



Clinical trial results:

A multicentre, phase II, open label, single arm study of pixantrone in patients with CD20-positive relapsed or refractory aggressive non-Hodgkin lymphoma treated with rituximab, ifosfamide and etoposide.

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2017-000719-17 |
| Trial protocol | FR BE |
| Global end of trial date | 19 December 2024 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 29 March 2026 |
| First version publication date | 29 March 2026 |

Trial information

Trial identification

| | |
|-----------------------|-------|
| Sponsor protocol code | PIVeR |
|-----------------------|-------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03458260 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | LYSARC |
| Sponsor organisation address | CH Lyon Sud – Bat 2D - 69495 PIERRE-BENITE Cedex - France, PIERRE-BENITE , France, 69495 |
| Public contact | Clinical Project Manager N. PRONINA, LYSARC, +33 (0)427 01 27 38, piver@lysarc.org |
| Scientific contact | Pr. L. Fornecker, LYSARC, +33 (0)427 01 27 38, lm.fornecker@icans.eu |

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 | 24 December 2024 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 19 December 2024 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to assess the efficacy of Pixantrone with rituximab, ifosfamide and etoposide as measured by the overall metabolic response (OMR) rate after 2 cycles of treatment or at permanent treatment discontinuation, whichever occurs first.

Protection of trial subjects:

sentence on rescue treatment ?

Background therapy:

Anthracycline-based regimens in combination with Rituximab are the standard of care in first-line for aggressive NHL. However, 30-40% will be refractory to first-line therapy or relapsed after standard first-line immunochemotherapy (R/R patients). Salvage chemotherapy followed by high-dose therapy and autologous stem-cells transplantation (HDT-ASCT) is the standard of care for eligible R/R patients.

Evidence for comparator:

There is currently no standard of care for patients with R/R aggressive NHL who are not eligible for HDT-ASCT procedure. Studies have demonstrated the possibility to combine Pixantrone with rituximab and other chemotherapeutic compounds in indolent and aggressive NHL. The combination of Rituximab, Ifosfamide and Etoposide is the backbone of several salvage regimens for relapsed/refractory DLBCL and will be tested in this study.

| | |
|---|-----------------|
| Actual start date of recruitment | 01 January 2018 |
| 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 | France: 71 |
| Country: Number of subjects enrolled | Belgium: 3 |
| Worldwide total number of subjects | 74 |
| EEA total number of subjects | 74 |

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 | 0 |

| | |
|---------------------------|----|
| months) | |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 17 |
| From 65 to 84 years | 55 |
| 85 years and over | 2 |

Subject disposition

Recruitment

Recruitment details:

Enrollment of PIVeR study was to be stopped once 84 evaluable patients were enrolled with an estimated recruitment period of 3 years. However, the recruitment was not as efficient as expected and it has been stopped on December 31st, 2021. A total of 74 patients were enrolled.

Pre-assignment

Screening details:

A total of 74 patients were enrolled.
16 patients were screen failed

Period 1

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

Arms

| | |
|-----------|---|
| Arm title | Pixantrone - rituximab - ifosfamide - etoposide |
|-----------|---|

Arm description:

Treatment will consist of 2 to 6 cycles of Pixantrone with rituximab, ifosfamide and etoposide (21-day cycle)

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Pixantrone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for injection |
| Routes of administration | Intravenous bolus use |

Dosage and administration details:

Dose for patients aged 18-69 : 80 mg/m²
Dose for patients aged 70 and + : 60 mg/m²

After reconstitution should be administered as a slow IV infusion over a period of 1 hour (+/- 10 minutes)

| | |
|--|---------------------------------------|
| Investigational medicinal product name | Rituximab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous bolus use |

Dosage and administration details:

Dosage 375 mg/m²

Administration : Chemotherapy products have been used according to summary of product characteristics.

| | |
|--|---|
| Investigational medicinal product name | Ifosfamide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for concentrate for solution for infusion |
| Routes of administration | Intravenous bolus use |

Dosage and administration details:

Chemotherapy products have been used according to summary of product characteristics.

Dose for pateints aged 18-69 : 1500 mg/m²
Dose for patients aged 70 and + : 1000mg/m²

| | |
|--|---|
| Investigational medicinal product name | Etoposide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for dispersion for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Chemotherapy products are to be used according to summary of product characteristics.

