Clinical trial results:
The combination of Lenalidomide and Dexamethasone with or without intensification by high-dose Melphalan in the treatment of multiple myeloma

Summary

EudraCT number	2008-004083-39
Trial protocol	DE
Global end of trial date	31 January 2020

Results information

Result version number	v1 (current)
This version publication date	09 June 2022
First version publication date	09 June 2022
Summary attachment (see zip file)	Justification no results in EudraCT (DSMM XIII_Sponsor Statment no results in EudraCT DB_23May2022.pdf)

Trial information

Trial identification

Sponsor protocol code	DSMM_XIII

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01090089
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GMIHO Gesellschaft für Medizinische Innovation – Hämatologie und Onkologie mbH
Sponsor organisation address	Almstadtstraße 7, Berlin, Germany, 10119
Public contact	GMIHO, GMIHO Gesellschaft für Medizinische Innovation – Hämatologie und Onkologie mbH, 0049 351 25 933100, info@gmiho.de
Scientific contact	GMIHO, GMIHO Gesellschaft für Medizinische Innovation – Hämatologie und Onkologie mbH, 0049 351 25 933100, info@gmiho.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	24 May 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of both treatment regimens with regard to progression-free survival.

Protection of trial subjects:

The conduct, documentation and evaluation of this study was compliant to Good Clinical Practice 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 adverse clinical experiences observed by the investigator and reported by the patient were recorded with details about duration and intensity of each episode as well as action taken related to the study drug and its outcome. The investigator had to evaluate each adverse experience for its relationship to the study drug and for its seriousness. Moreover, during and after each cycle the observed toxicity of treatment was considered for continuation of therapy and indicated dose modifications had to be performed. Furthermore, the investigator had to assess all abnormal laboratory results for their clinical significance. If any abnormal laboratory result considered clinically significant, the investigator had to provided details about the action taken in relation to the study drug and the outcome.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 March 2010
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: 348
Worldwide total number of subjects	348
EEA total number of subjects	348

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)	0
From 65 to 84 years	348
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Approximately 348 patient with multiple myeloma (MM) should screened for enrollment at 40 sites in Germany.

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?	Yes
Arm title	Arm A1

Arm description:

In patients in treatment arm A1 the therapy with lenalidomide and low-dose dexamethasone (Rd) were continued when stem cell mobilization and harvest of peripheral blood stem cells (PBSC) was finished, usually 3-4 weeks after the start of stem cell mobilization therapy. The study treatment with lenalidomide and low-dose dexamethasone was given until progression and stopped when progression was documented or when intolerable side effects occurred. Patients in arm A1 treated with autologous stem cell transplantation only in case of relapse or progression.

Arm type	Experimental
Investigational medicinal product name	Lenalidomide
Investigational medicinal product code	
Other name	Revlimid®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg orally once daily on days 1 to 21 of repeated 28 days cycles until progression or intolerable side effects

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

Dosage and administration details:

40 mg orally once daily on days 1, 8, 15 and 22 of repeated 28 days cycles until progression or intolerable side effects

Arm title	Arm A2

Arm description:

Patients in arm A2 received a tandem high-dose melphalan (140 mg/m²) with peripheral blood stem cell transplantation (PBSCT) after stem cell mobilization and PBSC. Accordingly, patients who had a sufficient stem cell transplant got the first melphalan (140 mg/m²) within 2-4 weeks after stem cell harvest. The second melphalan (140 mg/m²) was scheduled two months after the first melphalan (140 mg/m²). In treatment arm A2 lenalidomide (10 mg/day) maintenance was applied and started within 2-3 months from the second PBSCT for patients without signs of progression who had an adequate reconstitution of hematopoiesis post–transplant.

Arm type	Experimental

Investigational medicinal product name	Lenalidomide
Investigational medicinal product code	
Other name	Revlimid®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Mode of administration:
induction therapy: 25 mg orally once daily on days 1 to 21 of repeated 28 days cycles for 3 cycles
maintenance therapy: 10 mg orally once daily of repeated 28 days cycles until progression or intolerable side effects

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

Dosage and administration details:

induction therapy: 40 mg orally once daily on days 1, 8, 15 and 22 of repeated 28 days cycles for 3 cycles

Investigational medicinal product name	Melphalan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

first high-dose 140 mg/m² intravenous infusion followed by PBSCT 2-4 weeks after stem cell harvest; second high-dose 140 mg/m² intravenous infusion followed by PBSCT after 2 months of first high-dose 140 mg/m² administration

Number of subjects in period 1	Arm A1	Arm A2
Started	174	174
Completed	174	174

Baseline characteristics

End points

End points reporting groups

Reporting group title	Arm A1

Reporting group description:

In patients in treatment arm A1 the therapy with lenalidomide and low-dose dexamethasone (Rd) were continued when stem cell mobilization and harvest of peripheral blood stem cells (PBSC) was finished, usually 3-4 weeks after the start of stem cell mobilization therapy. The study treatment with lenalidomide and low-dose dexamethasone was given until progression and stopped when progression was documented or when intolerable side effects occurred. Patients in arm A1 treated with autologous stem cell transplantation only in case of relapse or progression.

Reporting group title	Arm A2

Reporting group description:

Patients in arm A2 received a tandem high-dose melphalan (140 mg/m²) with peripheral blood stem cell transplantation (PBSCT) after stem cell mobilization and PBSC. Accordingly, patients who had a sufficient stem cell transplant got the first melphalan (140 mg/m²) within 2-4 weeks after stem cell harvest. The second melphalan (140 mg/m²) was scheduled two months after the first melphalan (140 mg/m²). In treatment arm A2 lenalidomide (10 mg/day) maintenance was applied and started within 2-3 months from the second PBSCT for patients without signs of progression who had an adequate reconstitution of hematopoiesis post–transplant.

Primary: progression-free survival (PFS)

End point title	progression-free survival (PFS)

End point description:

End point type	Primary

End point timeframe:

from the time point of randomization until progression or intolerable side effects

End point values	Arm A1	Arm A2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	174		
Units: Number of patients				
number (not applicable)	174	174		

Statistical analyses

Statistical analysis title	No analysis
Comparison groups	Arm A1 v Arm A2
Number of subjects included in analysis	348
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	≤ 0.045
Method	t-test, 1-sided

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: until progression	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Frequency threshold for reporting non-serious adverse events: 0 %

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: Due to the COVID-19 pandemic and its lockdown and restrictions the planned monitoring activities could not be entirely performed. Therefore, no or limited source data verification (SDV) for endpoints at the sites were possible. Obligatory established hygienical concepts also resulted to significant delays in collecting remaining data. This led to the fact that the data for the final analysis were not available at the scheduled time.

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