Clinical trial results:
Exploration of TNF-alpha Blockade with golimumab in the Induction of Clinical Remission in Patients with Early peripheral SpondyloArthritis (SpA) according to ASAS-criteria ('CRESPA').

Summary

EudraCT number	2011-003678-97
Trial protocol	BE
Global end of trial date	30 April 2019

Results information

Result version number	v1 (current)
This version publication date	19 September 2021
First version publication date	19 September 2021

Trial information

Trial identification

Sponsor protocol code	AGO/2011/005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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	07 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 March 2019
Global end of trial reached?	Yes
Global end of trial date	30 April 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To explore the potential of an induction therapy with the TNF-blocking agent golimumab (Simponi® in a very early disease stage (less than 3 months of symptom duration) of patients with predominant peripheral Spondyloarthritis (SpA), classified according to the new ASAS-criteria.

In the open-label 'CRESPA-extension' part of the study, we want to investigate the long-term safety and efficacy of golimumab administered every 4 weeks at a dose of 50 mg subcutaneously (SC) for a total period of 116 weeks (104 weeks golimumab monotherapy + 12 weeks combination therapy with methotrexate 10-15 mg weekly).

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 October 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	29 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	60
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

84 patients were screened in the period from 01-10-2011 till 18-03-2019. 60 patients were included, 60 patients were randomised. 59 patients were included and completed the trial. End of trial notification was dated 18-03-2019 (last patient last visit) and submitted to EC and CA 23-05-2019.

Pre-assignment

Screening details:

Inclusion Criteria:
- ≥ 18 years of age
- meet the new Assessment of SpondyloArthritis (ASAS) criteria for peripheral spondyloarthritis:
-1 of the Peripheral Spondyloarthritis (SpA) features
- Onset of peripheral SpA symptoms ≤ 3 months prior to the screening visit
- active disease at screening and baseline

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The randomisation and blinding was completely performed by Theorem Clinical Research. The decision to unblind a patient will be made by the study physician and was extensively documented in the patient file. Theorem Clinical Research provided sealed envelopes which were kept in the clinical study master file at the department of Rheumatology, University Hospital Gent.

Arms

Are arms mutually exclusive?	Yes
Arm title	Baseline CRESPA study: Placebo

Arm description: -

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

Dosage and administration details:

The prefilled syringe with golimumab or placebo will be administrated subcutaneously every 4 weeks.

Arm title	Baseline CRESPA study: Golimumab 50mg (Simponi®)

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Simponi
Investigational medicinal product code	CAS 476181-74-5
Other name	golimumab
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

The prefilled syringe with golimumab or placebo will be administrated subcutaneously every 4 weeks.

Number of subjects in period 1	Baseline CRESPA study: Placebo	Baseline CRESPA study: Golimumab 50mg (Simponi®)
Started	20	40
Completed	20	40

Period 2	
Period 2 title	CERPA Study
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	CRESPA study: Placebo

Arm description: -

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

Dosage and administration details:

The prefilled syringe with golimumab or placebo will be administrated subcutaneously every 4 weeks.

Arm title	CRESPA study: Golimumab 50mg (Simponi®)

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Simponi
Investigational medicinal product code	CAS 476181-74-5
Other name	golimumab
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

The prefilled syringe with golimumab or placebo will be administrated subcutaneously every 4 weeks.

Number of subjects in period 2	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)
Started	20	40
Completed	20	39
Not completed	0	1
safety issues	-	1

Period 3

Period 3 title	CERPA extension
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Treatment arm

Arm description:

The 'CRESPA-Extension' part of the study is designed to investigate safety and long-term efficacy of golimumab in peripheral SpA patients with a major response to golimumab or a disease flare upon withdrawal of golimumab after reaching initial remission in the 'CRESPA' study. In the last 3 months of the CRESPA-Extension study part, golimumab treatment will be combined with methotrexate in order to explore the possibility that co-medication with methotrexate would allow for the discontinuation of golimumab treatment at week 116, thus providing clues of the potential of "biological-free" remission. 29 were not included in the extension study because of remission.

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

Dosage and administration details:

Methotrexate will be administered orally with a total weekly dosage of 10 to 15 mg, meaning 4 to 6 tablets of 2.5mg weekly (104 weeks golimumab monotherapy + 12 weeks combination therapy with methotrexate 10-15 mg weekly).

Investigational medicinal product name	Simponi
Investigational medicinal product code	CAS 476181-74-5
Other name	golimumab
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

The prefilled syringe with golimumab or placebo will be administrated subcutaneously every 4 weeks (104 weeks golimumab monotherapy + 12 weeks combination therapy with methotrexate 10-15 mg weekly).