Dosage for patients aged 18-69 : 150 mg/m²

Dosage for patients aged 70 and + : 100 mg/m²

| Number of subjects in period 1 | Pixantrone - rituximab - ifosfamide - etoposide |
|---|--|
| Started | 74 |
| Completed | 19 |
| Not completed | 55 |
| Consent withdrawn by subject | 1 |
| Physician decision | 1 |
| CAR-T cells | 3 |
| NO RESPONDER PATIENT | 3 |
| Adverse event, non-fatal | 10 |
| Death | 1 |
| PERSONAL REASON FOR THE PATIENT | 1 |
| PATIENT DECIDES TO STOP ALL LYMPHOMAS TREATMENTS | 1 |
| DEAUVILLE 4 | 1 |
| INSUFFICIENT RESPONSE AND CARDIAC COMORBIDITIES | 1 |
| ASCT | 3 |
| Lack of efficacy | 29 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Treatment |
|-----------------------|-----------|

Reporting group description: -

| Reporting group values | Treatment | Total | |
|------------------------|-----------|-------|--|
| Number of subjects | 74 | 74 | |
| Age categorical | | | |
| Units: Subjects | | | |
| From 18-70 years | 38 | 38 | |
| 71 years and over | 36 | 36 | |
| Age continuous | | | |
| Units: years | | | |
| median | 70 | | |
| full range (min-max) | 35 to 87 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 28 | 28 | |
| Male | 46 | 46 | |
| Ann Arbor stage | | | |
| Units: Subjects | | | |
| _I | 3 | 3 | |
| II | 9 | 9 | |
| III | 9 | 9 | |
| IV | 53 | 53 | |
| ECOG | | | |
| Units: Subjects | | | |
| _0 | 27 | 27 | |
| _1 | 35 | 35 | |
| _2 | 12 | 12 | |
| IPI | | | |
| Units: Subjects | | | |
| 0-2 | 25 | 25 | |
| 3-5 | 45 | 45 | |
| Missing | 4 | 4 | |
| aaIPI | | | |
| Units: Subjects | | | |
| 0-1 | 28 | 28 | |
| 2-3 | 42 | 42 | |
| Missing | 4 | 4 | |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Pixantrone - rituximab - ifosfamide - etoposide |
| Reporting group description: | |
| Treatment will consist of 2 to 6 cycles of Pixantrone with rituximab, ifosfamide and etoposide (21-day cycle) | |

Primary: OMR rate after 2 cycles according to local investigator

| | |
|--|--|
| End point title | OMR rate after 2 cycles according to local investigator ^[1] |
| End point description: | |
| Overall Metabolic Response rate by local investigator based on PET-CT scan according to Lugano classification (Cheson B. et al, JCO 2014). Patients without response assessment (i.e. response not evaluated or missing) due to whatever reason will be considered as non-responders. | |
| End point type | Primary |
| End point timeframe: | |
| After 2 cycles or at permanent treatment discontinuation, whichever occurs first. | |

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: The PIVeR trial was designed in order to detect an OMR increase in favor of the Pixantrone from 40% (null hypothesis) to 55% (alternative hypothesis), assuming an 80% power at a 5% (1-sided) significance level using a two-stage phase II design.

The null hypothesis was to be rejected if the lower limit of the 90%CI was $\geq 40\%$.

| | | | | |
|----------------------------------|---|--|--|--|
| End point values | Pixantrone - rituximab - ifosfamide - etoposide | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 74 | | | |
| Units: percent | | | | |
| number (confidence interval 90%) | 59.5 (49.2 to 69.1) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: CMR rate after 2 cycles according to local investigator

| | |
|---|---|
| End point title | CMR rate after 2 cycles according to local investigator |
| End point description: | |
| Complete Metabolic Response rate by local investigator based on PET-CT scan according to Lugano classification (Cheson B. et al, JCO 2014). Patients without response assessment (i.e. response not evaluated or missing) due to whatever reason will be considered as non-responders. | |
| End point type | Secondary |
| End point timeframe: | |
| After 2 cycles or at permanent treatment discontinuation, whichever occurs first. | |

| | | | | |
|----------------------------------|--|--|--|--|
| End point values | Pixantrone - rituximab - ifosfamide - etoposide | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 74 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | 18.9 (10.7 to 29.7) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: OMR rate after 2 cycles according to central review

| | |
|--|---|
| End point title | OMR rate after 2 cycles according to central review |
| End point description: | |
| Overall Metabolic Response rate according to central review based on PET-CT scan according to Lugano classification (Cheson B. et al, JCO 2014). | |
| Patients without response assessment (i.e. response not evaluated or missing) due to whatever reason will be considered as non-responders. | |
| End point type | Secondary |
| End point timeframe: | |
| After 2 cycles or at permanent treatment discontinuation, whichever occurs first. | |

| | | | | |
|----------------------------------|--|--|--|--|
| End point values | Pixantrone - rituximab - ifosfamide - etoposide | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 74 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | 47.3 (35.6 to 59.3) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: OMR rate at the timepoint of interest according to local investigator

| | | | | |
|-----------------|---|--|--|--|
| End point title | OMR rate at the timepoint of interest according to local investigator | | | |
|-----------------|---|--|--|--|

End point description:

Overall Metabolic Response rate by local investigator based on PET-CT scan according to Lugano classification (Cheson B. et al, JCO 2014).
Patients without response assessment (i.e. response not evaluated or missing) due to whatever reason will be considered as non-responders.

