Clinical trial results:
A MULTICENTER, OPEN LABEL STUDY OF VELCADE, MELPHALAN AND PREDNISONE (VMP) IN RELAPSED/REFRACTORY MULTIPLE MYELOMA PATIENTS

Summary

EudraCT number	2007-006123-13
Trial protocol	IT
Global end of trial date	01 October 2016

Results information

Result version number	v1 (current)
This version publication date	28 March 2023
First version publication date	28 March 2023

Trial information

Trial identification

Sponsor protocol code	MM-07-07

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, Data Center, 011 0243236, clinicaltrialoffice@emn.org
Scientific contact	Data Center, Data Center, 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	01 October 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Determine whether the association of VMP (with Melphalan at dose of 24 mg/28 days and Velcade 1.3 mg/m2, weekly) is safe and induces a significant rate of PR in patients with relapse/refractory myeloma.

Protection of trial subjects:

Under approval of Local Etical Commitee

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 March 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: 42
Worldwide total number of subjects	42
EEA total number of subjects	42

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	40
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Blood samples were collected at screening. During 28 days screeening incusion and excluson criteria was examinated

Period 1

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

Arms

Arm title	VMP ARM

Arm description:

Velcade Melphalan Prednisione

Arm type	Experimental
Investigational medicinal product name	Velcade
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1,3 mg/m2 milligram(s)/square meter daily
VMP: 4 cycles for 8 days
Maximum treatment duration according to the protocol: 52 Days

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

Dosage and administration details:

9 cycles
4mg daily

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

Dosage and administration details:

9 cycles

50mg daily

Number of subjects in period 1	VMP ARM
Started	42
Completed	42

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	42	42	
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)	0	0	
From 65-84 years	40	40	
85 years and over	2	2	
Age continuous Units: years			
median	73		
inter-quartile range (Q1-Q3)	70 to 79	-	
Gender categorical Units: Subjects			
Female	25	25	
Male	17	17	
Median previous lines therapy Units: Subjects			
One	31	31	
Two	11	11	

Subject analysis sets

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

Subject analysis set description:

In this trial, we started with a reduced dose of melphalan (24 mg for 28 days: 2 mg on Monday, Wednesday, and Friday every week), bortezomib (1.3 mg/m2 as a bolus intravenous injection on days 1, 8, 15, and 22), and prednisone (50 mg every other day) for a total of 9 cycles, as soon as the screening visits of the pretreatment period
had been completed

Reporting group values	VMP		
Number of subjects	42		
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)	0		
From 65-84 years	40		
85 years and over	2		
Age continuous			
Units: years			
median	73		
inter-quartile range (Q1-Q3)	70 to 79		
Gender categorical			
Units: Subjects			
Female	25		
Male	17		
Median previous lines therapy			
Units: Subjects			
One	31		
Two	11		

End points

End points reporting groups

Reporting group title	VMP ARM
Reporting group description: Velcade Melphalan Prednisione	
Subject analysis set title	VMP
Subject analysis set type	Intention-to-treat
Subject analysis set description: In this trial, we started with a reduced dose of melphalan (24 mg for 28 days: 2 mg on Monday, Wednesday, and Friday every week), bortezomib (1.3 mg/m2 as a bolus intravenous injection on days 1, 8, 15, and 22), and prednisone (50 mg every other day) for a total of 9 cycles, as soon as the screening visits of the pretreatment period had been completed	

Primary: ORR Rate

End point title	ORR Rate
End point description: Determine whether the association of VMP (with Melphalan at dose of 24 mg/28 days and VELCADE at 1.3 mg/m2, weekly) induces a significant rate of PR or better in patients with relapse/refractory myeloma.	
End point type	Primary
End point timeframe: 9 months	

End point values	VMP ARM	VMP		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	42	42		
Units: number				
number (not applicable)				
Yes	24	24		
No	18	18		

Statistical analyses

Statistical analysis title	only descriptive
Statistical analysis description: only descriptive	
Comparison groups	VMP ARM v VMP
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0 [2]
Method	only descriptive
Parameter estimate	only descriptive
Point estimate	57

Confidence interval	
level	Other: 0 %
sides	2-sided
lower limit	57
upper limit	57

Notes:
[1] - only descriptive
[2] - only descriptive

Secondary: PFS

End point title	PFS

End point description:
Determine the durations of progression-free survival (PFS)

End point type	Secondary

End point timeframe:
37 months

End point values	VMP ARM	VMP		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	42	42		
Units: month				
median (confidence interval 95%)	18 (12.8 to 20.2)	18 (12.8 to 20.2)		

Statistical analyses

Statistical analysis title	only descriptive

Statistical analysis description:
only descriptive

Comparison groups	VMP ARM v VMP
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0 [4]
Method	only descriptive
Parameter estimate	only descriptive
Point estimate	18
Confidence interval	
level	Other: 0 %
sides	2-sided
lower limit	18
upper limit	18

Notes:
[3] - only descriptive
[4] - only descriptive

Secondary: OS

End point title	OS
End point description: Determine the OS	
End point type	Secondary
End point timeframe: 37 monhts	

End point values	VMP ARM	VMP		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	42	42		
Units: month				
median (confidence interval 95%)	30 (17.2 to 37)	30 (17.2 to 37)		

Statistical analyses

Statistical analysis title	only descriptive
Statistical analysis description: only descriptive	
Comparison groups	VMP ARM v VMP
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0 [6]
Method	only descriptive
Parameter estimate	only descriptive
Point estimate	30
Confidence interval	
level	Other: 0 %
sides	2-sided
lower limit	30
upper limit	30

Notes:

[5] - only descriptive

[6] - only descriptive

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 37 months	
Assessment type	Systematic

Dictionary used	
Dictionary name	no dictionary
Dictionary version	0

Reporting groups	
Reporting group title	VMP Arm

Reporting group description: -

Serious adverse events	VMP Arm		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 42 (19.05%)		
number of deaths (all causes)	24		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Heart failure			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hemorrhagic erosive gastritis			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			

subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
COPD exacerbation			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchopneumonia			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
H1N1 influenza			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	VMP Arm		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 42 (100.00%)		
Nervous system disorders			
Neuropathic pruritus	Additional description: Real AE is Neuropathic Pain (10054095) by MedDRA. Not reported in this system		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Paraesthesia			

subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	7		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	28 / 42 (66.67%)		
occurrences (all)	28		
Neutropenia			
subjects affected / exposed	14 / 42 (33.33%)		
occurrences (all)	14		
Thrombocytopenia			
subjects affected / exposed	26 / 42 (61.90%)		
occurrences (all)	26		
General disorders and administration site conditions			
Haematoma			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Pyrexia			
subjects affected / exposed	8 / 42 (19.05%)		
occurrences (all)	8		
Fatigue			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	8 / 42 (19.05%)		
occurrences (all)	8		
Diarrhoea			
subjects affected / exposed	10 / 42 (23.81%)		
occurrences (all)	10		
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		

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