Clinical trial results:
A randomized placebo-controlled phase II study of clarithromycin or placebo combined with VCD induction therapy prior to high-dose melphalan with stem cell support in patients with newly diagnosed multiple myeloma

Summary

EudraCT number	2014-002187-32
Trial protocol	DK
Global end of trial date	01 June 2018

Results information

Result version number	v1 (current)
This version publication date	03 December 2018
First version publication date	03 December 2018
Summary attachment (see zip file)	PubMed abstract (Abstract.pdf)

Trial information

Trial identification

Sponsor protocol code	DMSG03/14

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02573935
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Aalborg University Hospital
Sponsor organisation address	Mølllleparkvej 4, Aalborg, Denmark, 9000
Public contact	Clinical Trial Unit Hematology, Danish Myeloma Study Group, +45 97663880, henrik.gregersen@rn.dk
Scientific contact	Clinical Trial Unit Hematology, Danish Myeloma Study Group, +45 97663880, henrik.gregersen@rn.dk

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 June 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 June 2018
Global end of trial reached?	Yes
Global end of trial date	01 June 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of our study was to evaluate the effect of clarithromycin in combination with VCD induction therapy in patients with newly diagnosed multiple myeloma

Protection of trial subjects:

Robust rules for concomitant medication. Frequent ECG during early phase of trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 58
Worldwide total number of subjects	58
EEA total number of subjects	58

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)	39
From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Myeloma patients eligible for high-dose melphalan with stem cell support

Pre-assignment

Screening details:

Myeloma patients eligible for high-dose melphalan with stem cell support

Pre-assignment period milestones

Number of subjects started	58
Number of subjects completed	

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Clarithromycin

Arm description:

Combination of clarithromycin and VCD

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

Dosage and administration details:

500 mg twice daily for 63 days

Arm title	Placebo

Arm description:

Combination of placebo and VCD

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 Tablet twice daily for 63 days

Number of subjects in period 1	Clarithromycin	Placebo
Started	27	31
Completed	22	28
Not completed	5	3
Adverse event, non-fatal	5	3

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	58	58	
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		0	
85 years and over		0	
Age continuous Units: years			
median	63		
inter-quartile range (Q1-Q3)	55 to 66	-	
Gender categorical Units: Subjects			
Female	18	18	
Male	40	40	

Subject analysis sets

Subject analysis set title	Clarithromycin effect
Subject analysis set type	Full analysis

Subject analysis set description:

Analysis of effect of clarithromycin added to VCD

Reporting group values	Clarithromycin effect		
Number of subjects	58		
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			

From 65-84 years 85 years and over			

Age continuous Units: years median inter-quartile range (Q1-Q3)	 63 55 to 66		
Gender categorical Units: Subjects			
Female Male	18 40		

End points

End points reporting groups

Reporting group title	Clarithromycin
Reporting group description: Combination of clarithromycin and VCD	
Reporting group title	Placebo
Reporting group description: Combination of placebo and VCD	
Subject analysis set title	Clarithromycin effect
Subject analysis set type	Full analysis
Subject analysis set description: Analysis of effect of clarithromycin added to VCD	

Primary: VGPR or better response after VCD induction

End point title	VGPR or better response after VCD induction
End point description:	
End point type	Primary
End point timeframe: VGPR or better response after VCD induction	

End point values	Clarithromycin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	31		
Units: VGPR or better response after VCD induct	12	16		

Statistical analyses

Statistical analysis title	Fisher’s exact test
Comparison groups	Clarithromycin v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Fisher exact

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From inclusion until completion of 4.VCD, equalling 84 days	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	NCI CTC
Dictionary version	4
Reporting groups	
Reporting group title	Clarithromycin
Reporting group description: Combination of clarithromycin and VCD	
Reporting group title	Placebo
Reporting group description: Combination of placebo and VCD	

Serious adverse events	Clarithromycin	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 27 (59.26%)	16 / 31 (51.61%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	1	1	
Gastrointestinal disorders			
Abdominal pain, neutropenic enterocolitis, paralytic ileus or peptic ulcer			
subjects affected / exposed	9 / 27 (33.33%)	2 / 31 (6.45%)	
occurrences causally related to treatment / all	9 / 9	2 / 2	
deaths causally related to treatment / all	1 / 1	1 / 1	
Infections and infestations			
Septicemia			
subjects affected / exposed	5 / 27 (18.52%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	5 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 27 (7.41%)	5 / 31 (16.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Clarithromycin	Placebo	
Total subjects affected by non-serious adverse events subjects affected / exposed	26 / 27 (96.30%)	28 / 31 (90.32%)	
Cardiac disorders Hypotension subjects affected / exposed occurrences (all)	6 / 27 (22.22%) 6	1 / 31 (3.23%) 1	
Nervous system disorders Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	15 / 27 (55.56%) 15	8 / 31 (25.81%) 8	
Blood and lymphatic system disorders Thrombocytopenia subjects affected / exposed occurrences (all) Anemia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all)	13 / 27 (48.15%) 13 14 / 27 (51.85%) 14 12 / 27 (44.44%) 12	7 / 31 (22.58%) 7 11 / 31 (35.48%) 11 13 / 31 (41.94%) 13	
Renal and urinary disorders Peripheral edema subjects affected / exposed occurrences (all)	12 / 27 (44.44%) 12	8 / 31 (25.81%) 8	
Psychiatric disorders Psychiatric symptoms subjects affected / exposed occurrences (all)	6 / 27 (22.22%) 6	3 / 31 (9.68%) 3	
Infections and infestations Infection subjects affected / exposed occurrences (all)	23 / 27 (85.19%) 23	24 / 31 (77.42%) 24	

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? Yes

Date	Interruption	Restart date
16 September 2016	The study was prematurely stopped for safety reasons after the inclusion of 58 patients (36% of the planned study population).	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study included only 58 of planned patients

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30123673

http://www.ncbi.nlm.nih.gov/pubmed/30230047