Number of subjects in period 3[1]	Treatment arm
Started	31
Completed	28
Not completed	3
safety issues	1
pregnancy on 13-03-2016	1
Lost to follow-up	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 29 were not included in the extension study because of remission.

Baseline characteristics

Reporting groups	
Reporting group title	Baseline CRESPA study: Placebo
Reporting group description: -	
Reporting group title	Baseline CRESPA study: Golimumab 50mg (Simponi®)
Reporting group description: -	

Reporting group values	Baseline CRESPA study: Placebo	Baseline CRESPA study: Golimumab 50mg (Simponi®)	Total
Number of subjects	20	40	60
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	42.3	38.3	
standard deviation	± 13.7	± 13.2	-
Gender categorical Units: Subjects			
Female	13	26	39
Male	7	14	21
HLA B27 positive Units: Subjects			
yes	13	20	33
no	7	20	27
Concomitant NSAIDs use at baseline, Units: Subjects			
yes	18	32	50
no	2	8	10
Anterior uveitis, past or present Units: Subjects			
yes	0	1	1
no	20	39	59
IBD, past or present Units: Subjects			
yes	1	0	1
no	19	40	59
Preceding infection			

Units: Subjects			
yes	2	6	8
no	18	34	52
Skin and/or nail psoriasis Units: Subjects			
yes	8	17	25
no	12	23	35
patients with elevated CRP (≥5 mg/L) Units: Subjects			
yes	15	24	39
no	5	16	21
Sacroiliitis on MRI Units: Subjects			
yes	9	12	21
no	11	28	39
Family history of SpA Units: Subjects			
yes	8	13	21
no	12	27	39
Inflammatory back pain (history/presence) Units: Subjects			
yes	2	5	7
no	18	35	53
Symptom duration Units: weeks			
arithmetic mean	4.4	5.2	
standard deviation	± 2	± 2.8	-
NSAID index Units: index			
median	100	89.3	
inter-quartile range (Q1-Q3)	65.1 to 100	35 to 100	-

End points

End points reporting groups

Reporting group title	Baseline CRESPA study: Placebo
Reporting group description: -	
Reporting group title	Baseline CRESPA study: Golimumab 50mg (Simponi®)
Reporting group description: -	
Reporting group title	CRESPA study: Placebo
Reporting group description: -	
Reporting group title	CRESPA study: Golimumab 50mg (Simponi®)
Reporting group description: -	
Reporting group title	Treatment arm

Reporting group description:

The 'CRESPA-Extension' part of the study is designed to investigate safety and long-term efficacy of golimumab in peripheral SpA patients with a major response to golimumab or a disease flare upon withdrawal of golimumab after reaching initial remission in the 'CRESPA' study. In the last 3 months of the CRESPA-Extension study part, golimumab treatment will be combined with methotrexate in order to explore the possibility that co-medication with methotrexate would allow for the discontinuation of golimumab treatment at week 116, thus providing clues of the potential of "biological-free" remission. 29 were not included in the extension study because of remission.

Primary: Clinical Remission Status at week 24

End point title	Clinical Remission Status at week 24

End point description:

The primary endpoint of the study is the induction of clinical remission (complete resolution of synovitis/dactylitis/enthesitis which was present at baseline) and prevention of newly developing peripheral and/or axial spondylarthritis signs). The primary analysis will be a comparison at 24 weeks of the percentage of patients in clinical remission in the group treated with the Tumor Necrosis Factor (TNF)-blocking agent versus placebo.

End point type	Primary

End point timeframe:

At week 24

End point values	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	40		
Units: number (n)	4	30		

Statistical analyses

Statistical analysis title	Clinical Remission Status
Comparison groups	CRESPA study: Placebo v CRESPA study: Golimumab 50mg (Simponi®)

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Fisher exact

Secondary: Patient global assessment of disease activity at week 24

End point title	Patient global assessment of disease activity at week 24
End point description:	

End point type	Secondary
End point timeframe:	
At week 24	

End point values	Baseline CRESPA study: Placebo	Baseline CRESPA study: Golimumab 50mg (Simponi®)	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	40	20	40
Units: 0–10 NRS scale				
median (inter-quartile range (Q1-Q3))	8 (4 to 9)	7 (5 to 8)	6 (4 to 8)	1 (0 to 3)

Statistical analyses

Statistical analysis title	PGA of disease activity
Comparison groups	Baseline CRESPA study: Golimumab 50mg (Simponi®) v Baseline CRESPA study: Placebo v CRESPA study: Placebo v CRESPA study: Golimumab 50mg (Simponi®)
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)

Secondary: Patient global assessment of pain at week 24

End point title	Patient global assessment of pain at week 24
End point description:	

