Clinical trial results:
Phase II multicentric study to evaluate the efficacy and the safety of Bendamustine in adjunct to Etoposide, Aracytabin and Melphalan (BeEAM) as a preparative regimen for autologous stem cell transplantation in refractory/relapsed aggressive B-cell non-Hodgkin lymphoma patients.

Summary

EudraCT number	2011-001246-14
Trial protocol	IT
Global end of trial date	22 February 2021
Results information	
Result version number	v1 (current)
This version publication date	26 August 2022
First version publication date	26 August 2022
Summary attachment (see zip file)	EBMT 2020 abstract (https_www.abstractserver.com_ebmt2020_absmgm_printprevi Protocol synopsys (Amendment 1 protocol synopsis.pdf)

Trial information

Trial identification	
Sponsor protocol code	701
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	AORMN Hospital
Sponsor organisation address	Piazzale Cinelli 4, Pesaro, Italy,
Public contact	Hematology Clinical Trial Office, Presidio Ospedaliero"San Salvatore/Ospedali Riuniti Marche Nord", +39 0721364022, alessandro.isidori@ospedalimarchenord.it
Scientific contact	Hematology Clinical Trial Office, Presidio Ospedaliero"San Salvatore/Ospedali Riuniti Marche Nord", +39 0721364022, alessandro.isidori@ospedalimarchenord.it

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	30 July 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 February 2021
Global end of trial reached?	Yes
Global end of trial date	22 February 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the 1-year complete remission (CR) rate.

Protection of trial subjects:

No specific measure was put in place to protect trial subjects, in addition to standard of care.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2011
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	Italy: 66
Worldwide total number of subjects	66
EEA total number of subjects	66

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)	57
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

According to Amendment 1, sent to the Italian Regulatoy Authority (AIFA)on october 20th, 2020, 66 patients were enrolled in the trial between June 2011 and november 20th, 2018. All patients were enrolled in Italy.

Pre-assignment

Screening details:

73 patients were screened. 7/73 patients did not meet one or more of the inclusion or exclusion criteria, and were consequently not enrolled in the trial. 66 patients were finally enrolled.

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	Treatment arm

Arm description:

This was a single arm trial testing the the efficacy and the safety of Bendamustine in adjunct to Etoposide, Aracytabin and Melphalan (BeEAM) as a preparative regimen for autologous stem cell transplantation in refractory/relapsed aggressive B-cell non-Hodgkin lymphoma patients.

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

Dosage and administration details:

Bendamustine was used in adjunct to other drugs in the conditioning regimen for autologosu stem cell transplantation in resistant/refractory non Hodking lymphoma patients, as follows:
• Bendamustine 200 mg/m2
on day -7 and -6
• Aracytin 400 mg/m2 from day -5 to day -2
• Etoposide 200 mg/m2
from day -5 to day -2
• Melphalan 140 mg/m2
on day -1
• Autologous stem cell transplantation on day 0

Number of subjects in period 1	Treatment arm
Started	66
Completed	66

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	66	66	
Age categorical			
Patients aged 18-70 were considered to be enrolled in the trial			
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)	57	57	
From 65-84 years	9	9	
85 years and over	0	0	
Gender categorical			
Both males and females patients were enrolled in the trial			
Units: Subjects			
Female	30	30	
Male	36	36	

End points

End points reporting groups

Reporting group title	Treatment arm

Reporting group description:

This was a single arm trial testing the the efficacy and the safety of Bendamustine in adjunct to Etoposide, Aracytabin and Melphalan (BeEAM) as a preparative regimen for autologous stem cell transplantation in refractory/relapsed aggressive B-cell non-Hodgkin lymphoma patients.

Primary: Complete remission rate

End point title	Complete remission rate[1]

End point description:

The primary endpoint of the study was to evaulate the 1-year complete remission (CR) rate.

End point type	Primary

End point timeframe:

12 months (1 year).

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: This was a single arm study designed according to the Fleming's Method. OS and EFS was estimated according to Kaplan–Mayer method. The log rank test was used to assess the significance of differences for each prognostic factor in the univariate analysis. The Cox proportional hazards regression model and the logistic regression models was used to assess how patients' characteristics predict EFS and OS.

End point values	Treatment arm			
Subject group type	Reporting group			
Number of subjects analysed	66			
Units: percentage	82			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Adverse event reporting was performed from April 1st, 2011 to February 22nd, 2021. Adverse events were notified to Mundipharma Pharmacovigilance office (producer of Bendamustine), to the following email EUDrugSafety@mundipharma-rd.eu

Adverse event reporting additional description:

Please refer to Mundipharma Pharmacovigilance office for a detailed report on AE and SAE, because we do not have this information available.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.0

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: Adverse events were notified to Mundipharma Pharmacovigilance office (producer of Bendamustine), to the following email EUDrugSafety@mundipharma-rd.eu

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 October 2020	Due to a delay in the accrual of patients, related to the advent of CART cell therapies in this patient population, we decided to reduce the number of subjects by lowering the statystical power of the trial, in order to allow patients to receive CART instead of autologous stem cell transplantation, if available. According, we changed the statistycal analysis as follow: "Fixing the lowest acceptable rate as 55% and the successful rate as 70%, with a significance level alpha=0.05 and a power 1-beta =0.80, the sample size was estimated in 64 patients. Considering a possible drop-out rate of 3%, the number of patients entering the protocol is fixed to 66."

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported