



Clinical trial results:

BENEFIT - A multicenter phase II study evaluating BeEAM (Bendamustine, Etoposide, Cytarabine, Melphalan) prior to autologous stem cell transplant for first and second chemosensitive relapses in patients with follicular lymphoma

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2013-000076-16 |
| Trial protocol | FR |
| Global end of trial date | 08 October 2018 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 17 March 2021 |
| First version publication date | 17 March 2021 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | ET13-01 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02008006 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Centre Léon Bérard |
| Sponsor organisation address | 28 rue Laennec, LYON, France, 69008 |
| Public contact | DRCI, Centre Léon Bérard, 33 (0)478 78 28 28, DRCIreglementaire@lyon.unicancer.fr |
| Scientific contact | DRCI, Centre Léon Bérard, 33 (0)478 78 28 28, DRCIreglementaire@lyon.unicancer.fr |

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 | 08 November 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 07 October 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 08 October 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the efficacy of BeEAM (bendamustine, etoposide, cytarabine and melphalan) regimen prior to autologous stem cell transplant for first and second chemosensitive relapses in patients with follicular lymphoma (WHO grade 1, 2, 3a) by measuring the event-free survival define by relapse (for complete responders at the beginning of treatment), progression, death from any cause and initiation of a new therapy.

Protection of trial subjects:

Patients achieving a complete or partial response after salvage treatment according to 2007 Cheson international response criteria and being eligible for transplant will proceed to the inclusion visit. The inclusion will be performed after salvage treatment before HDT.

The investigator or designee staff will have to proceed to the following information/procedures during the inclusion visit:

- Inform the patient of the treatments, the objectives and the design of the study, answer to questions and sign with him/her the informed consent form (ICF). The investigator must not start any study related procedure before ICF is signed and dated by both patient (or impartial witness, if applicable) and investigator
- Check the eligibility criteria list

Inclusion visit

Patient registration

Assessment during study treatment (BeEAM treatment)

Hematological assessment post ASCT

Day 100 assessment after ASCT

Long-term follow up

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 18 June 2014 |
| 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: 21 |
| Worldwide total number of subjects | 21 |
| EEA total number of subjects | 21 |

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) | 21 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

First and second chemosensitive relapses in patients with WHO grade 1, 2 and 3a follicular lymphoma
Adult patients aged from 18 to 65 years with previously treated follicular lymphoma (WHO grade 1, 2, 3a) without contraindication to autologous stem cell transplantation (ASCT) in first and second chemosensitive relapses

Period 1

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

Arms

| | |
|-----------|--------------|
| Arm title | Experimental |
|-----------|--------------|

Arm description:

The proposed trial is a single arm, multicenter, open-label, phase II study.

Patients will be pre-treated with a salvage treatment. Then, patients will be consolidated by BeEAM regimen prior to ASCT:

- Bendamustine (160 mg/m² from day -8 to -7)
- Etoposide (200 mg/m² from day -6 to day -3: 100mg/m² every 12h)
- Cytarabine (400 mg/m² from day -6 to day -3: 200 mg/m² every 12h)
- Melphalan (140 mg/m² on day -2)

ASCT will be performed according to standard recommendations. After ASCT, administration of any other chemotherapy agents or regimen is not allowed. During the study, 9 visits will be performed after ASCT during 4 years:

- At D100 and M6,
- Then every 6 months (M12, M18, M24, M30, M36, M42 and M48)

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

Dosage and administration details:

Rutiximab- based salvage treatment and mobilization procedure before ASCT

Conditioning regimen: BeEAM

Patients will be consolidated by BeEAM regimen prior to ASCT:

- Bendamustine (160 mg/m² from day -8 and -7)
- Etoposide (200 mg/m² from day -6 to day -3)
- Cytarabine (400 mg/m² from day -6 to day -3)
- Melphalan (140 mg/m² on day -2)

ASCT

Management after ASCT

| Number of subjects in period 1 ^[1] | Experimental |
|--|--------------|
| | |
| Started | 20 |
| Completed | 20 |

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: One patient was enrolled before the inclusions were suspended and he did not receive the study treatment. The analysis population consists of the 20 patients treated.