End point type	Secondary
End point timeframe:	
At week 24	

End point values	Baseline CRESPA study: Placebo	Baseline CRESPA study: Golimumab 50mg (Simponi®)	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	40	20	40
Units: 0–10 NRS scale				
median (inter-quartile range (Q1-Q3))	6 (4 to 8)	5 (4 to 7)	6 (3 to 7)	2 (0 to 4)

Statistical analyses

Statistical analysis title	PGA of pain
Comparison groups	Baseline CRESPA study: Placebo v Baseline CRESPA study: Golimumab 50mg (Simponi®) v CRESPA study: Placebo v CRESPA study: Golimumab 50mg (Simponi®)
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)

Secondary: The improvement in the tender joint count at week 24

End point title	The improvement in the tender joint count at week 24
End point description:	
End point type	Secondary
End point timeframe:	
At week 24	

End point values	Baseline CRESPA study: Placebo	Baseline CRESPA study: Golimumab 50mg (Simponi®)	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	40	20	40
Units: tender joint count				
median (inter-quartile range (Q1-Q3))	4 (2 to 9)	5 (3 to 8)	5 (1 to 7)	0 (0 to 2)

Statistical analyses

Statistical analysis title	tender joint count
Comparison groups	Baseline CRESPA study: Placebo v Baseline CRESPA study: Golimumab 50mg (Simponi®) v CRESPA study: Placebo v CRESPA study: Golimumab 50mg (Simponi®)
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)

Secondary: The improvement in the swollen joint count at week 24

End point title	The improvement in the swollen joint count at week 24
End point description:	
End point type	Secondary
End point timeframe:	
At week 24	

End point values	Baseline CRESPA study: Placebo	Baseline CRESPA study: Golimumab 50mg (Simponi®)	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	40	20	40
Units: swollen joint count				
median (inter-quartile range (Q1-Q3))	3 (2 to 5)	4 (2 to 5)	1 (0 to 6)	0 (0 to 1)

Statistical analyses

Statistical analysis title	swollen joint count
Comparison groups	CRESPA study: Placebo v CRESPA study: Golimumab 50mg (Simponi®) v Baseline CRESPA study: Placebo v Baseline CRESPA study: Golimumab 50mg (Simponi®)
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)

Secondary: The improvement in dactylitis at week 24

End point title	The improvement in dactylitis at week 24

End point description:

End point type	Secondary

End point timeframe:

At week 24

End point values	Baseline CRESPA study: Placebo	Baseline CRESPA study: Golimumab 50mg (Simponi®)	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	40	20	40
Units: patients with dactylitis	9	15	12	7

Statistical analyses

Statistical analysis title	patients with dactylitis
Comparison groups	Baseline CRESPA study: Placebo v Baseline CRESPA study: Golimumab 50mg (Simponi®) v CRESPA study: Placebo v CRESPA study: Golimumab 50mg (Simponi®)
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Fisher exact

Secondary: The improvement in enthesitis at week 24

End point title	The improvement in enthesitis at week 24

End point description:

End point type	Secondary

End point timeframe:

At week 24

End point values	Baseline CRESPA study: Placebo	Baseline CRESPA study: Golimumab 50mg (Simponi®)	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	39	20	40
Units: patients with enthesitis	9	16	16	7

Statistical analyses

Statistical analysis title	Patients with enthesitis
Comparison groups	Baseline CRESPA study: Placebo v Baseline CRESPA study: Golimumab 50mg (Simponi®) v CRESPA study: Placebo v CRESPA study: Golimumab 50mg (Simponi®)
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Fisher exact

Secondary: Patients achieving Peripheral Spondyloarthritis Response Criteria pSpARC 40 at week 24

End point title	Patients achieving Peripheral Spondyloarthritis Response Criteria pSpARC 40 at week 24
End point description:	
End point type	Secondary
End point timeframe: At week 24	

End point values	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	40		
Units: number (n)	3	20		

Statistical analyses

Statistical analysis title	pSpARC 40%
Comparison groups	CRESPA study: Placebo v CRESPA study: Golimumab 50mg (Simponi®)

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011
Method	Fisher exact

Secondary: Patients achieving Peripheral Spondyloarthritis Response Criteria pSpARC 50 at week 24

End point title	Patients achieving Peripheral Spondyloarthritis Response Criteria pSpARC 50 at week 24

End point description:

End point type	Secondary

End point timeframe:

At week 24

End point values	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	40		
Units: number (n)	3	22		

Statistical analyses

Statistical analysis title	pSpARC 50%
Comparison groups	CRESPA study: Placebo v CRESPA study: Golimumab 50mg (Simponi®)
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	Fisher exact

Secondary: Patients achieving Peripheral Spondyloarthritis Response Criteria pSpARC 70 at week 24

