Clinical trial results:
Brentuximab vedotin as consolidation treatment in patients with stage I/II Hodgkin's lymphoma and FDG-PET positivity after 2 cycles of ABVD

Summary

EudraCT number	2013-000734-35
Trial protocol	FR BE
Global end of trial date	09 July 2020

Results information

Result version number	v1 (current)
This version publication date	17 July 2021
First version publication date	17 July 2021

Trial information

Trial identification

Sponsor protocol code	BRAPP2

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02298283
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	LYSARC
Sponsor organisation address	Centre Hospitalier Lyon-Sud Bâtiment 2D , PIERRE-BÉNITE Cedex, France, 69495
Public contact	Clinical Project Management, LYSARC, brapp2@lysarc.org
Scientific contact	Pauline BRICE Coordinating Investigator, LYSA HDJ Hématologie Hôpital Saint Louis, pauline.brice@aphp.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	09 July 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Progression free survival (PFS) at 2 years in patients with stage I/II Hodgkin’s lymphoma and FDG-PET positivity after 2 cycles of ABVD receiving brentuximab vedotin as consolidation treatment

Protection of trial subjects:

TBC by Project Manager

Background therapy:

ABVD: Adriamycin, Bleomycin, Vinblastine and DTIC/Dacarbazine
BEACOPPescalated: Bleomycin, Etoposide, Doxorubicin, Cyclophosphamide, Vincristine, Procarbazine and Prednisone
IFRT (Involved Field Radiotherapy)

Evidence for comparator:

Not Applicable

Actual start date of recruitment	09 April 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	France: 47
Country: Number of subjects enrolled	Belgium: 1
Worldwide total number of subjects	48
EEA total number of subjects	48

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)	47

From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

FRANCE from 09/04/2015 to 04/04/2018
BELGIUM on 29/01/2018

Pre-assignment

Screening details:

Inclusion following FDG-PET positivity after 2 cycles of ABVD => 49 patients enrolled
One patient withdrew his consent before induction treatment => 47 patients in Induction

Period 1

Period 1 title	Induction
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not Applicable

Arms

Arm title	BEACOPP + IFRT

Arm description: -

Arm type	Experimental
Investigational medicinal product name	BEACOPP
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cyclophosphamide	1250 mg/m²	i.v.	D1
Doxorubicin	35 mg/m²	i.v.	D1
Vincristine	1.4 mg/m²	i.v.(max.2mg)	D8
Bléomycine	10 mg/m²	i.v	J8
Etoposide	200 mg/m²/j	i.v.	D1 à D3
Procarbazine	100 mg/m²/j	p.o.	D1 à D7
Prednisone	40 mg/m²/j	p.o.	D1 à D7
G-CSF 5 µg/kg/j		s.c.	J9 until GB 1.0x109/L

2 cycles of 21 days

Number of subjects in period 1	BEACOPP + IFRT
Started	48
Completed	41
Not completed	7
Consent withdrawn by subject	1
Progression	4
Lack of efficacy	1

Protocol deviation	1

Period 2	
Period 2 title	Consolidation
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not Applicable

Arms

Arm title	Brentuximab vedotin

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Brentuximab Vedotin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.8 mg/kg starting 4 to 6 weeks after standard radiotherapy.
8 cycles, one cycle is 3 weeks

Number of subjects in period 2	Brentuximab vedotin
Started	41
Completed	35
Not completed	6
Consent withdrawn by subject	1
Adverse event, non-fatal	4
Progression	1

Baseline characteristics

Reporting groups

Reporting group title	Induction

Reporting group description: -

Reporting group values	Induction	Total	
Number of subjects	48	48	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	36		
inter-quartile range (Q1-Q3)	24 to 42	-	
Gender categorical Units: Subjects			
Female	23	23	
Male	25	25	

Subject analysis sets

Subject analysis set title	Efficacy set
Subject analysis set type	Full analysis

Subject analysis set description:

The efficacy set includes all included patients who have received at least one administration of brentuximab vedotin treatment.

Subject analysis set title	Safety set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety set is defined as all patients who have received at least one dose of brentuximab vedotin.

Reporting group values	Efficacy set	Safety set	
Number of subjects	41	41	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	33.8	33.8	
inter-quartile range (Q1-Q3)	24 to 36	24 to 36	
Gender categorical Units: Subjects			
Female	22	22	
Male	19	19	

End points

End points reporting groups

Reporting group title	BEACOPP + IFRT
Reporting group description: -	
Reporting group title	Brentuximab vedotin
Reporting group description: -	
Subject analysis set title	Efficacy set
Subject analysis set type	Full analysis
Subject analysis set description:	
The efficacy set includes all included patients who have received at least one administration of brentuximab vedotin treatment.	
Subject analysis set title	Safety set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety set is defined as all patients who have received at least one dose of brentuximab vedotin.	

Primary: PFS at 2 years according to investigator assessment

End point title	PFS at 2 years according to investigator assessment[1]
End point description:	
Progression free survival (PFS) is defined as the time from the date of the first cycle of ABVD to the first observation of documented disease progression or death due to any cause. If a subject has not progressed or died, PFS is censored at the time of last visit with adequate assessment.	
End point type	Primary
End point timeframe:	
at 2 years	

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: As per internal LYSARC guidelines, no statistical analysis to be specified for Phase II trial with only one arm and survival endpoint as primary endpoint.

