Clinical trial results:
A PHASE II STUDY OF THE CLINICAL ACTIVITY AND SAFETY OF ACTINOMYCIN D IN PATIENTS WITH RELAPSED/REFRACTORY ACUTE MYELOID LEUKEMIA WITH NUCLEOPHOSMIN (NPM1) GENE MUTATION

Summary

EudraCT number	2014-000693-18
Trial protocol	IT
Global end of trial date	19 July 2016

Results information

Result version number	v1 (current)
This version publication date	06 February 2021
First version publication date	06 February 2021

Trial information

Trial identification

Sponsor protocol code	ActD-AML-PG01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University of Perugia, Department of Medicine
Sponsor organisation address	Piazzale severi n°1, Perugia, Italy,
Public contact	Sezione di Ematologia e Immunologia, University of Perugia, Department of Medicine, +39 0755783190,
Scientific contact	Sezione di Ematologia e Immunologia, University of Perugia, Department of Medicine, +39 0755783190,

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	06 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 July 2016
Global end of trial reached?	Yes
Global end of trial date	19 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the anti-tumor activity of the intravenously administered single agent actinomycin D in AML patients carrying the NPM1 mutations fulfilling the eligibility criteria for enrollment in this study.

Protection of trial subjects:

Normal clinical practice

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 March 2014
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: 10
Worldwide total number of subjects	10
EEA total number of subjects	10

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)	6
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 10 patients with relapsed/refractory acute myeloid leukemia with mutated NPM1 were recruited between June 28, 2014 and February 20, 2016. All patients were enrolled and treated at Santa Maria della Misericordia hospital in Perugia, Italy.

Pre-assignment

Screening details:

All patients meeting the inclusion criteria were sucesfully screened. No screening failure was reported.

Period 1

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

Arms

Arm title	Single Arm

Arm description:

10 patients treated with the study drug in a Phase II trial

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

Dosage and administration details:

15 mcg/Kg/day, single administration, for 5 consecutive days. Dose cap 2 mg/day.

Number of subjects in period 1	Single Arm
Started	10
Completed	9
Not completed	1
Adverse event, serious fatal	1

Baseline characteristics

Reporting groups

Reporting group title	Phase II clinical trial

Reporting group description: -

Reporting group values	Phase II clinical trial	Total	
Number of subjects	10	10	
Age categorical Units: Subjects			
Age > 18 years	10	10	
Age continuous Units: years median full range (min-max)	 66.5 53 to 75	 -	
Gender categorical Units: Subjects			
Female Male	6 4	6 4	

Subject analysis sets

Subject analysis set title	Complete Response Rate
Subject analysis set type	Full analysis

Subject analysis set description:

Four of nine evaluable patients obtained a complete response (including both complete remission and complete remission with incomplete hematological recovery).

Reporting group values	Complete Response Rate		
Number of subjects	9		
Age categorical Units: Subjects			
Age > 18 years	9		
Age continuous Units: years median full range (min-max)	 66 53 to 75		
Gender categorical Units: Subjects			
Female Male	5 4		

End points

End points reporting groups

Reporting group title	Single Arm

Reporting group description:

10 patients treated with the study drug in a Phase II trial

Subject analysis set title	Complete Response Rate
Subject analysis set type	Full analysis

Subject analysis set description:

Four of nine evaluable patients obtained a complete response (including both complete remission and complete remission with incomplete hematological recovery).

Primary: Complete Response Rate

End point title	Complete Response Rate[1]

End point description:

End point type	Primary

End point timeframe:

July 28, 2014 to April 20, 2016. This is the time frame between the response assessment in the first and last patients included in the study.

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: This phase II pilot study was designed applying the Simon's minimax two-stage model. We calculated a sample size that would be sufficient to accept the alternative hypothesis (CR/CRi rate after one or two induction cycles equals to or higher than 45%) and reject the null hypothesis (CR/CRi rate equals or lower than 10%), with an alfa level of 0.05 and a beta level of 0.2. The study drug was considered Worth of further investigation in CR/CRi was obtained in at least 3 patients.

End point values	Single Arm	Complete Response Rate		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9	9		
Units: % patients	44	44		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: June 28, 2014 to July 19, 2016	
Assessment type	Systematic
Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.03
Reporting groups	
Reporting group title	single arm study

Reporting group description: -

Serious adverse events	single arm study		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 10 (10.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Infections and infestations			
Sepsis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	single arm study		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)		
Cardiac disorders			
Electrocardiogram QT interval abnormal			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Syncope			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	3		

fever subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Gastrointestinal disorders oral mucositis subjects affected / exposed occurrences (all) diarrhea subjects affected / exposed occurrences (all) vomiting subjects affected / exposed occurrences (all) nausea subjects affected / exposed occurrences (all)	 8 / 10 (80.00%) 12 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1 2 / 10 (20.00%) 2		
Hepatobiliary disorders Transaminases increased subjects affected / exposed occurrences (all) bilirubin increased subjects affected / exposed occurrences (all)	 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1		
Skin and subcutaneous tissue disorders Skin disorder subjects affected / exposed occurrences (all)	 4 / 10 (40.00%) 6		
Renal and urinary disorders Urinary tract infection subjects affected / exposed occurrences (all)	 2 / 10 (20.00%) 4		
Infections and infestations febrile neutropenia subjects affected / exposed occurrences (all) sepsis	 7 / 10 (70.00%) 12 		

subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
Viral infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
pneumonia			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hyponatraemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 February 2015	Response assessment to be performed after either one or two induction cycles, instead of after one induction cycle.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported