



Clinical trial results:

A prospective phase II study of bendamustine in patients aged over 60 years with classical Hodgkin lymphoma treated by prednisone, vinblastine, and doxorubicin

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2014-001002-17 |
| Trial protocol | BE |
| Global end of trial date | 10 November 2020 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 04 June 2022 |
| First version publication date | 04 June 2022 |

Trial information

Trial identification

| | |
|-----------------------|------|
| Sponsor protocol code | PVAB |
|-----------------------|------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02414568 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | LYSARC |
| Sponsor organisation address | Centre hospitalier Lyon Sud, 165 chemin du grand Revoyet, LYON, France, 69495 |
| Public contact | Fabienne Morand (Project Manager), LYSARC , 33 (0)472 66 38 53, fabienne.morand@lysarc.org |
| Scientific contact | Fabienne Morand (Project Manager), LYSARC , 33 (0)472 66 38 53, fabienne.morand@lysarc.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 | 10 November 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 10 November 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary endpoint of the study is to assess the Complete Metabolic Response (CMR) rate at the final evaluation after completion of study treatment (after 6 cycles of study treatment or at premature treatment discontinuation) defined according to Lugano Classification (PET-CT-Based response).

Protection of trial subjects:

An ICF explaining the procedures of the study, including the potential hazards, was reviewed and approved by the IEC prior to its use. Before entering the study, the ICF was read by and explained to all subjects. Each subject had ample opportunity to ask questions and was assured of the right to withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision.

Each subject was required to sign an ICF to participate in the study. Two specific ICFs, for the collection of biological samples and for a genetic study for medical purposes, were also required to be signed by each subject willing to participate in these studies. Each subject received a copy of each signed and dated ICF.

Background therapy:

Prednisone, vinblastine and doxorubicin were not tested and were given to patients as standard treatment.

Evidence for comparator:

No comparator was used.

| | |
|---|--------------|
| Actual start date of recruitment | 17 July 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 | Belgium: 10 |
| Country: Number of subjects enrolled | France: 80 |
| Worldwide total number of subjects | 90 |
| EEA total number of subjects | 90 |

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) | 26 |
| From 65 to 84 years | 60 |
| 85 years and over | 4 |

Subject disposition

Recruitment

Recruitment details:

Date of recruitment :

First inclusion : France 17JUL2015 / Belgium 18DEC2015

Last inclusion : France 31JUL2018 / Belgium 16MAY2018

Pre-assignment

Screening details:

Number of patients screened : 99 patients

- 9 patient not included

Number of patients included: 90 patients

- 1 patient with no study drug administration

Number of patients in the Full Analysis Set : 89 patients

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 | Experimental |
|-----------|--------------|

Arm description:

Patients with at least one administration of study treatment

| | |
|--|----------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Bendamustine Hydrochloride |
| Investigational medicinal product code | 3543-75-7 |
| Other name | |
| Pharmaceutical forms | Powder for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

bendamustine is injected via IV only at J1 with a dose at 120mg/m² every 3 week during 4 or 6 cycles

| Number of subjects in period 1 ^[1] | Experimental |
|---|--------------|
| Started | 89 |
| Completed | 78 |
| Not completed | 11 |
| Adverse event, serious fatal | 2 |
| Consent withdrawn by subject | 1 |
| Adverse event, non-fatal | 6 |
| concurrent illness | 1 |
| Lack of efficacy | 1 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 90 patients were included in the study. However, one patient had no study drug administration and was not included in the full analysis set. This is the reason why only 89 patients were analyzed.

Baseline characteristics

Reporting groups

Reporting group title

Overall trial

Reporting group description: -

| Reporting group values | Overall trial | Total | |
|---|---------------|-------|--|
| Number of subjects | 89 | 89 | |
| Age categorical | | | |
| 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) | 26 | 26 | |
| From 65-84 years | 59 | 59 | |
| 85 years and over | 4 | 4 | |
| Age continuous | | | |
| Units: years | | | |
| median | 68 | | |
| full range (min-max) | 61 to 88 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 31 | 31 | |
| Male | 58 | 58 | |

End points

End points reporting groups

| | |
|--|--------------|
| Reporting group title | Experimental |
| Reporting group description: | |
| Patients with at least one administration of study treatment | |

Primary: Complete metabolic response rate at the end of study treatment

| | |
|-----------------|---|
| End point title | Complete metabolic response rate at the end of study treatment ^[1] |
|-----------------|---|