End point values	Efficacy set			
Subject group type	Subject analysis set			
Number of subjects analysed	41			
Units: percent				
number (confidence interval 95%)	90.0 (75.5 to 96.1)			

Attachments (see zip file)	PFS/Figure 166102.jpeg

Statistical analyses

No statistical analyses for this end point

Secondary: CRR at the end of treatment according to Cheson 2007

End point title	CRR at the end of treatment according to Cheson 2007
End point description:	
Assessment of response is based on the International Workshop to Standardize Response criteria for	

NHL (Criteria for evaluation of response in Non-Hodgkin’s lymphoma (Cheson, 2007)).
Patient with “not-evaluated” response or without response assessment (due to whatever reason) are considered as missing and are not included in the calculation of complete response rate (CRR).

End point type	Secondary

End point timeframe:

At the end of treatment i.e. after 8 cycles of brentuximab vedotin or after last treatment dose in case of permanent treatment discontinuation

End point values	Efficacy set			
Subject group type	Subject analysis set			
Number of subjects analysed	39			
Units: percent				
number (confidence interval 95%)	87.2 (72.57 to 95.70)			

Statistical analyses

No statistical analyses for this end point

Secondary: OS at 2 years

End point title	OS at 2 years

End point description:

OVerall survival (OS) is measured from the date of the first cycle of ABVD to the date of death from any cause. Alive patients are censored at their last follow-up date.

End point type	Secondary

End point timeframe:

at 2 years

End point values	Efficacy set			
Subject group type	Subject analysis set			
Number of subjects analysed	41			
Units: percent				
number (confidence interval 95%)	97.5 (83.5 to 99.6)			

Attachments (see zip file)	OS/Figure 176222.jpeg

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Before treatment = between informed consent and BEACOPP C1D1
Induction = between 1st administration of BEACOPP and 1st administration of brentuximab vedotin
Consolidation = from 1st administration of brentuximab vedotin
Overall

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23

Reporting groups

Reporting group title	Before treatment
Reporting group description: -	
Reporting group title	Induction
Reporting group description: -	
Reporting group title	Consolidation
Reporting group description: -	
Reporting group title	Overall

Reporting group description: -

Serious adverse events	Before treatment	Induction	Consolidation
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 41 (2.44%)	12 / 41 (29.27%)	3 / 41 (7.32%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Papillary thyroid cancer			
subjects affected / exposed	1 / 41 (2.44%)	1 / 41 (2.44%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Radiation pneumonitis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Venous thrombosis			

subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Hospitalisation			
subjects affected / exposed	0 / 41 (0.00%)	1 / 41 (2.44%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 41 (0.00%)	5 / 41 (12.20%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	6 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile bone marrow aplasia			
subjects affected / exposed	0 / 41 (0.00%)	3 / 41 (7.32%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 41 (0.00%)	1 / 41 (2.44%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 41 (0.00%)	1 / 41 (2.44%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bartholinitis			

subjects affected / exposed	0 / 41 (0.00%)	1 / 41 (2.44%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 41 (2.44%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Overall		
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 41 (36.59%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Papillary thyroid cancer			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Radiation pneumonitis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Venous thrombosis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Hospitalisation			

subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	5 / 41 (12.20%)		
occurrences causally related to treatment / all	6 / 6		
deaths causally related to treatment / all	0 / 0		
Febrile bone marrow aplasia			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bartholinitis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 41 (2.44%)		
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	Before treatment	Induction	Consolidation
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	23 / 41 (56.10%)
Nervous system disorders			
Nervous system disorders	Additional description: Neuropathy peripheral		
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	12 / 41 (29.27%)
occurrences (all)	0	0	14
Blood and lymphatic system disorders			
Blood and lymphatic system disorders	Additional description: Neutropenia Leukopenia Lymphopenia		
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	3 / 41 (7.32%)
occurrences (all)	0	0	4
General disorders and administration site conditions			
General disorders and administration site conditions	Additional description: Asthenia Chest discomfort Oedema peripheral		
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	3 / 41 (7.32%)
occurrences (all)	0	0	3
Gastrointestinal disorders			
Gastrointestinal disorders	Additional description: Constipation		
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders	Additional description: Lung disorder Pulmonary embolism Rhinorrhoea		
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	3 / 41 (7.32%)
occurrences (all)	0	0	3
Infections and infestations			
Infections and infestations	Additional description: Bronchitis Herpes zoster Influenza Nasopharyngitis Sinusitis Urinary tract infection Viral infection Vulvovaginal mycotic infection		
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	8 / 41 (19.51%)
occurrences (all)	0	0	10

Non-serious adverse events	Overall		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 41 (56.10%)		
Nervous system disorders			

Nervous system disorders	Additional description: Neuropathy peripheral		
subjects affected / exposed	12 / 41 (29.27%)		
occurrences (all)	14		
Blood and lymphatic system disorders			
Blood and lymphatic system disorders	Additional description: Neutropenia Leukopenia Lymphopenia		
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	4		
General disorders and administration site conditions			
General disorders and administration site conditions	Additional description: Asthenia Chest discomfort Oedema peripheral		
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Gastrointestinal disorders			
Gastrointestinal disorders	Additional description: Constipation		
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders	Additional description: Lung disorder Pulmonary embolism Rhinorrhoea		
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Infections and infestations			
Infections and infestations	Additional description: Bronchitis Herpes zoster Influenza Nasopharyngitis Sinusitis Urinary tract infection Viral infection Vulvovaginal mycotic infection		
subjects affected / exposed	8 / 41 (19.51%)		
occurrences (all)	10		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 October 2014	New version of the protocol V2 => V3 : change in inclusion and Exclusion criteria and biological exams New version of ICF
06 November 2014	New version of ICF (new exams tab)
05 November 2015	New Investigators Brochure Version 13 (ICF modification + addendum)
23 February 2017	New country involved in the study : Belgium New version of protocol V5 Clarification regarding one inclusion criteria

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported