Clinical trial results:
A randomised comparison of daily 25 mg versus 5 mg lenalidomide as maintenance therapy after high-dose therapy and autologous stem cell transplantation in patients with multiple myeloma.

Summary

EudraCT number	2007-003945-33
Trial protocol	DE
Global end of trial date	22 June 2017

Results information

Result version number	v1 (current)
This version publication date	08 October 2020
First version publication date	08 October 2020
Summary attachment (see zip file)	LenaMain Results Summary (Summary results_LenaMain V01-F 16JUN2018.pdf)

Trial information

Trial identification

Sponsor protocol code	RV-MM-PI-280

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00891384
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gesellschaft für Medizinische Innovation –Hämatologie und Onkologie mbH (GMIHO)
Sponsor organisation address	Almstadtstraße 7, Berlin, Germany, 10119
Public contact	Medical Consulting, Gesellschaft für Medizinische Innovation –Hämatologie und Onkologie mbH (GMIHO), +49 35125933100, info@gmiho.de
Scientific contact	Prof. Dr. Guido Kobbe, Department of Hematology, Oncology and Clinical Immunology Heinrich-Heine-University, +49 211 8117720, Kobbe@med.uni-duesseldorf.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 June 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 June 2017
Global end of trial reached?	Yes
Global end of trial date	22 June 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Compare the event-free survival (EFS) of patients with multiple myeloma who receive two different dose levels (25 vs. 5 mg daily) of lenalidomide as maintenance therapy after first line high-dose therapy and autologous stem cell transplantation.

Protection of trial subjects:

The conduct, evaluation, and documentation of this study, was in compliance with the Good Clinical Practice Guidelines and under the guiding principles detailed in the Declaration of Helsinki. The study was also be carried out in keeping with applicable local law(s) and regulation(s) as well as GDPR. All toxicities were monitored and patients who had rash, myelotoxicity of grade 2 or more, thrombo-embolic events of grade 2 or more, neuropathy of grade two or more, bradycardia of grade 3 or more, change in performance status, transfusion requirement, bleeding complications grade 3 or more and infections grade 3 or more were examined.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 June 2009
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	Germany: 188
Worldwide total number of subjects	188
EEA total number of subjects	188

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)	144
From 65 to 84 years	44
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 6 study sites in Germany. From 04 June 2009 until 01 February 2015 on a total of 194 patients were included.

Pre-assignment

Screening details:

Inclusion of 194 patients was planned, and the analysis of the primary endpoint was planned to be done after at least 96 subjects have developed disease progression. 194 patients were included and 188 are eligible for the analysis of the primary endpoint as there were 6 screening failures.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Arm A

Arm description:

Oral lenalidomide was given on day 1 of cycle 1 of consolidation therapy at a dose of 25 mg daily for 21 days every 28 days. After 6 cycles of consolidation therapy patients were treated in Arm A and received 25 mg lenalidomide daily for 21 days every 28 days. Treatment was continued as tolerated until disease progression developed.

Arm type	Experimental
Investigational medicinal product name	Lenalidomide
Investigational medicinal product code	
Other name	Revlimid®
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

All patients started with consolidation therapy. Consolidation therapy consisted of 6 cycles of lenalidomide 25 mg daily for 21 days every 28 days. After consolidation therapy patients treated with 25 mg lenalidomide daily for 21 days every 28 days. Maintenance therapy was continued until disease progression occured or untolerable side effects occur despite of dose reduction or the study ends.

Arm title	Arm B

Arm description:

Oral lenalidomide was given on day 1 of cycle 1 of consolidation therapy at a dose of 25 mg daily for 21 days every 28 days. After 6 cycles of consolidation therapy patients were treated in Arm B and received 5 mg lenalidomide daily for 21 days every 28 days. Treatment was continued as tolerated until disease progression developed.

