investigations Lymphocyte count decreased subjects affected / exposed occurrences (all) | 14 / 16 (87.50%) 21 | | |
| Weight decreased subjects affected / exposed occurrences (all) | 5 / 16 (31.25%) 5 | | |
| Neutrophil count decreased subjects affected / exposed occurrences (all) | 4 / 16 (25.00%) 4 | | |
| White blood cell count decreased subjects affected / exposed occurrences (all) | 3 / 16 (18.75%) 4 | | |
| Haemoglobin decreased subjects affected / exposed occurrences (all) | 2 / 16 (12.50%) 3 | | |
| Platelet count decreased subjects affected / exposed occurrences (all) | 2 / 16 (12.50%) 3 | | |
| Blood bilirubin decreased subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | | |
| Blood glucose decreased subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | | |
| Blood magnesium decreased subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | | |
| Blood potassium decreased | | | |

| | | | |
|--|---|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Blood sodium decreased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 16 (6.25%)</p> <p>1</p> <p>1 / 16 (6.25%)</p> <p>1</p> | | |
| <p>Cardiac disorders</p> <p>Palpitations</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 16 (6.25%)</p> <p>1</p> | | |
| <p>Nervous system disorders</p> <p>Headache</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Ataxia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Cognitive disorder</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dizziness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dysaesthesia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 16 (12.50%)</p> <p>3</p> <p>1 / 16 (6.25%)</p> <p>1</p> <p>1 / 16 (6.25%)</p> <p>1</p> <p>1 / 16 (6.25%)</p> <p>1</p> <p>1 / 16 (6.25%)</p> <p>1</p> | | |
| <p>Blood and lymphatic system disorders</p> <p>Febrile neutropenia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 16 (6.25%)</p> <p>1</p> | | |
| <p>Ear and labyrinth disorders</p> <p>Hypoacusis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vertigo</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 16 (6.25%)</p> <p>1</p> <p>1 / 16 (6.25%)</p> <p>1</p> | | |
| <p>Eye disorders</p> | | | |

| | | | |
|----------------------------------|-----------------|--|--|
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Eyelid oedema | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 6 / 16 (37.50%) | | |
| occurrences (all) | 16 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | | |
| occurrences (all) | 3 | | |
| Constipation | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | | |
| occurrences (all) | 3 | | |
| Vomiting | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | | |
| occurrences (all) | 5 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 3 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 2 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Stomatitis | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | | |
| occurrences (all) | 3 | | |
| Onychoclasia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Pain of skin | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 2 | | |
| Palmar erythema | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Pityriasis rosea | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Pruritus | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Rash macular | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Skin reaction | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Trichorrhhexis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Urticaria | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|--|----------------------|--|--|
| Musculoskeletal chest pain subjects affected / exposed occurrences (all) | 2 / 16 (12.50%) 2 | | |
| Myalgia subjects affected / exposed occurrences (all) | 2 / 16 (12.50%) 2 | | |
| Pain in extremity subjects affected / exposed occurrences (all) | 2 / 16 (12.50%) 2 | | |
| Arthralgia subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | | |
| Back pain subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | | |
| Groin pain subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | | |
| Infections and infestations | | | |
| Oral herpes subjects affected / exposed occurrences (all) | 2 / 16 (12.50%) 2 | | |
| Central line infection subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | | |
| Herpes zoster subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | | |
| Metabolism and nutrition disorders | | | |
| Anorexia subjects affected / exposed occurrences (all) | 2 / 16 (12.50%) 2 | | |

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

None reported