Clinical trial results:
LENALIDOMIDE MAINTENANCE IN MULTIPLE MYELOMA PATIENTS ACHIEVING AT LEAST VGPR AFTER INDUCTION THERAPY: MINIMAL RESIDUAL DISEASE MONITORING

Summary

EudraCT number	2012-004063-52
Trial protocol	IT
Global end of trial date	31 August 2017

Results information

Result version number	v1 (current)
This version publication date	21 January 2023
First version publication date	21 January 2023

Trial information

Trial identification

Sponsor protocol code	RV-MM-PI-0694

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03433365
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	FONDAZIONE EMN ITALY ONLUS
Sponsor organisation address	Via Saluzzo 1/A, Torino, Italy, 10125
Public contact	Data Center, Fondazione EMN Italy ONLUS, 011 0243236, clinicaltrialoffice@emn.org
Scientific contact	Data Center, Fondazione EMN Italy ONLUS, 011 0243236, clinicaltrialoffice@emn.org

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	02 December 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 August 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1.To evaluate the activity of Lenalidomide on tumour load during maintenance phase analysing; 2.To verify whether molecular remissions obtained during maintenance therapy with Lenalidomide-based regimen are associated with a prolonged PFS.

Protection of trial subjects:

Under approval of Local Etical Commitee

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2012
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	Italy: 73
Worldwide total number of subjects	73
EEA total number of subjects	73

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)	73
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

NA

Period 1

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

Arms

Arm title	MRD analysis

Arm description:

MRD analysis

Arm type	NOT APPLICABLE
Investigational medicinal product name	No intervention_Observational study
Investigational medicinal product code	O
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

No intervention_Observational study
Potential study subjects will sign an informed consent prior undergoing any study related procedure. Patients enrolled in this study will receive Lenalidomide-based regimen as maintenance therapy according to their previous decided therapeutic schedule. All consecutive patients treated with Lenalidomide-based regimen as maintenance therapy and with inclusion criteria will be asked to participate to this study.

To collect 2 samples for MRD analysis in patients treated with Lenalidomide

Number of subjects in period 1	MRD analysis
Started	73
Completed	73

Baseline characteristics

Reporting groups

Reporting group title	Pre-maintenance

Reporting group description: -

Reporting group values	Pre-maintenance	Total	
Number of subjects	73	73	
Age categorical 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)	73	73	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
median	57		
inter-quartile range (Q1-Q3)	53 to 61	-	
Gender categorical Units: Subjects			
Female	36	36	
Male	37	37	
ISS Stage Units: Subjects			
Stage I	30	30	
Stage II	33	33	
Stage III	10	10	

Subject analysis sets

Subject analysis set title	Pre-maintenance
Subject analysis set type	Per protocol

Subject analysis set description:

The MRD population was defined as patients who had an available MRD sample before and/or after starting maintenance.

Reporting group values	Pre-maintenance		
Number of subjects	73		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	73		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
median	57		
inter-quartile range (Q1-Q3)	53 to 61		
Gender categorical			
Units: Subjects			
Female	36		
Male	37		
ISS Stage			
Units: Subjects			
Stage I	30		
Stage II	33		
Stage III	10		

End points

End points reporting groups

Reporting group title	MRD analysis
Reporting group description: MRD analysis	
Subject analysis set title	Pre-maintenance
Subject analysis set type	Per protocol
Subject analysis set description: The MRD population was defined as patients who had an available MRD sample before and/or after starting maintenance.	

Primary: MRD conversion ASO-RQ-PCR

End point title	MRD conversion ASO-RQ-PCR[1]
End point description: PFS analysis among patients with persistent MRD negativity and patients who turned to MRD positive by ASO-RQ-PCR	
End point type	Primary
End point timeframe: 40 months	
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: Statistical analysis and P value are not reported since the system give me an error that I'm not able to understand and fix. All p values are reported in the publication	

End point values	Pre-maintenance			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: time to event endpoint				
median (inter-quartile range (Q1-Q3))				
m-CR	70 (70 to 70)			
no m-CR	27.2 (21.5 to 40.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival ASO-RQ-PCR

End point title	Progression Free Survival ASO-RQ-PCR
End point description: PFS was calculated from the date of BM sampling before maintenance to the date of progression or death or the date the patient was last known to be in remission.	
End point type	Secondary
End point timeframe: 40 Months	

End point values	Pre-maintenance			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: Time to event Endpoint				
median (confidence interval 95%)				
m-CR No m-CR	70 (70 to 70) 26 (26 to 26)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival MFC

End point title	Progression Free Survival MFC

End point description:

PFS was calculated from the date of BM sampling before maintenance to the date of progression or death or the date the patient was last known to be in remission.

End point type	Secondary

End point timeframe:

40 months

End point values	Pre-maintenance			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: Time to event				
median (inter-quartile range (Q1-Q3))				
flow-CR No flow-CR	70 (70 to 70) 19.5 (19.5 to 19.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Comparison of MFC and ASO-RQ-PCR Analyses

End point title	Comparison of MFC and ASO-RQ-PCR Analyses

End point description:

The Pearson correlation coefficient (r) was used to compare methods of MRD analysis (ASORQ-PCR and MFC)

End point type	Secondary

End point timeframe:

40 monts

End point values	Pre-maintenance			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: rho correlation				
number (confidence interval 95%)	0.9 (0.89 to 0.93)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival ASO-RQ-PCR

End point title	Overall Survival ASO-RQ-PCR

End point description:

OS was calculated from the date of BM sampling before maintenance to the date of death or the date the patient was last known to be alive.

End point type	Secondary

End point timeframe:

40 months

End point values	Pre-maintenance			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: Time to event ednpoint				
median (inter-quartile range (Q1-Q3))				
m-CR	70 (70 to 70)			
No m-CR	59.3 (59.3 to 59.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival MFC

End point title	Overall Survival MFC

End point description:

OS was calculated from the date of BM sampling before maintenance to the date of death or the date the patient was last known to be alive.

End point type	Secondary

End point timeframe:

40 months

End point values	Pre-maintenance			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: Time to event				
median (inter-quartile range (Q1-Q3))				
flow-CR	70 (70 to 70)			
No flow-CR	60.4 (59.4 to 60.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: MRD conversion MFC

End point title	MRD conversion MFC

End point description:

PFS analysis among patients with persistent MRD negativity and patients who turned to MRD positive by MFC

End point type	Secondary

End point timeframe:

40 monhts

End point values	Pre-maintenance			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: time to event				
median (inter-quartile range (Q1-Q3))				
m -CR	70 (70 to 70)			
no m-CR	35.3 (22.6 to 35.3)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]
Timeframe for reporting adverse events:
Not applicable for this study
Adverse event reporting additional description:
Not applicable for this study. Assessment type, Dictioanry are mandatory, but filled in only to save page. AE is not collected

Assessment type	Non-systematic

Dictionary used

Dictionary name	NO AE
Dictionary version	0

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

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: AE is not collected and so analyzed for this study

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 April 2017	- Updated Sponsor Name and Contact - Added "study Commitees" A steering committee that includes a subset of investigators in this study and representatives from Sponsor will be formed to provide advice on the conduct of the study and publications." - Added "If the serum and urine M-protein are unmeasurabled a > 90% decrease in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria."

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported