Clinical trial results:
A PHASE II,MULTI-CENTER, OPEN LABEL STUDY OF ORAL LBH589 PLUS MELPHALAN, PREDNISONE AND THALIDOMIDE (LB-MPT)IN ADVANCED, REFRACTORY MULTIPLE MYELOMA PATIENTS.

Summary

EudraCT number	2007-007939-29
Trial protocol	IT
Global end of trial date	11 April 2017

Results information

Result version number	v1 (current)
This version publication date	29 March 2023
First version publication date	29 March 2023

Trial information

Trial identification

Sponsor protocol code	CLBH589BIT01T

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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	31 May 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 April 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Determine whether the combination LB-MPT (with escalating dose of LB589) is safe and effective in advanced/refractory MM patients.

Protection of trial subjects:

Under approval of Local Etical Commitee

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 May 2008
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: 31
Worldwide total number of subjects	31
EEA total number of subjects	31

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	31
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The pre-treatment period includes the screening visit, performed at study entry. After providing written informed consent to participate in the study, patients will be evaluated for study eligibility

Pre-assignment period milestones

Number of subjects started	31
Number of subjects completed	31

Period 1

Period 1 title	Treatment
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	LB-MPT

Arm description:

LBH589, melphalan, prednisone, thalidomide

Arm type	Experimental
Investigational medicinal product name	LBH589
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Level 0 = starting dose LBH589 = 15 mg once daily on days 1, 3, 5, 8, 10, 12, 15, 17, 19 followed by 9-day rest period (day 20 through 28).
Level – 1 LBH589 = 10 mg once daily on days 1, 3, 5, 8, 10, 12, 15, 17, 19 followed by 9-day rest period (day 20 through 28).
Level + 1 LBH589 = 20 mg once daily on days 1, 3, 5, 8, 10, 12, 15, 17, 19 followed by 9-day rest period (day 20 through 28).

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

Dosage and administration details:

Melphalan will be given orally at the dose of 0.18 mg/Kg for 4 days. Each cycle will be repeated every 28 days for a total of 6 courses.

Investigational medicinal product name	Thalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Thalidomide will be given orally at the dose of 50 mg/day continuously.

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

Dosage and administration details:

Prednisone will be given orally at the dose of 1,5 mg/Kg for 4 days followed by a 24-day rest period (days 5 through 28). Each cycle will be repeated every 28 days for a total of 6 courses.

Number of subjects in period 1	LB-MPT
Started	31
Completed	10
Not completed	21
Adverse event, serious fatal	1
Consent withdrawn by subject	1
Adverse event, non-fatal	8
Lack of efficacy	11

Period 2

Period 2 title	Maintenance
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	LB-P

Arm description: -

Arm type	Experimental
Investigational medicinal product name	LBH589
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

LBH589 at the dose used for LB-MPT daily on days 1, 3, 5, 8, 10, 12, 15, 17, 19 followed by 9-day rest period (day 20 through 28) continuously until development of PD.

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

Dosage and administration details:

Prednisone 25 mg daily, on days 1, 3, 5 every week continuously until development of PD.

Number of subjects in period 2	LB-P
Started	10
Completed	0
Not completed	10
Adverse event, serious fatal	1
Adverse event, non-fatal	1
Lack of efficacy	8

Baseline characteristics

Reporting groups	
Reporting group title	LB-MPT
Reporting group description:	
LBH589, melphalan, prednisone, thalidomide	

Reporting group values	LB-MPT	Total	
Number of subjects	31	31	
Age categorical Units: Subjects			
Adults (18-64 years)	9	9	
From 65-84 years	22	22	
85 years and over	0	0	
Age continuous Units: years			
median	70		
full range (min-max)	40 to 81	-	
Gender categorical Units: Subjects			
Female	15	15	
Male	16	16	
ISS Stage Units: Subjects			
ISS I	17	17	
ISS II	10	10	
ISS III	4	4	
Disease status Units: Subjects			
Untested relapse	22	22	
Refractory	9	9	
Performance status (WHO) Units: Subjects			
0-1	20	20	
2-4	11	11	
Myeloma type Units: Subjects			
IgG	22	22	
IgA	6	6	
Light chain only	3	3	

Subject analysis sets	
Subject analysis set title	LB-MPT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Patient that are eligible	

Reporting group values	LB-MPT		
Number of subjects	31		
Age categorical Units: Subjects			
Adults (18-64 years)	9		
From 65-84 years	22		
85 years and over	0		
Age continuous Units: years			
median	70		
full range (min-max)	40 to 81		
Gender categorical Units: Subjects			
Female	15		
Male	16		
ISS Stage Units: Subjects			
ISS I	17		
ISS II	10		
ISS III	4		
Disease status Units: Subjects			
Untested relapse	22		
Refractory	9		
Performance status (WHO) Units: Subjects			
0-1	20		
2-4	11		
Myeloma type Units: Subjects			
IgG	22		
IgA	6		
Light chain only	3		

End points

End points reporting groups	
Reporting group title	LB-MPT
Reporting group description: LBH589, melphalan, prednisone, thalidomide	
Reporting group title	LB-P
Reporting group description: -	
Subject analysis set title	LB-MPT
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patient that are eligible	

Primary: grade 3-4 non-hematologic toxicity	
End point title	grade 3-4 non-hematologic toxicity
End point description:	
End point type	Primary
End point timeframe: 4 years	

End point values	LB-MPT	LB-MPT		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	31	31		
Units: Patients				
Yes	6	6		
No	25	25		

Statistical analyses

Statistical analysis title	No statistical analysis
Statistical analysis description: No statistical analysis	
Comparison groups	LB-MPT v LB-MPT
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0 [2]
Method	No statistical analysis
Parameter estimate	No statistical analysis
Point estimate	6

Confidence interval	
level	Other: 0 %
sides	2-sided
lower limit	6
upper limit	6
Variability estimate	Standard deviation
Dispersion value	0

Notes:

[1] - No statistical analysis

[2] - No statistical analysis

Primary: PR Rate

End point title	PR Rate

End point description:

End point type	Primary

End point timeframe:

4 years

End point values	LB-MPT	LB-MPT		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	31	31[3]		
Units: Patients				
>= PR	12	12		
< PR	19	19		

Notes:

[3] - 31

Statistical analyses

Statistical analysis title	No statistical analysis
Comparison groups	LB-MPT v LB-MPT
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.001 [5]
Method	No statistical analysis
Parameter estimate	No statistical analysis
Point estimate	12
Confidence interval	
level	Other: 0 %
sides	2-sided
lower limit	12
upper limit	12
Variability estimate	Standard error of the mean
Dispersion value	0

Notes:
[4] - No statistical analysis
[5] - No statistical analysis

Secondary: PFS

End point title	PFS

End point description:

End point type	Secondary

End point timeframe:
1 year

End point values	LB-MPT			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: percent				
number (not applicable)	59			

Statistical analyses

No statistical analyses for this end point

Secondary: OS

End point title	OS

End point description:

End point type	Secondary

End point timeframe:
1 year

End point values	LB-MPT			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: percent				
number (not applicable)	63			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
End of trial	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0
Reporting groups	
Reporting group title	LB-MPT
Reporting group description:	
LBH589, melphalan, prednisone, thalidomide	

Serious adverse events	LB-MPT		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 31 (45.16%)		
number of deaths (all causes)	29		
number of deaths resulting from adverse events	2		
Investigations			
Blood pressure decreased			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Ischaemia			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Presyncope			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	2 / 31 (6.45%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	7 / 31 (22.58%)			
occurrences causally related to treatment / all	6 / 14			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	7 / 31 (22.58%)			
occurrences causally related to treatment / all	5 / 10			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
General disorders and administration site conditions				
Fatigue				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	2 / 31 (6.45%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Cough				

subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Pulmonary alveolar haemorrhage			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		

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

Non-serious adverse events	LB-MPT		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 31 (96.77%)		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	28 / 31 (90.32%)		
occurrences (all)	31		
Thrombocytopenia			
subjects affected / exposed	27 / 31 (87.10%)		
occurrences (all)	31		
Neutropenia			
subjects affected / exposed	25 / 31 (80.65%)		
occurrences (all)	31		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	10 / 31 (32.26%)		
occurrences (all)	31		
Asthenia			
subjects affected / exposed	9 / 31 (29.03%)		
occurrences (all)	31		
Pain			

subjects affected / exposed	5 / 31 (16.13%)		
occurrences (all)	31		
Oedema			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	31		
Fatigue			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	31		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	6 / 31 (19.35%)		
occurrences (all)	31		
Nausea			
subjects affected / exposed	5 / 31 (16.13%)		
occurrences (all)	31		
Diarrhoea			
subjects affected / exposed	4 / 31 (12.90%)		
occurrences (all)	31		
Vomiting			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	31		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 31 (12.90%)		
occurrences (all)	31		
Dyspnoea			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	31		
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	5 / 31 (16.13%)		
occurrences (all)	31		
Hyperkalaemia			
subjects affected / exposed	5 / 31 (16.13%)		
occurrences (all)	31		
Decreased appetite			

subjects affected / exposed	4 / 31 (12.90%)		
occurrences (all)	31		
Hyperglycaemia			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	31		

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/22335534