Clinical trial results:
Scintigraphic detection of tumor necrosis factor with radioactive labeled TNF-blocker in patients with active rheumatoid arthritis and active axial and peripheric spondyloarthropathy.

Summary

EudraCT number	2009-017998-37
Trial protocol	BE
Global end of trial date	26 March 2019

Results information

Result version number	v1 (current)
This version publication date	18 April 2022
First version publication date	18 April 2022

Trial information

Trial identification

Sponsor protocol code	AGO/2009/015

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01590966
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ghent University Hospital
Sponsor organisation address	Corneel Heymanslaan 10, Ghent, Belgium, 9000
Public contact	Hiruz CTU, Ghent University Hospital, 32 93320500, hiruz.ctu@uzgent.be
Scientific contact	Hiruz CTU, Ghent University Hospital, 32 93320500, hiruz.ctu@uzgent.be

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	26 March 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 March 2019
Global end of trial reached?	Yes
Global end of trial date	26 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a proof-of-concept study of in vivo detection of TNF by immunoscintigraphy of a radiolabelled TNF inhibitor in RA and SpA, and correlate this with clinical, imaging findings and therapeutic outcome

Protection of trial subjects:

Ethics review and approval, informed consent, supportive care and routine monitoring.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2012
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	Belgium: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	19
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

20 patients were included in the period from 01-05-2012 till 26-03-2019. End of trial notification was dated 26-03-2019 (last patient last visit) and submitted to EC and CA 22-08-2019.

Pre-assignment

Screening details:

- age 18 - 70 years
- diagnosed with rheumatoid arthrosis according to the ACR-criteria, OR diagnosed with axial spondyloarthropathy according to the ASAS criteria OR with peripheral spondylarthropathy
- no active tuberculosis
- no pregnant women or women not using contraceptives when applicable

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	RA patients

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Cimzia
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

200 mg every 2 weeks

Arm title	Peripheral SpA patients

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Cimzia
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

200 mg every 2 weeks

Arm title	Axial SpA patients

Arm description: -

Arm type	Experimental

Investigational medicinal product name	Cimzia
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

200 mg every 2 weeks

Number of subjects in period 1	RA patients	Peripheral SpA patients	Axial SpA patients
Started	5	6	9
Completed	5	6	9

Baseline characteristics

Reporting groups	
Reporting group title	RA patients
Reporting group description: -	
Reporting group title	Peripheral SpA patients
Reporting group description: -	
Reporting group title	Axial SpA patients
Reporting group description: -	

Reporting group values	RA patients	Peripheral SpA patients	Axial SpA patients
Number of subjects	5	6	9
Age categorical Units: Subjects			
Adults (18-64 years)	4	6	9
From 65-84 years	1	0	0
Age continuous Units: years			
arithmetic mean	56.24	40.97	37.1
standard deviation	± 7.8	± 7.7	± 9.1
Gender categorical Units: Subjects			
Female	4	4	2
Male	1	2	7

Reporting group values	Total		
Number of subjects	20		
Age categorical Units: Subjects			
Adults (18-64 years)	19		
From 65-84 years	1		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	10		
Male	10		

Subject analysis sets	
Subject analysis set title	All patients at baseline
Subject analysis set type	Full analysis
Subject analysis set description: 5 patients with RA (ACR EULAR criteria), 5 patients with PsA (Caspar criteria) and 10 patients with axSpA (ASAS criteria)	
Subject analysis set title	All patients in treatment at week 24

Subject analysis set type	Full analysis

Subject analysis set description:

Correlation between in vivo detection of TNF by immunoscintigraphy and therapeutic outcome

Reporting group values	All patients at baseline	All patients in treatment at week 24	
Number of subjects	20	20	
Age categorical Units: Subjects			
Adults (18-64 years)	19	19	
From 65-84 years	1	1	
Age continuous Units: years			
arithmetic mean	43.0	43.0	
standard deviation	± 10.1	± 10.1	
Gender categorical Units: Subjects			
Female	8	8	
Male	12	12	

End points

End points reporting groups

Reporting group title	RA patients
Reporting group description: -	
Reporting group title	Peripheral SpA patients
Reporting group description: -	
Reporting group title	Axial SpA patients
Reporting group description: -	
Subject analysis set title	All patients at baseline
Subject analysis set type	Full analysis
Subject analysis set description:	
5 patients with RA (ACR EULAR criteria), 5 patients with PsA (Caspar criteria) and 10 patients with axSpA (ASAS criteria)	
Subject analysis set title	All patients in treatment at week 24
Subject analysis set type	Full analysis
Subject analysis set description:	
Correlation between in vivo detection of TNF by immunoscintigraphy and therapeutic outcome	

Primary: DAS 28 at week 24

End point title	DAS 28 at week 24[1][2]
End point description:	
End point type	Primary
End point timeframe:	
at week 24	

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: No statistical analysis was done, only the calculation of the mean DAS 28 values at week 24
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was done, only the calculation of the mean DAS 28 values at week 24

End point values	RA patients			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: DAS 28 units	3			

Statistical analyses

No statistical analyses for this end point

Primary: ASDAS

End point title	ASDAS[3][4]
End point description:	

