Clinical trial results:
Brentuximab vedotin or B-CAP in the treatment of older patients with newly diagnosed classical Hodgkin Lymphoma – a GHSG-NLG Intergroup Phase II trial –

Summary

EudraCT number	2013-003990-89
Trial protocol	DE NO SE DK FI
Global end of trial date	16 November 2022

Results information

Result version number	v1 (current)
This version publication date	27 July 2023
First version publication date	27 July 2023
Summary attachment (see zip file)	Clinical_Study_Report_B-CAP_V1.0 (Clinical_Study_Report_B-CAP_V1.0.pdf)

Trial information

Trial identification

Sponsor protocol code	Uni-Koeln-1707

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02191930
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	German Hodgkin Study Group
Sponsor organisation address	Kerpener Str. 62 50924 Köln, Cologne, Germany,
Public contact	German Hodgkin Study Group, German Hodgkin Study Group, 0049 221478 88200, ghsg@uk-koeln.de
Scientific contact	German Hodgkin Study Group, German Hodgkin Study Group, 0049 221478 88200, ghsg@uk-koeln.de

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	16 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 March 2022
Global end of trial reached?	Yes
Global end of trial date	16 November 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of the B-CAP trial was to establish a well-known and tolerable CHOP regimen with the highly active brentuximab vedotin that might be a valuable option for the treatment of older HL patients. The primary objectives were to show efficacy of B-CAP in older patients with advanced-stage cHL, and to show efficacy of brentuximab vedotin monotherapy in older cHL patients not eligible to receive poly-chemotherapy. Secondary objectives were to show the safety and feasibility of B-CAP and brentuximab vedotin monotherapy.

Protection of trial subjects:

Insurance protection for the patients participating in this trial in Germany is provided by HDI Gerling Versicherung AG, insurance policy no. 57 010309 03010.
Insurance protection for the patients participating in this trial in Sweden, Denmark and Finland is provided by HDI-Gerling Industrial Insurance Co – UK Branch, insurance policy no. 390-01163636-14004.
Insurance protection for the patients participating in this trial in Norway is in accordance with the Product Liability Act in the Drug Insurance.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 November 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 29
Country: Number of subjects enrolled	Norway: 9
Country: Number of subjects enrolled	Finland: 7
Country: Number of subjects enrolled	Denmark: 14
Country: Number of subjects enrolled	Sweden: 11
Worldwide total number of subjects	70
EEA total number of subjects	70

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)	20
From 65 to 84 years	46
85 years and over	4

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	70
Number of subjects completed	70

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	B-CAP

Arm description:

Patients with ECOG of 2 or less (3 or less if caused by HL) and CIRS-G score of 6 or less (overall) and 3 or less per organ system receive 6 cycles of B-CAP (Brentuximab vedotin, cyclophosphamide, doxorubicine, predniso(lo)ne). Cycle length is 21 days

Arm type	Experimental
Investigational medicinal product name	Brentuximab-Vedotin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Brentuximab vedotin is administered as a 30-minute infusion. The patient should be observed for 60 minutes following the first infusion of brentuximab vedotin. During this observation period, the i.v. line should remain open for at least one hour to allow administration of i.v. drugs if necessary. All supportive measures consistent with optimal patient care will be given throughout the study according to institutional standards. Medications for infusion-related reactions, such as epinephrine, antihistamines, and corticosteroids, should be available for immediate use.

Arm title	Brentuximab vedotin monotherapy

Arm description:

Patients with CIRS-G score of 7 or more receive Brentuximab Vedotin as single agent therapy for up to 16 cycles. Cycle length is 21 days.

Arm type	Not eligible for B-CAP
Investigational medicinal product name	Brentuximab-Vedotin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Brentuximab vedotin is administered as a 30-minute infusion. The patient should be observed for 60 minutes following the first infusion of brentuximab vedotin. During this observation period, the i.v. line should remain open for at least one hour to allow administration of i.v. drugs if necessary. All supportive measures consistent with optimal patient care will be given throughout the study according

to institutional standards. Medications for infusion-related reactions, such as epinephrine, antihistamines, and corticosteroids, should be available for immediate use.

Number of subjects in period 1	B-CAP	Brentuximab vedotin monotherapy
Started	50	20
Completed	48	18
Not completed	2	2
Adverse event, serious fatal	1	-
Consent withdrawn by subject	1	-
Protocol deviation	-	2

Baseline characteristics

Reporting groups	
Reporting group title	B-CAP
Reporting group description:	
Patients with ECOG of 2 or less (3 or less if caused by HL) and CIRS-G score of 6 or less (overall) and 3 or less per organ system receive 6 cycles of B-CAP (Brentuximab vedotin, cyclophosphamide, doxorubicine, predniso(lo)ne). Cycle length is 21 days	
Reporting group title	Brentuximab vedotin monotherapy
Reporting group description:	
Patients with CIRS-G score of 7 or more receive Brentuximab Vedotin as single agent therapy for up to 16 cycles. Cycle length is 21 days.	