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

End point timeframe:

After 2 cycles, for patients who did not respond after 2 cycles.

After 2 cycles, for patients responders after 2 cycles and eligible for ASCT.

After 6 cycles, for patients responders after 2 cycles and not eligible for ASCT.

| | | | | |
|----------------------------------|--|--|--|--|
| End point values | Pixantrone - rituximab - ifosfamide - etoposide | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 74 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | 39.2 (28 to 51.2) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: OMR rate at the end of treatment according to local investigator

| | |
|-----------------|--|
| End point title | OMR rate at the end of treatment according to local investigator |
|-----------------|--|

End point description:

Overall Metabolic Response rate by local investigator based on PET-CT scan according to Lugano classification (Cheson B. et al, JCO 2014).
Patients without response assessment (i.e. response not evaluated or missing) due to whatever reason will be considered as non-responders.

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

End point timeframe:

At the end of treatment or at permanent treatment discontinuation, whichever occurs first.

| | | | | |
|----------------------------------|--|--|--|--|
| End point values | Pixantrone - rituximab - ifosfamide - etoposide | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 74 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | 37.8 (26.8 to 49.9) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival

| | |
|-----------------|---------------------------|
| End point title | Progression Free Survival |
|-----------------|---------------------------|

End point description:

PFS is defined as the time (years) from inclusion into the study to the first observation of documented disease progression or death due to any cause.

If a subject has not progressed or died, PFS will be censored at the date of tumor assessment.

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

End point timeframe:

Since inclusion.

| | | | | |
|----------------------------------|--|--|--|--|
| End point values | Pixantrone - rituximab - ifosfamide - etoposide | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 74 | | | |
| Units: percent | | | | |
| median (confidence interval 95%) | 0.26 (0.21 to 0.47) | | | |

| | |
|-----------------------------------|------------------------|
| Attachments (see zip file) | PFS/Figure 170302.jpeg |
|-----------------------------------|------------------------|

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

| | |
|-----------------|------------------|
| End point title | Overall Survival |
|-----------------|------------------|

End point description:

Overall survival will be measured (in years) from the date of inclusion to the date of death from any cause.

Alive patients will be censored at the date of last contact.

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

End point timeframe:

Since inclusion.

| | | | | |
|----------------------------------|--|--|--|--|
| End point values | Pixantrone - rituximab - ifosfamide - etoposide | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 74 | | | |
| Units: percent | | | | |
| median (confidence interval 95%) | 1.6 (1.16 to 3.04) | | | |

| | |
|-----------------------------------|-----------------------|
| Attachments (see zip file) | OS/Figure 170402.jpeg |
|-----------------------------------|-----------------------|

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 drug administration.

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

Dictionary used

| | |
|-----------------|-------|
| Dictionary name | CTCAE |
|-----------------|-------|

| | |
|--------------------|-----|
| Dictionary version | 4.0 |
|--------------------|-----|

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Pixantrone - rituximab - ifosfamide - etoposide |
|-----------------------|---|

Reporting group description:

Treatment will consist of 2 to 6 cycles of Pixantrone with rituximab, ifosfamide and etoposide (21-day cycle)

| Serious adverse events | | Pixantrone - rituximab - ifosfamide - etoposide | | |
|---|--|---|--|--|
| Total subjects affected by serious adverse events | | | | |
| subjects affected / exposed | | 29 / 74 (39.19%) | | |
| number of deaths (all causes) | | 48 | | |
| number of deaths resulting from adverse events | | 13 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | | |
| NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) | | | | |
| subjects affected / exposed | | 6 / 74 (8.11%) | | |
| occurrences causally related to treatment / all | | 1 / 6 | | |
| deaths causally related to treatment / all | | 0 / 4 | | |
| Injury, poisoning and procedural complications | | | | |
| INJURY, POISONING AND PROCEDURAL COMPLICATIONS | | | | |
| subjects affected / exposed | | 1 / 74 (1.35%) | | |
| occurrences causally related to treatment / all | | 0 / 1 | | |
| deaths causally related to treatment / all | | 0 / 0 | | |
| Cardiac disorders | | | | |
| CARDIAC DISORDERS | | | | |
| subjects affected / exposed | | 6 / 74 (8.11%) | | |
| occurrences causally related to treatment / all | | 5 / 7 | | |
| deaths causally related to treatment / all | | 0 / 1 | | |