End point type	Primary

End point timeframe:

at week 24

Notes:

[3] - 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: No statistical analysis was done, only the calculation of the mean ASDAS values at week 24

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was done, only the calculation of the mean ASDAS values at week 24

End point values	Peripheral SpA patients			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: ASDAS units	2			

Statistical analyses

No statistical analyses for this end point

Primary: ASDAS

End point title	ASDAS[5][6]

End point description:

End point type	Primary

End point timeframe:

at week 24

Notes:

[5] - 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: No statistical analysis was done, only the calculation of the mean ASDAS values at week 24

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was done, only the calculation of the mean ASDAS values at week 24

End point values	Axial SpA patients			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: ASDAS units	2			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Overall study

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Overall study

Reporting group description: -

Serious adverse events	Overall study		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 20 (15.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
transsphenoidal resection of macro-adenoma of the pituitary gland			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Prepatellar bursitis right knee			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prepatellar bursitis left knee			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Septic prepatellar bursitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Infections and infestations			
Viral gastro-enteritis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Overall study		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 20 (80.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast abces			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Erytheem injection place			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
abdominal pain			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Malaise			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
syncope			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Mastitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Angina			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Extreme fatigue			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Rhinitis allergic			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Labored breathing			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Common cold			
subjects affected / exposed	10 / 20 (50.00%)		
occurrences (all)	10		
Pharyngitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Psychiatric disorders			
Terrors			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Anxiety			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Blood and lymphatic system disorders Fall and hematoma subjects affected / exposed occurrences (all) Bleeding crusts at nasal musoca subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Ear and labyrinth disorders Otitis subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Esophagus spasm subjects affected / exposed occurrences (all) Gastro-enteritis subjects affected / exposed occurrences (all) Epigastric pain subjects affected / exposed occurrences (all) Reflux oesofagitis subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 3 / 20 (15.00%) 3 1 / 20 (5.00%) 1 2 / 20 (10.00%) 2 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 2 / 20 (10.00%) 2		
Skin and subcutaneous tissue disorders Pruritis subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1		

Eczema subjects affected / exposed occurrences (all) Vesicular rash subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2 1 / 20 (5.00%) 1		
Renal and urinary disorders Cystitis subjects affected / exposed occurrences (all) Uriniary tract infection subjects affected / exposed occurrences (all) Pyelonefritis subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1 3 / 20 (15.00%) 3 1 / 20 (5.00%) 1		
Endocrine disorders Increase mucus production subjects affected / exposed occurrences (all) Night sweating subjects affected / exposed occurrences (all)	 2 / 20 (10.00%) 2 1 / 20 (5.00%) 1		
Musculoskeletal and connective tissue disorders Bursitis trochanteriac subjects affected / exposed occurrences (all) Spasm subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Infections and infestations Bronchial infection subjects affected / exposed occurrences (all) CMV infection	 2 / 20 (10.00%) 2 		

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Mycosis pubis region			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Viral infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
wound infection PIP2 right			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Flu			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Zona thoracalis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Clostridium difficile infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 June 2013	This amendment includes an addition to the informed consent and protocol that a few drops of perchlorate be added prior to the injection of the screening agent to prevent uptake of free isotope into the thyroid and gastrointestinal structures. It has also been added to both documents that from the 9th patient onwards, the scintigraphy session will contain a maximum of 3 time points instead of 2 as the 24h images are too important to drop. In addition, it is now clearly stated in the informed consent that if nuclear medicine deems it necessary for a good interpretation of the images, a SPECT/CT scan can be performed as well.
06 November 2013	This amendment removes the option to stop Cimzia after 2 consecutive visits of clinical remission because the study population has insufficient statistical power to answer this specific question. Obviously, an individual study patient can always opt to stop treatment in the event of remission. In addition, the possibility is offered to continue treating patients who have a good clinical response but are not yet eligible for reimbursement. Furthermore, 6 patients who have failed on an anti-TNF treatment (other than Cimzia) will also be added. The other changes are mainly administrative simplifications by removing repetitions in the protocol
21 August 2014	This amendment adds 5 patients with Crohn's Disease and 5 patients with erosive hand osteoarthritis. In this proof of concept study, the scanning procedure will be performed in all additional patients. Only in the Crohn's disease patients will a treatment with the TNF-blocker Cimzia® be administered after the scan procedure, since this is standard treatment for Crohn's disease. The patients with erosive hand arthrosis will not be treated with the TNF blocker Cimzia® as this is not a standard treatment for erosive hand arthrosis.
13 May 2016	This amendment requests that the maintenance dose for the Crohn's group of patients be adjusted in accordance with the Cimzia® label, available on the FDA site. The FDA approved maintenance dose for this indication is 400 mg every 4 weeks as opposed to 200 mg every 4 weeks.
07 April 2017	This amendment requests to increase the number of patients with Axial Spondyloarthritis who have failed anti-TNF treatment. Currently this was anticipated to be 4 patients (2 radiographic and 2 non-radiographic) . We had planned to increase the number for this group to "up to 10 patients". This will increase the final predetermined number of patients in the study from 36 to 44.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27403334