Baseline characteristics

End points

End points reporting groups

| | |
|--|--------------|
| Reporting group title | Experimental |
| Reporting group description: | |
| The proposed trial is a single arm, multicenter, open-label, phase II study. Patients will be pre-treated with a salvage treatment. Then, patients will be consolidated by BeEAM regimen prior to ASCT: | |
| - Bendamustine (160 mg/m ² from day -8 to -7) | |
| - Etoposide (200 mg/m ² from day -6 to day -3: 100mg/m ² every 12h) | |
| - Cytarabine (400 mg/m ² from day -6 to day -3: 200 mg/m ² every 12h) | |
| - Melphalan (140 mg/m ² on day -2) | |
| ASCT will be performed according to standard recommendations. After ASCT, administration of any other chemotherapy agents or regimen is not allowed. During the study, 9 visits will be performed after ASCT during 4 years: | |
| - At D100 and M6, | |
| - Then every 6 months (M12, M18, M24, M30, M36, M42 and M48) | |

Primary: Primary end point

| | |
|--|----------------------------------|
| End point title | Primary end point ^[1] |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| Event-free survival define by relapse (for complete responders at the beginning of treatment), progression, death from any cause and initiation of a new therapy | |

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: Qualitative variables will be described using frequency and percentage distributions. Quantitative data will be described using the number of observations, mean, standard deviation, median, minimum and maximum values, and the number of missing data if appropriate. Patient characteristics and other baseline data will be summarized. The date of inclusion (beginning of BeEAM regimen) will serve as a reference for calculation of durations unless otherwise indicated.

| | | | | |
|-----------------------------|-----------------|--|--|--|
| End point values | Experimental | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 20 | | | |
| Units: month | 20 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

The investigator collects (spontaneous patient report or questioning) and immediately notifies the sponsor of all SAEs, in a written report, whether or not they are deemed to be attributable to research and which occur during the study

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

Dictionary used

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|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 21.0 |

Frequency threshold for reporting non-serious adverse events: 5 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: All 20 patients treated experienced one or more adverse events. For the 20 patients at least one of the events was related to the study treatment and all also had at least one grade ≥ 3 AE. 16 patients reported at least one SAE during the study including 3 patients with two SAEs, 2 patients with 4 SAEs and one patient with 5 SAEs, for a total of 29 SAEs.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 07 July 2015 | Extend the duration of inclusions by one year |
| 03 November 2015 | Response to the ANSM's request dated 09/08/2015 to amend the protocol (criteria for non-inclusion) following the occurrence of 2 cases of veno-occlusive disease related to the treatment and our declaration of a new fact of security of 08/05/2015 Addition of three exclusion criteria: History of chronic liver disease, excessive alcohol consumption and History of veno-occlusive disease (VOD) or sinusoidal obstruction syndrome (SOS) |
| 15 April 2016 | Temporary stop of the trial and establishment of an independent monitoring committee |
| 19 September 2016 | Resumption after temporary stop of the trial and modification requested by the independent monitoring committee |
| 12 December 2017 | Recruitment was temporarily interrupted on 09/25/17 due to poor recruitment in this study (21 patients included out of the 50 expected) and the expiration of the treatment units on 09/30/17. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|------------------|--|--------------|
| 24 November 2017 | A monitoring committee was held on 04/18/2016 (19 patients included including 18 treated) following the occurrence of the 2 new safety facts. This committee recommended "Temporary stopping of recruitment pending the collection of additional information" (the Promoter had already suspended inclusions since 02/12/2016). On June 16, 2016 the committee met again and it was decided to continue the test with amendment. The final discontinuation of the study was decided on 24/11/2017 before reaching the number of patients provided for in the protocol. | - |

Notes:

Limitations and caveats

None reported