Reporting group values	B-CAP	Brentuximab vedotin monotherapy	Total
Number of subjects	50	20	70
Age categorical			
Age categorial			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	19	1	20
From 65-84 years	31	15	46
85 years and over	0	4	4
Age continuous			
Age continuous			
Units: years			
median	66	80.50	
standard deviation	± 5.8	± 6.9	-
Gender categorical			
Units: Subjects			
Female	23	7	30
Male	27	13	40

Subject analysis sets	
Subject analysis set title	B-CAP Group
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Intention to treat (ITT): 48	

Subject analysis set title	BV Group
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Intention to treat (ITT): 18	

Reporting group values	B-CAP Group	BV Group	
Number of subjects	48	18	
Age categorical			
Age categorial			
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)	19	1	
From 65-84 years	29	13	
85 years and over	0	4	
Age continuous			
Age continuous			
Units: years			
median	66.0	82.0	
standard deviation	± 5.9	± 7.1	
Gender categorical			
Units: Subjects			
Female	23	7	
Male	26	12	

End points

End points reporting groups

Reporting group title	B-CAP

Reporting group description:

Patients with ECOG of 2 or less (3 or less if caused by HL) and CIRS-G score of 6 or less (overall) and 3 or less per organ system receive 6 cycles of B-CAP (Brentuximab vedotin, cyclophosphamide, doxorubicine, predniso(lo)ne). Cycle length is 21 days

Reporting group title	Brentuximab vedotin monotherapy

Reporting group description:

Patients with CIRS-G score of 7 or more receive Brentuximab Vedotin as single agent therapy for up to 16 cycles. Cycle length is 21 days.

Subject analysis set title	B-CAP Group
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Intention to treat (ITT): 48

Subject analysis set title	BV Group
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Intention to treat (ITT): 18

Primary: objective response rate (ORR)

End point title	objective response rate (ORR)[1]

End point description:

End point type	Primary

End point timeframe:

Primary endpoint of the study is the objective response rate (ORR), defined as the proportion of patients having CR, CRr or PR in the centrally reviewed restaging after six cycles of chemotherapy.

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: Arms have not been compared because the BV Mono Arm is not a comparison Arm. BV Mono Arm has been created for patients that were not eligible for chemotherapy (B-CAP).

End point values	B-CAP Group	BV Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48	18		
Units: patients				
CR	21	4		
PR	26	7		
Progressive disease	1	4		
missed restaging after chemotherapy	0	2		
no change in tumor growth	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The investigator has to report every serious adverse event and every pregnancy directly (within one working day) to the Trial Chairman.
Every SAE has to be reported immediately using an SAE form and has to be sent to the stated address.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.2

Reporting groups

Reporting group title	B-CAP
Reporting group description: -	
Reporting group title	BV Mono
Reporting group description: -	

Serious adverse events	B-CAP	BV Mono	
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 49 (57.14%)	13 / 19 (68.42%)	
number of deaths (all causes)	9	7	
number of deaths resulting from adverse events	1	3	
Vascular disorders			
Jugular vein thrombosis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			

subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	3 / 49 (6.12%)	2 / 19 (10.53%)	
occurrences causally related to treatment / all	2 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 49 (0.00%)	2 / 19 (10.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonia			
subjects affected / exposed	1 / 49 (2.04%)	2 / 19 (10.53%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			

subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	12 / 49 (24.49%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	10 / 12	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal angina			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epigastric discomfort			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Erysipelas			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Dysuria			

subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Abscess soft tissue			
subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infection			
subjects affected / exposed	2 / 49 (4.08%)	3 / 19 (15.79%)	
occurrences causally related to treatment / all	1 / 2	3 / 3	
deaths causally related to treatment / all	1 / 1	3 / 3	
Pneumonia			
subjects affected / exposed	1 / 49 (2.04%)	2 / 19 (10.53%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	3 / 49 (6.12%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	1 / 49 (2.04%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonas infection			
subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 49 (0.00%)	2 / 19 (10.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	B-CAP	BV Mono	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 49 (10.20%)	5 / 19 (26.32%)	
Vascular disorders			
Stasis dermatitis			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Therapeutic embolisation			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Oedema			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Catheter site infection			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Immune system disorders			
Sarcoidosis			

subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Psychiatric disorders			
Nervousness			
subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Investigations			
White blood cell count decreased			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Polyneuropathy			
subjects affected / exposed	1 / 49 (2.04%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 49 (2.04%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Dry mouth			
subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Back pain			

subjects affected / exposed	1 / 49 (2.04%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Bone pain			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Myopathy			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Infections and infestations			
Wound infection			
subjects affected / exposed	1 / 49 (2.04%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Fungal infection			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Weight fluctuation			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Weight loss poor			
subjects affected / exposed	0 / 49 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported