Clinical trial results:
Safety and efficacy of interleukin-1 inhibitor anakinra for the amelioration of fever during neutropenia and mucositis in patients with multiple myeloma receiving an autologous hematopoietic stem cell transplantation after high-dose melphalan.

Summary

EudraCT number	2016-004419-11
Trial protocol	NL
Global end of trial date	03 April 2020

Results information

Result version number	v1 (current)
This version publication date	29 August 2021
First version publication date	29 August 2021

Trial information

Trial identification

Sponsor protocol code	SC35

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03233776
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Radboud university medical center
Sponsor organisation address	Geert Grooteplein Zuid 8, Nijmegen, Netherlands, 6525 GA
Public contact	Trialbureau Hematologie-Oncologie, Radboud university medical center, +31 243614794, trialbureauhemat-onco@radboudumc.nl
Scientific contact	Trialbureau Hematologie-Oncologie, Radboud university medical center, +31 243614794, trialbureauhemat-onco@radboudumc.nl

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 May 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 April 2020
Global end of trial reached?	Yes
Global end of trial date	03 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the safety and efficacy of anakinra in patients with multiple myeloma receiving high-dose melphalan (HDM) in the preparation for an autologous hematopoietic stem cell transplantation (SCT).

Protection of trial subjects:

Adverse events were monitored and recorded. The study was monitored by an independent monitor.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2017
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	Netherlands: 9
Worldwide total number of subjects	9
EEA total number of subjects	9

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)	4
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

105 patients were considered for inclusion. 79 were not selected because of comorbidities, inclusion in other trials, not interested, treatment in other hospitals, completion of study etc. 26 patients were selected for screening of whom 9 were included. The other 17 patients were not interested, did not fulfill the criteria or were not needed.

Pre-assignment period milestones

Number of subjects started	9
Number of subjects completed	9

Period 1

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

Blinding implementation details:

The results of the investigational blood cultures are blinded.

Arms

Arm title	All subjects

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Anakinra
Investigational medicinal product code	
Other name	Kineret
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects will be treated with anakinra in an increasing dose, according to 3+3 design. Predefined doses of anakinra are 100 mg, 200 mg and 300 mg. Subjects will receive anakinra once daily, starting on day -2, until day +12. Subjects will receive an intravenous dose of anakinra, given in a volume of 50 mL, administered with an infusion speed of 30 ml/hour, through a central venous catheter.

Number of subjects in period 1	All subjects
Started	9
Completed	9

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	9	9	
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			
arithmetic mean	67.67		
standard deviation	± 6.325	-	
Gender categorical Units: Subjects			
Female	3	3	
Male	6	6	

Subject analysis sets	
Subject analysis set title	100mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

First group of subjects treated with 100mg Anakinra.

Subject analysis set title	200mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Second group of subjects treated with 200mg Anakinra.

Subject analysis set title	300mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Third group of subjects treated with 300mg Anakinra.

Reporting group values	100mg	200mg	300mg
Number of subjects	3	3	3

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			
arithmetic mean	59.33	66.67	59.00
standard deviation	± 9.018	± 1.155	± 4.583
Gender categorical Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	All subjects
Reporting group description: -	
Subject analysis set title	100mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: First group of subjects treated with 100mg Anakinra.	
Subject analysis set title	200mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Second group of subjects treated with 200mg Anakinra.	
Subject analysis set title	300mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Third group of subjects treated with 300mg Anakinra.	

Primary: Safety

End point title	Safety[1]

End point description:

All subjects who have received study medication in this study will be part of the safety and tolerability evaluation. Adverse events will be monitored throughout the study.
Safety measurements: Non-hematological grade 3-4 side effects will be graded according to the common toxicity criteria (CTCAE) and will be reported as DLT. Hematologically, period to neutrophil recovery will be recorded. Finally, serious infections and opportunistic infections will be recorded.

End point type	Primary

End point timeframe:

Adverse events will be recorded from day of admission (day -3) until 30 days following the last dose of the investigational treatment. Adverse events occurring after 30 days should also be recorded if considered at least possibly related to the treatment

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 is not applicable for this endpoint. For safety, DLTs, SAEs and SUSARs were scored. These did not occur in any dose group.

End point values	All subjects	100mg	200mg	300mg
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	3	3	3
Units: number of events	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Maximum tolerated dose

End point title	Maximum tolerated dose[2]

End point description:

End point type	Primary

End point timeframe:

Not applicable

Notes:

[2] - 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 is not applicable for this endpoint. The maximum tolerated dose was concluded to be 300 mg, since no DLTs occurred in any dose group, and 300 mg was the maximum dose tested.

End point values	All subjects	100mg	200mg	300mg
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	3	3	3
Units: mg				
number (not applicable)				
Tolerated	9	3	3	3
Not tolerated	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events will be recorded from day of admission (day -3) until 30 days following the last dose of the investigational treatment. Adverse events occurring after 30 days should also be recorded if considered at least possibly related to the treatment

Assessment type	Systematic

Dictionary used

Dictionary name	NCI-CTCAE
Dictionary version	4.0

Reporting groups

Reporting group title	All subjects

Reporting group description: -

Serious adverse events	All subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	All subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)		
Investigations			
White blood cells decreased	Additional description: Scored as 'white blood cells decreased' or 'decreased white cell count'		
subjects affected / exposed	9 / 9 (100.00%)		
occurrences (all)	9		
Hypokalaemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Lymphocyte count decreased	Additional description: Scored as 'lymphocyte count decreased' or 'lymphopenia'		
subjects affected / exposed	9 / 9 (100.00%)		
occurrences (all)	9		
Neutrophil count decreased	Additional description: Scored as 'neutrophil count decreased' or 'neutropenia'		

subjects affected / exposed	9 / 9 (100.00%)		
occurrences (all)	9		
Platelet count decreased	Additional description: Scored as 'platelet count decreased' or 'trombocytopenia'		
subjects affected / exposed	9 / 9 (100.00%)		
occurrences (all)	9		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Vascular access complication			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Nervous system disorders			
Vasovagal reaction			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	3		
Febrile neutropenia			
subjects affected / exposed	8 / 9 (88.89%)		
occurrences (all)	8		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 9 (66.67%)		
occurrences (all)	6		
Nausea			
subjects affected / exposed	8 / 9 (88.89%)		
occurrences (all)	8		
Oral mucositis			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		

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