Arm type	Experimental
Investigational medicinal product name	Lenalidomide
Investigational medicinal product code	
Other name	Revlimid®
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

All patients started with consolidation therapy. Consolidation therapy consisted of 6 cycles of lenalidomide 25 mg daily for 21 days every 28 days. After consolidation therapy patients treated with 5 mg lenalidomide daily for 21 days every 28 days. Maintenance therapy was continued until disease progression occured or untolerable side effects occur despite of dose reduction or the study ends.

Number of subjects in period 1	Arm A	Arm B
Started	94	94
Completed	94	94

Baseline characteristics

Reporting groups	
Reporting group title	Arm A
Reporting group description:	
Oral lenalidomide was given on day 1 of cycle 1 of consolidation therapy at a dose of 25 mg daily for 21 days every 28 days. After 6 cycles of consolidation therapy patients were treated in Arm A and received 25 mg lenalidomide daily for 21 days every 28 days. Treatment was continued as tolerated until disease progression developed.	
Reporting group title	Arm B
Reporting group description:	
Oral lenalidomide was given on day 1 of cycle 1 of consolidation therapy at a dose of 25 mg daily for 21 days every 28 days. After 6 cycles of consolidation therapy patients were treated in Arm B and received 5 mg lenalidomide daily for 21 days every 28 days. Treatment was continued as tolerated until disease progression developed.	

Reporting group values	Arm A	Arm B	Total
Number of subjects	94	94	188
Age categorical 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)	72	72	144
From 65-84 years	22	22	44
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	38	34	72
Male	56	60	116

End points

End points reporting groups

Reporting group title	Arm A

Reporting group description:

Oral lenalidomide was given on day 1 of cycle 1 of consolidation therapy at a dose of 25 mg daily for 21 days every 28 days. After 6 cycles of consolidation therapy patients were treated in Arm A and received 25 mg lenalidomide daily for 21 days every 28 days. Treatment was continued as tolerated until disease progression developed.

Reporting group title	Arm B

Reporting group description:

Oral lenalidomide was given on day 1 of cycle 1 of consolidation therapy at a dose of 25 mg daily for 21 days every 28 days. After 6 cycles of consolidation therapy patients were treated in Arm B and received 5 mg lenalidomide daily for 21 days every 28 days. Treatment was continued as tolerated until disease progression developed.

Primary: Event-free Survival (EFS)

End point title	Event-free Survival (EFS)

End point description:

The primary efficacy endpoint was event-free survival (EFS) from the time point of randomisation, where death or progress counted as events.

End point type	Primary

End point timeframe:

from randomisation until the 96th patient experienced relapse

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	94		
Units: 10	94	94		

Statistical analyses

Statistical analysis title	Primary statistical analysis
Comparison groups	Arm A v Arm B
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	Logrank

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: from randomisation until experienced relapse	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Frequency threshold for reporting non-serious adverse events: 3 %

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: The majority of the AEs of a grade ≥ 3 were of the System Organ Class Blood/Bone Marrow, where the most common AEs of a grade ≥ 3 indicate a decrease in Neutrophils/granulocytes (ANC/AGC) or Leukocytes (total WBC) (graded according to the NCI CTCAE v3.0). The safety analysis indicated that in Arm A (25 mg lenalidomide daily) the number of patients with at least one adverse event (AE) of a grade ≥ 3 was higher than in Arm B (5 mg lenalidomide daily) (84 (87.5%) vs. 62 (64.58%).

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 April 2009	Protocol Version 20, 06.03.2009: Changing of Sponsor`s Address; MRT with contrast material
12 July 2012	Protocol Version 21, 18.06.2012: Changing of Sponsor`s Address; changing of the manufacturing of Lenalidomide-> Bottles to blister
07 November 2012	Protocol Version 23, 02.10.2012: Different reasons of dosis reduction; recommendation on treatment of Infections; new study site
05 April 2013	Protocol Version 24, 15.01.2013: new study site
12 September 2013	Protocol Version 26, 21.08.2013: recommendation on prior therapy new SmPC
04 August 2014	Protocol Version 27, 02.06.2014: new SmPC
01 August 2016	Protocol Version 29, 06.07.2016: new PPP (Pregnancy Prevention Plan)

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/32817078