Clinical trial results: *An open-label, single-arm, phase II, prospective, pilot study of tocilizumab in patients with Erdheim-Chester disease*

Summary

EudraCT number*	2012-003151-11
Trial protocol	ECD-TCZ-01
Global end of trial date*	30/11/2016

Trial information

Trial identification

Sponsor protocol code*	ECD-TCZ-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01727206
WHO universal trial number (UTN)	-

Notes:

Sponsors details*

Sponsor organisation name	IRCCS Ospedale San Raffaele
Sponsor organisation address	Via Olgettina, 60, Milano, Italy, 20132
Public contact	Simone Casiraghi casiraghi.simone@hsr.it 02 2643 3828
Scientific contact	Prof. Lorenzo Dagna dagna.lorenzo@unisr.it 02 2643 3828

Notes: n.a.

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

Results analysis stage

Analysis stage*	Final
Date of interim/final analysis*	30/05/2017
Is this the analysis of the primary completion data?*	Yes
Global end of trial reached?*	Yes
Global end of trial date*	30/11/2016
Was the trial ended prematurely?	No

General information about the trial

Main objective of the trial*: The study aims to evaluate the efficacy and safety profile of treatment with tocilizumab in adult patients with Erdheim-Chester disease with extraskeletal involvement. Efficacy will be assessed by measuring the effect of treatment on the size of measurable lesions, using two-dimensional assessments, as well as on functional indices objectively measurable through laboratory and/or functional tests (such as, for example – if altered at enrollment – renal or cardiac function indices). The effects of treatment on symptom control and on the quality of life of patients will also be assessed. Treatment safety will be determined by analyzing adverse events and related laboratory safety parameters.

Actual start date of recruitment*	07/11/2012
Long term follow-up planned*	No
If Yes, rationale:	Safety Efficacy Ethical reason Regulatory reason Scientific research
Duration	30 months
Independent data monitoring committee (IDMC) involvement?*	No
Protection of trial subjects*:	Enrolled patients were allowed on a stable dose of steroids (maximum 10 mg/day of prednisone) and/or methotrexate, provided these medications had been administered for at least 4 months
Background therapy:	
Evidence for comparator:	n.a.

Population of trial subjects

Subjects enrolled per country

Country:	Italy
Planned number of subjects	6
Actual Number of subjects enrolled*	3
Worldwide total number of subjects	3
EEA total number of subjects	3

Subjects enrolled per age group

In utero*	0
Preterm newborn - gestational age < 37wks*	0
Newborns (0-27 days)*	0
Infants and toddlers (28 days-23months)*	0
Children (2-11 years)*	0
Adolescents (12-17 years)*	0
Adults (18-64 years)*	2
From 65 to 84 years*	1
85 years and over*	0

Subject disposition

Recruitment details:

This is a monocentric study, time of enrollment has been defined in 20 months.

Pre-assignment - *Screening details*:

- Patients aged >= 18 years of age able to understand and sign an informed consent;

- diagnosis of ECD documented histologically;

- advanced stage of the disease limited to the skeleton, with at least one measurable lesion;

- progression of the disease during the therapies most commonly used today (e.g. corticosteroids, interferon-alpha, methotrexate) or with a location (CNS or cardiac for example) known to be unresponsive to any of the treatments currently available;

- if women of childbearing age, a negative pregnancy test and the possibility of reliably excluding the onset of pregnancy for the entire duration of the study.

Period 1

Period title*	Overall Trial
Is this the baseline period?	
Allocation method*	Not applicable
Blinding used*	Not blinded

Arms

Arm title*	Experimental arm - Tocilizumab
Arm description:	Tocilizumab
Arm type*	Experimental
Investigational medicinal product name*	Tocilizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms*	Solution
Routes of administration*	Intravenous
Dosage and administration details*	8 mg/kg i.v. at day 0 and week 4, 8, 12, 16, 20

Number of subjects in period	Arm Title (overall population)	Arm Title *(repeat for each arms if applicable)*
Started*	3	
Completed*	3	
Subject non-completion reason (if applicable)		
AE, non fatal		
AE, fatal		
Consent withdrawn by subject		
Lack of efficacy		
Lost to follow up		
Physician decision		
Pregnancy		
Protocol Deviation		
Other		

