Clinical trial results:
Bendamustine, Prednisone and Velcade® for first-line treatment of patients with symptomatic multiple myeloma not eligible for high-dose chemotherapy followed by autologous stem cell transplantation (BPV).

Summary

EudraCT number	2013-005485-19
Trial protocol	DE
Global end of trial date	23 August 2018

Results information

Result version number	v1 (current)
This version publication date	28 April 2022
First version publication date	28 April 2022
Summary attachment (see zip file)	BPVSummary (BPVSummary.pdf)

Trial information

Trial identification

Sponsor protocol code	BPV

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02237261
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Heidelberg University Hospital
Sponsor organisation address	Im Neuenheimer Feld 672, Heidelberg, Germany, 69120
Public contact	GMMG Studiensekretariat Medizinische Klinik V und Nationales Centrum für Tumorerkrankungen, Universitätsklinikum Heidelberg INF130.3 69120 Heidelberg Germany, +49 6221 568198, S.GMMG@med.uni-heidelberg.de
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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	11 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 August 2018
Global end of trial reached?	Yes
Global end of trial date	23 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of the study is to demonstrate the efficacy of BPV to efficiently decrease myeloma tumor burden.

Protection of trial subjects:

Safety date were reviewed by a DSMB

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 November 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	Germany: 46
Worldwide total number of subjects	46
EEA total number of subjects	46

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)	2
From 65 to 84 years	44
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

For recruitment patients diagnosed with multiple myeloma requiring systemic treatment (in accordance to CRAB criteria) were informed regarding the trial and offered to undergo screening examination for inclusion. Written informed consent was mandatory for inclusion into the trial.

Pre-assignment

Screening details:

Prior to inclusion, patients had to be registered at the GMMG by fax, including information regarding eligibility criteria and the investigational site. Also, data of the following parameters were transmitted:
Serum M-protein (concentration of monoclonal protein in serum)
Urine M-protein (Bence Jones)
sFLC in case of hyposecretory myeloma.

Period 1

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

Arms

Arm title	Treatment arm

Arm description:

First line treatment of patients with symptomatic multiple myeloma

Arm type	Experimental
Investigational medicinal product name	bendamustine
Investigational medicinal product code	LO1AA09
Other name	Levact(R)
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

All patients received bendamustine in a dose of 90 mg/m2 body surface area (BSA).
Bendamustine was administered by i.v. infusion over 30-60 minutes.

Investigational medicinal product name	prednisone
Investigational medicinal product code	H02AB07
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

60mg/m² as Tablets days 1-4

Investigational medicinal product name	bortezomib
Investigational medicinal product code	ATC code LO1AA09
Other name	Velcade ®
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

All patients received bortezomib in a dose of 1.3 mg/m2 body surface area (BSA) as a subcutaneous injection.

Number of subjects in period 1	Treatment arm
Started	46
Completed	46

Baseline characteristics

Reporting groups	
Reporting group title	Treatment
Reporting group description:	
Treatment group only (no comparator)	

Reporting group values	Treatment	Total	
Number of subjects	46	46	
Age categorical Units: Subjects			
Adults (18-64 years)	2	2	
From 65-84 years	44	44	
Gender categorical Units: Subjects			
Female	27	27	
Male	19	19	

Subject analysis sets	
Subject analysis set title	Per Protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
Of all patients included, 33 fulfilled the criteria of the per-protocol analysis set, in particular the completion of 3 cycles of treatment.	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
In this data set, all 46 patients included were analysed.	

Reporting group values	Per Protocol	ITT	
Number of subjects	33	46	
Age categorical Units: Subjects			
Adults (18-64 years)	0	2	
From 65-84 years	33	44	
Gender categorical Units: Subjects			
Female	23	27	
Male	10	19	

End points

End points reporting groups

Reporting group title	Treatment arm

Reporting group description:

First line treatment of patients with symptomatic multiple myeloma

Subject analysis set title	Per Protocol
Subject analysis set type	Per protocol

Subject analysis set description:

Of all patients included, 33 fulfilled the criteria of the per-protocol analysis set, in particular the completion of 3 cycles of treatment.

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

In this data set, all 46 patients included were analysed.

Primary: Overall response rate PP

End point title	Overall response rate PP[1]

End point description:

The overall response rate (ORR) was defined as PR or better during the 9 treatment cycles. Response to treatment was evaluated according to IMWG criteria. The PP population was defined as those patients in the ITT population who completed at least 3 cycles of BPV therapy and were evaluable for response without major protocol violations. Best response was used to calculate ORR.

End point type	Primary

End point timeframe:

during 9 treatment cycles

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: There was only one treatment arm in this study (no control group). The following estimate was calculated in comparison to a predefined ORR of 67%.
The 95% one-sided confidence interval was identified as mean 0.7879, lower 0.6495, and p-value 0.0876. Despite the positive therapeutic results for the PP population, the statistical analysis could not confirm a statistically significant increase in ORR above 67% as predefined to reject the H0 hypothesis.

End point values	Per Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	33			
Units: Patients				
near complete response	9			
very good partial response	9			
partial response	8			
minimal response	5			

Attachments (see zip file)	BPV_analysisPP.png

Statistical analyses

No statistical analyses for this end point

Secondary: renal outcome

End point title	renal outcome

End point description:

to investigate the percentage of patients with recovery/improvement of renal function (for patients with impaired renal function at baseline, n= 19)

End point type	Secondary

End point timeframe:

during treatment cycles

End point values	Treatment arm	ITT		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	19[2]	19[3]		
Units: number of patients				
non-responder	8	8		
responder	11	11		

Notes:

[2] - patients with impaired renal function at baseline

[3] - Only patients with renal impairment at baseline were analysed

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events that have a start date during or within 30 days after end of treatment.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1/21.0

Reporting groups	
Reporting group title	Safety population
Reporting group description:	
Fatal adverse events.	

Serious adverse events	Safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 46 (50.00%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events	2		
Injury, poisoning and procedural complications			
Injury,poisoning,procedural complications			
subjects affected / exposed	2 / 46 (4.35%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac			
subjects affected / exposed	4 / 46 (8.70%)		
occurrences causally related to treatment / all	1 / 7		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Nervous system disorders			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrointestinal			

subjects affected / exposed	5 / 46 (10.87%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
respiratory,thoracic,mediastinal			
subjects affected / exposed	2 / 46 (4.35%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	1 / 1		
Hepatobiliary disorders			
Hepatobiliary disorders			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Psychiatric disorders			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infections and infestations			
subjects affected / exposed	11 / 46 (23.91%)		
occurrences causally related to treatment / all	0 / 12		
deaths causally related to treatment / all	1 / 1		

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

Non-serious adverse events	Safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 46 (78.26%)		
Vascular disorders			
Vascular disorder			
subjects affected / exposed	4 / 46 (8.70%)		
occurrences (all)	4		
Nervous system disorders			

Nervous system subjects affected / exposed occurrences (all)	7 / 46 (15.22%) 7		
Blood and lymphatic system disorders Blood and lymphatic system subjects affected / exposed occurrences (all)	11 / 46 (23.91%) 11		
Gastrointestinal disorders Gastrointestinal subjects affected / exposed occurrences (all)	3 / 46 (6.52%) 3		
Infections and infestations Infections and infestations subjects affected / exposed occurrences (all)	12 / 46 (26.09%) 12		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 April 2016	Reduction of sample size

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32155662