End point description:

According to Lugano Classification (PET-CT based response)

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

At the end of study treatment (after 6 cycles of study treatment or at premature treatment discontinuation)

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: Non-comparative phase II study. The confidence interval is included in the primary endpoint.

| | | | | |
|-----------------------------|-----------------|--|--|--|
| End point values | Experimental | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 89 | | | |
| Units: Percentage | | | | |
| CMR | 69 | | | |
| Not CMR | 20 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PFS at 4 years

| | |
|-----------------|----------------|
| End point title | PFS at 4 years |
|-----------------|----------------|

End point description:

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

End point timeframe:

From the date of inclusion to the date of first documented disease progression, relapse or death from any cause, whatever the event that occurs first.

| | | | | |
|----------------------------------|---------------------|--|--|--|
| End point values | Experimental | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 89 | | | |
| Units: percentage | | | | |
| number (confidence interval 50%) | 50.3 (38.9 to 60.6) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DFS at 4 years

| | |
|--|----------------|
| End point title | DFS at 4 years |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| From the time of attainment of CMR (according to the Lugano Classification; PET-CT-Based response) to the date of first documented disease progression, relapse or death from any cause. | |

| | | | | |
|------------------------------------|---------------------|--|--|--|
| End point values | Experimental | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 89 | | | |
| Units: percentage | | | | |
| number (confidence interval 62.8%) | 62.8 (49.4 to 73.6) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: OS at 4 years

| | |
|--|---------------|
| End point title | OS at 4 years |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| from the date of inclusion to the date of death from any cause. Alive patients will be censored at their last date of contact. | |

| | | | | |
|----------------------------------|-------------------|--|--|--|
| End point values | Experimental | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 89 | | | |
| Units: percentage | | | | |
| number (confidence interval 69%) | 69 (56.6 to 78.5) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the date of informed consent signature to 30 days after last study drug administration

Adverse event reporting additional description:

After the last drug administration, only the SAEs with the AEs corresponding are reported

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

Dictionary used

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

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|--------------------|----|
| Dictionary version | 24 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | Safety analysis |
|-----------------------|-----------------|

Reporting group description: -

| Serious adverse events | Safety analysis | | |
|---|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 28 / 89 (31.46%) | | |
| number of deaths (all causes) | 24 | | |
| number of deaths resulting from adverse events | 4 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oesophageal carcinoma | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infusion related reaction | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 2 / 89 (2.25%) | | |
| occurrences causally related to treatment / all | 2 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac valve disease | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiogenic shock | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Nervous system disorders | | | |
| Brain stem haematoma | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 4 / 89 (4.49%) | | |
| occurrences causally related to treatment / all | 5 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 89 (3.37%) | | |
| occurrences causally related to treatment / all | 4 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Febrile bone marrow aplasia | | | |
| subjects affected / exposed | 2 / 89 (2.25%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|--|----------------|--|--|
| Leukopenia | | | |
| subjects affected / exposed | 2 / 89 (2.25%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bone marrow failure | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| histiocytosis hematophagic | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Strangulated hernia | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Gastrointestinal disorders | | | |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Obstructive defaecation | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oesophagitis | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Pneumonitis | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Suicide attempt | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Pyelonephritis | | | |
| subjects affected / exposed | 2 / 89 (2.25%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Septic shock | | | |
| subjects affected / exposed | 2 / 89 (2.25%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 89 (2.25%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bacterial prostatitis | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bacterial sepsis | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Citrobacter sepsis | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 1 / 89 (1.12%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Clostridium difficile colitis | | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Device related infection | | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Escherichia bacteraemia | | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Escherichia infection | | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Escherichia pyelonephritis | | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Escherichia sepsis | | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fungal infection | | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Prostatitis Escherichia coli | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Safety analysis | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 86 / 89 (96.63%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Oesophageal carcinoma | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 5 / 89 (5.62%) | | |
| occurrences (all) | 5 | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 2 / 89 (2.25%) | | |
| occurrences (all) | 2 | | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Strangulated hernia | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|--|---------------------|--|--|
| Acute respiratory distress syndrome subjects affected / exposed occurrences (all) | 1 / 89 (1.12%) 1 | | |
| Pleural effusion subjects affected / exposed occurrences (all) | 1 / 89 (1.12%) 1 | | |
| Pneumonitis subjects affected / exposed occurrences (all) | 1 / 89 (1.12%) 1 | | |
| Pulmonary embolism subjects affected / exposed occurrences (all) | 1 / 89 (1.12%) 1 | | |
| Pulmonary oedema subjects affected / exposed occurrences (all) | 1 / 89 (1.12%) 1 | | |
| Psychiatric disorders Suicide attempt subjects affected / exposed occurrences (all) | 1 / 89 (1.12%) 1 | | |
| Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all) | 1 / 89 (1.12%) 1 | | |
| Infusion related reaction subjects affected / exposed occurrences (all) | 1 / 89 (1.12%) 1 | | |
| Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all) | 2 / 89 (2.25%) 3 | | |
| Cardiac valve disease subjects affected / exposed occurrences (all) | 1 / 89 (1.12%) 1 | | |
| Cardiogenic shock subjects affected / exposed occurrences (all) | 1 / 89 (1.12%) 1 | | |