| | | | |
|--|---|--|--|
| Nervous system disorders NERVOUS SYSTEM DISORDERS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 74 (1.35%) 0 / 1 0 / 0 | | |
| Blood and lymphatic system disorders BLOOD AND LYMPHATIC SYSTEM DISORDERS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 8 / 74 (10.81%) 7 / 9 0 / 0 | | |
| General disorders and administration site conditions GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 4 / 74 (5.41%) 3 / 4 1 / 2 | | |
| Gastrointestinal disorders GASTROINTESTINAL DISORDERS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 74 (1.35%) 1 / 1 1 / 1 | | |
| Respiratory, thoracic and mediastinal disorders RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 4 / 74 (5.41%) 0 / 4 0 / 1 | | |
| Renal and urinary disorders RENAL AND URINARY DISORDERS subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 74 (2.70%) 0 / 2 0 / 0 | | |
| Infections and infestations INFECTIOUS AND INFESTATIONS | | | |

| | | | |
|--|------------------|--|--|
| subjects affected / exposed | 17 / 74 (22.97%) | | |
| occurrences causally related to treatment / all | 6 / 19 | | |
| deaths causally related to treatment / all | 0 / 4 | | |
| Metabolism and nutrition disorders METABOLISM AND NUTRITION DISORDERS | | | |
| subjects affected / exposed | 1 / 74 (1.35%) | | |
| 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 | Pixantrone - rituximab - ifosfamide - etoposide | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 56 / 74 (75.68%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) | | | |
| subjects affected / exposed | 6 / 74 (8.11%) | | |
| occurrences (all) | 6 | | |
| Vascular disorders VASCULAR DISORDERS | | | |
| subjects affected / exposed | 2 / 74 (2.70%) | | |
| occurrences (all) | 2 | | |
| General disorders and administration site conditions GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | | | |
| subjects affected / exposed | 8 / 74 (10.81%) | | |
| occurrences (all) | 9 | | |
| Respiratory, thoracic and mediastinal disorders RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS | | | |
| subjects affected / exposed | 6 / 74 (8.11%) | | |
| occurrences (all) | 6 | | |
| Investigations | | | |

| | | | |
|---|-----------------------------------|--|--|
| <p>INVESTIGATIONS</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 74 (2.70%)</p> <p>2</p> | | |
| <p>Injury, poisoning and procedural complications</p> <p>INJURY, POISONING AND PROCEDURAL COMPLICATIONS</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 74 (1.35%)</p> <p>1</p> | | |
| <p>Cardiac disorders</p> <p>CARDIAC DISORDERS</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>7 / 74 (9.46%)</p> <p>9</p> | | |
| <p>Nervous system disorders</p> <p>NERVOUS SYSTEM DISORDERS</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>4 / 74 (5.41%)</p> <p>6</p> | | |
| <p>Blood and lymphatic system disorders</p> <p>BLOOD AND LYMPHATIC SYSTEM DISORDERS</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>34 / 74 (45.95%)</p> <p>83</p> | | |
| <p>Gastrointestinal disorders</p> <p>GASTROINTESTINAL DISORDERS</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>6 / 74 (8.11%)</p> <p>8</p> | | |
| <p>Renal and urinary disorders</p> <p>RENAL AND URINARY DISORDERS</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 74 (2.70%)</p> <p>2</p> | | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 74 (1.35%)</p> <p>1</p> | | |
| <p>Infections and infestations</p> <p>INFECTIONS AND INFESTATIONS</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>22 / 74 (29.73%)</p> <p>25</p> | | |
| <p>Metabolism and nutrition disorders</p> | | | |

| | | | |
|---------------------------------------|----------------|--|--|
| METABOLISM AND NUTRITION DISORDERS | | | |
| subjects affected / exposed | 5 / 74 (6.76%) | | |
| occurrences (all) | 6 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 27 July 2018 | Protocol v2.0 - addition of a third treatment cycle for patients eligible for autologous stem cell transplantation, prior to conditioning therapy. Initially, only two cycles were planned. The relatively long interval between the second cycle and transplantation allows for the administration of an additional cycle in routine practice. |
| 03 January 2019 | Protocol v3.0 - Patient age limitation to 80 years - Modification of the pixantrone dose for patients 70 years of age or older: the IDMC recommends reducing the dose to 60 mg/m ² for patients aged 70 years or older |
| 27 September 2024 | Protocol v4.0 Reduction of the study duration to 6 years |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|-----------------|---|--------------|
| 11 January 2022 | premature end of recruitment : 74 patients enrolled instead of 89 | - |

Notes:

Limitations and caveats

None reported