Clinical trial results:
Randomized phase II Trial comparing Lenalidomide with lowdose dexamethasone versus Lenalidomide in Second Line Multiple Myeloma (MM)

Summary

EudraCT number	2010-021857-38
Trial protocol	SE DK
Global end of trial date	20 November 2015

Results information

Result version number	v1 (current)
This version publication date	11 January 2020
First version publication date	11 January 2020
Summary attachment (see zip file)	summary (summary.pdf)

Trial information

Trial identification

Sponsor protocol code	PI-RV-MM-10-07

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Karolinska univ. hospital
Sponsor organisation address	141 86, Stockholm, Sweden,
Public contact	Hareth Nahi, Karolinska universe. hospital, +46 737121465, hareth.nahi@sll.se
Scientific contact	Hareth Nahi, Karolinska Inst, +46 737121465, hareth.nahi@sll.se

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	10 January 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 November 2015
Global end of trial reached?	Yes
Global end of trial date	20 November 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess efficacy (TTP) of maintenance treatment with lenalidomide alone compared to a regimen with lenalidomide and low dose dexamethasone

Protection of trial subjects:

Subjects were be fully informed of the risks and requirements of the study and, during the study, subjects were given any new information that may affect their decision to continue participation. They were told that their consent to participate in the study is voluntary and may be withdrawn at any time with no reason given and without penalty or loss of benefits to which they would otherwise be entitled. Only subjects who were fully able to understand the risks, benefits, and potential adverse events of the study, and provide their consent voluntarily will be enrolled.

Background therapy:

In order to achieve a response of best possible quality as soon as possible the combination of lenalidomide and dexamethasone works synergistically to reduce the tumor burden by several mechanisms adding up to a fast tumoricidal effect.

Evidence for comparator:

The mechanism of action of lenalidomide has a duality of effects: it directly leads to tumour cell death and improves the immune system to keep the tumour in remission (Chanan-Khan 2008). When combined with dexamethasone, lenalidomide therapy provides sustained control of multiple myeloma in relapsed/refractory patients who have received at least one prior therapy (San M 2009). Unlike chemotherapy, lenalidomide stimulates the immune response while also demonstrating tumoricidal activity (ChananKhan 2008, Schütt 2006). Additionally lenalidomide has a well-characterized safety profile, even with longer-term use (San Miguel JF et al. Haematologica. 2009)

Actual start date of recruitment	01 March 2011
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	Norway: 9
Country: Number of subjects enrolled	Sweden: 47
Country: Number of subjects enrolled	Denmark: 6
Worldwide total number of subjects	62
EEA total number of subjects	62

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)	52
From 65 to 84 years	8
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Patients who are in at least PR and have received lenalidomide as 2nd line treatment for MM will were recruited.

Pre-assignment

Screening details:

A written informed consent must be obtained before any study-specific screening procedures are performed.

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	Len/dex

Arm description:

treatment with Lenalidomide and dexamethasone

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

Dosage and administration details:

P.O. 25mg

Arm title	Lenalidomide

Arm description:

Treatment with Lenalidomide only

Arm type	study arm

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Len/dex	Lenalidomide
Started	31	31
Completed	31	31

Baseline characteristics

Reporting groups	
Reporting group title	Len/dex
Reporting group description: treatment with Lenalidomide and dexamethasone	
Reporting group title	Lenalidomide
Reporting group description: Treatment with Lenalidomide only	

Reporting group values	Len/dex	Lenalidomide	Total
Number of subjects	31	31	62
Age categorical			
Len			
Units: Subjects			
Adults (18-64 years)	20	22	42
From 65-84 years	9	8	17
85 years and over	2	1	3
Gender categorical Units: Subjects			
Female	17	16	33
Male	14	15	29

End points

End points reporting groups

Reporting group title	Len/dex
Reporting group description:	
treatment with Lenalidomide and dexamethasone	
Reporting group title	Lenalidomide
Reporting group description:	
Treatment with Lenalidomide only	

Primary: TTP

End point title	TTP
End point description:	
After 26 months' median follow-up, median TTP was 24·9 months (12·5–not calculable) versus not reached with Len versus Len+Dex	
End point type	Primary
End point timeframe:	
From randomisation until 24m from the last patient randomised	

End point values	Len/dex	Lenalidomide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31[1]	31		
Units: months				
number (not applicable)	30	25		

Notes:

[1] - The actual value is nor reached

Statistical analyses

Statistical analysis title	methods
Statistical analysis description:	
Graphs were generated and statistical analyses performed by GraphPad Prism (GraphPad Software Inc. La Jolla, CA, USA) and FlowJo X software (TreeStar Inc. OR, USA).	
Comparison groups	Lenalidomide v Len/dex
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 1 [3]
Method	Logrank
Parameter estimate	Hazard ratio (HR)

Notes:

[2] - comparison between len and len/dex

[3] - <0.05

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From signed inform consent until end of the trail

Adverse event reporting additional description:

. The most common haematologic TEAEs during the observational study were thrombocytopenia (38%), anaemia (30%), and neutropenia (13%). Febrile neutropenia was reported in only 2% of the observational study population. Upper respiratory tract infection was the most common non-haematologic TEAE (15%). Thromboembolic events occurred in seven patients

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	2

Reporting groups

Reporting group title	Fatigue

Reporting group description:

standard arm

Serious adverse events	Fatigue		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 31 (16.13%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Pneumonia	Additional description: 1(3%) in the Len and 5(16%) in the len/dex		
subjects affected / exposed	5 / 31 (16.13%)		
occurrences causally related to treatment / all	5 / 5		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Fatigue		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 31 (19.35%)		
Psychiatric disorders			
Fatigue	Additional description: Was equal between the arms, 6 (19%)		
subjects affected / exposed	6 / 31 (19.35%)		
occurrences (all)	6		

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