| | | | |
|--------------------------------------|------------------|--|--|
| Nervous system disorders | | | |
| Brain stem haematoma | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Polyneuropathy | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Blood and lymphatic system disorders | | | |
| Lymphopenia | | | |
| subjects affected / exposed | 73 / 89 (82.02%) | | |
| occurrences (all) | 125 | | |
| Leukopenia | | | |
| subjects affected / exposed | 29 / 89 (32.58%) | | |
| occurrences (all) | 75 | | |
| Neutropenia | | | |
| subjects affected / exposed | 25 / 89 (28.09%) | | |
| occurrences (all) | 71 | | |
| Anaemia | | | |
| subjects affected / exposed | 12 / 89 (13.48%) | | |
| occurrences (all) | 15 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 5 / 89 (5.62%) | | |
| occurrences (all) | 8 | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 4 / 89 (4.49%) | | |
| occurrences (all) | 5 | | |
| Febrile bone marrow aplasia | | | |
| subjects affected / exposed | 2 / 89 (2.25%) | | |
| occurrences (all) | 2 | | |
| Bone marrow failure | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Histiocytosis | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |

| | | | |
|--|---|--|--|
| Inguinal hernia subjects affected / exposed occurrences (all) | 1 / 89 (1.12%) 1 | | |
| Obstructive defaecation subjects affected / exposed occurrences (all) | 1 / 89 (1.12%) 1 | | |
| Oesophagitis subjects affected / exposed occurrences (all) | 1 / 89 (1.12%) 1 | | |
| Skin and subcutaneous tissue disorders Rash maculo-papular subjects affected / exposed occurrences (all) | 1 / 89 (1.12%) 1 | | |
| Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all) Renal failure subjects affected / exposed occurrences (all) | 1 / 89 (1.12%) 1 1 / 89 (1.12%) 1 | | |
| Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) cystitis subjects affected / exposed occurrences (all) Fungal infection subjects affected / exposed occurrences (all) Pyelonephritis subjects affected / exposed occurrences (all) Rhinitis | 4 / 89 (4.49%) 4 4 / 89 (4.49%) 6 2 / 89 (2.25%) 2 2 / 89 (2.25%) 2 2 / 89 (2.25%) 2 | | |

| | | | |
|-------------------------------|----------------|--|--|
| subjects affected / exposed | 2 / 89 (2.25%) | | |
| occurrences (all) | 2 | | |
| Septic shock | | | |
| subjects affected / exposed | 2 / 89 (2.25%) | | |
| occurrences (all) | 2 | | |
| Bacterial prostatitis | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Bacterial sepsis | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Citrobacter sepsis | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Device related infection | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Escherichia bacteraemia | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Escherichia infection | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Escherichia pyelonephritis | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Escherichia sepsis | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Infection | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Lung infection | | | |

| | | | |
|------------------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Prostatitis Escherichia coli | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Pseudomonas infection | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Tuberculosis | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 2 / 89 (2.25%) | | |
| occurrences (all) | 2 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 2 / 89 (2.25%) | | |
| occurrences (all) | 2 | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 89 (1.12%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 24 January 2018 | This amendment was due to a safety alert for bendamustine. A warning and a course of action regarding the risk of opportunistic infections reported during the safety alert have been added to the protocol. |
| 22 September 2020 | Addition of 2 exploratory objectives, to analyze centrally and independently of the first results obtained, the PET scans of the patients included in the study. Furthermore, the efficacy population, on which the sensitivity analyses of the primary endpoint was performed, was modified to include patients with non-evaluable responses at the end of treatment, in order to limit the bias of the analysis. |

Notes:

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.

No limitations and caveats.

Notes: