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 regiment 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
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- 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:

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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 questionning) and immediately notifies the sponsor of all SAEs, in a written report, wether or not theay are deemed to be attributable to research and wich occur during the study

Assessment type	Systematic

Dictionary used

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