Baseline characteristics

Reporting groups* Overall cohort	
Reporting group title*	Not applicable
Number of subjects at the baseline*	

Reporting group description: *You can report per arm in the baseline period or for the overall baseline period*

Subject analysis sets

Add a subject analysis set if you wish to report on groups different from the reporting group defined above (repeat if applicable)

Subject analysis set title*	Not applicable
Subject analysis set type*	Full Analysis Intention to treat Per protocol Safety analysis Sub-group analysis
Subject analysis set description*	Not applicable
Number of subjects in subjects analysis set*	Not applicable

Age characteristics*

Complete either the age categorical, age continuous or complete both these characteristics in order to collect values for the reporting groups and optionally the subject analysis sets.

	Characteristic title*	Units*	Age categories*
Age categorical	Not applicable	Not applicable	Not applicable

	Characteristic title*	Units*	Central tendency*	Dispersion type*
Age continuous	Overall cohort	Years Months Weeks Days	Arithmetic Mean Median least square mean geometric mean log mean	full range (min-max) standard deviation inter quartile range

Gender characteristics*

	Characteristic title*	Units*	Gender categories*
Gender categorical	Not applicable		Female Male

Study specific characteristics

	Characteristic title*	Units *	Categories*	Number of subject for each categories
Study specific categorical	Not applicable			
Study specific categorical				
Study specific categorical				

Study specific categorical				
Study specific categorical				

End points

Add subject analysis set if you wish to report on groups different form reporting groups defined above

Subject analysis set title*	Not applicable
Subject analysis set type*	Full Analysis Intention to treat Per protocol Safety analysis Sub-group analysis
Subject analysis set description*	Not applicable
Number of subject in subject analysis set *	

End points definitions

End point title*	Not applicable	
		Values
Countable or measurable?*	*Select countable when the end point represents data that contains distinct values.*	-
If countable, Countable units*:	Not applicable	
If measurable, Measurable units*	Not applicable	
Measure type*:	Number Arithmetic Mean Median least square mean geometric mean log mean	
Precision/dyspersion type*	Not applicable	

End point type*	Primary Secondary Other pre-specified Post Hoc

End point timeframe*:

Use categories only if the data for the end point can be categorized

Category title

Specify the groups of subjects applicable to this end point

Reporting groups*			
Period	Not applicable		
Arms	Not applicable		
subject analysis sets	Not applicable		

Adverse events

Adverse events information

Timeframe for reporting adverse events*: *Enter the time point(s) or time period for AE assessment*

First patient first visit: 07/11/2012
Last recruitment date: 17/05/2013
Study closure: 30/11/2016

Adverse event reporting additional description: No adverse events reported.

Assessment type*	Systematic or Non Systematic
Frequency threshold for reporting non-serious adverse events*	*Enter the frequency of non SAE that are reported in the results database for all arms or reporting groups*

Dictionary used

Dictionary name*	MedDRA or CTCAE
Dictionary version*	

Adverse events reporting group definition

Use arms from baseline period as reporting groups
OR

Reporting group title*: *Overall cohort*

For this reporting group, provide the following totals:

Subject exposed*	
Subjects affected by non -SAE*	
Total number of deaths (all causes)*	
Total number of deaths resulting from adverse event*	

Serious adverse event details and values

System organ class*:

Event term*:

Values for serious adverse event per reporting group *

Reporting groups	Subjects affected number	Subjects exposed number	Occurrences all number	Occurrences causally related to treatment number	Fatalities number	Fatalities causally related to treatment number

Non - Serious adverse event details and values

System organ class*:

Event term*:

Values for non-serious adverse event per reporting group*

Threshold for non-serious adverse event reporting is:

Reporting groups	Subjects affected number	Subjects exposed number	Occurrences all number

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol*? No

Date	Amendment

Notes:

Interruptions (globally)

Were there any global interruptions to the trial*? No

If Yes, Interruption date

Interruption descrption

Limitations and caveats

None reported

Online references

Enter PubMed identifier (PMID)

PMID: 28680751