End point title	Patients achieving Peripheral Spondyloarthritis Response Criteria pSpARC 70 at week 24

End point description:

End point type	Secondary

End point timeframe: At week 24

End point values	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	40		
Units: number (n)	3	16		

Statistical analyses

Statistical analysis title	pSpARC 70%
Comparison groups	CRESPA study: Placebo v CRESPA study: Golimumab 50mg (Simponi®)
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.077
Method	Fisher exact

Secondary: Patient global assessment of disease activity at week 12

End point title	Patient global assessment of disease activity at week 12
End point description:	
End point type	Secondary
End point timeframe: At week 12	

End point values	Baseline CRESPA study: Placebo	Baseline CRESPA study: Golimumab 50mg (Simponi®)	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	40	20	40[1]
Units: 0–10 NRS scale				
median (inter-quartile range (Q1-Q3))	8 (4 to 9)	7 (5 to 8)	6 (4 to 7)	2 (1 to 5)

Notes:

[1] - 40

Statistical analyses

Statistical analysis title	PGA of disease activity
Comparison groups	Baseline CRESPA study: Placebo v Baseline CRESPA study: Golimumab 50mg (Simponi®) v CRESPA study: Placebo v CRESPA study: Golimumab 50mg (Simponi®)
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Wilcoxon (Mann-Whitney)

Secondary: Patient global assessment of pain at week 12

End point title	Patient global assessment of pain at week 12
End point description:	
End point type	Secondary
End point timeframe:	
At week 12	

End point values	Baseline CRESPA study: Placebo	Baseline CRESPA study: Golimumab 50mg (Simponi®)	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	40	20	40
Units: 0–10 NRS scale				
median (inter-quartile range (Q1-Q3))	6 (4 to 8)	5 (4 to 7)	6 (3 to 7)	1 (1 to 4)

Statistical analyses

Statistical analysis title	PGA of pain
Comparison groups	Baseline CRESPA study: Placebo v Baseline CRESPA study: Golimumab 50mg (Simponi®) v CRESPA study: Placebo v CRESPA study: Golimumab 50mg (Simponi®)
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)

Secondary: The improvement in the tender joint count at week 12

End point title	The improvement in the tender joint count at week 12

End point description:

End point type	Secondary

End point timeframe:

At week 12

End point values	Baseline CRESPA study: Placebo	Baseline CRESPA study: Golimumab 50mg (Simponi®)	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	40	20	40
Units: tender joint count				
median (inter-quartile range (Q1-Q3))	4 (2 to 9)	5 (3 to 8)	4 (1 to 11)	0 (0 to 2)

Statistical analyses

Statistical analysis title	tender joint count
Comparison groups	Baseline CRESPA study: Placebo v Baseline CRESPA study: Golimumab 50mg (Simponi®) v CRESPA study: Placebo v CRESPA study: Golimumab 50mg (Simponi®)
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Wilcoxon (Mann-Whitney)

Secondary: The improvement in the swollen joint count at week 12

End point title	The improvement in the swollen joint count at week 12

End point description:

End point type	Secondary

End point timeframe:

At week 12

End point values	Baseline CRESPA study: Placebo	Baseline CRESPA study: Golimumab 50mg (Simponi®)	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	40	20	40
Units: swollen joint count				

median (inter-quartile range (Q1-Q3))	3 (2 to 5)	4 (2 to 5)	2 (0 to 7)	0 (0 to 0)

Statistical analyses

Statistical analysis title	swollen joint count
Comparison groups	Baseline CRESPA study: Placebo v Baseline CRESPA study: Golimumab 50mg (Simponi®) v CRESPA study: Placebo v CRESPA study: Golimumab 50mg (Simponi®)
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)

Secondary: The improvement in dactylitis at week 12

End point title	The improvement in dactylitis at week 12
End point description:	
End point type	Secondary
End point timeframe:	
At week 12	

End point values	Baseline CRESPA study: Placebo	Baseline CRESPA study: Golimumab 50mg (Simponi®)	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	40	20	40
Units: patients with dactylitis	9	15	8	3

Statistical analyses

Statistical analysis title	Patients with dactylitis
Comparison groups	Baseline CRESPA study: Golimumab 50mg (Simponi®) v CRESPA study: Placebo v Baseline CRESPA study: Placebo v CRESPA study: Golimumab 50mg (Simponi®)

Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Fisher exact

Secondary: The improvement in enthesitis at week 12

End point title	The improvement in enthesitis at week 12
End point description:	

End point type	Secondary
End point timeframe:	
At week 12	

End point values	Baseline CRESPA study: Placebo	Baseline CRESPA study: Golimumab 50mg (Simponi®)	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	40	20	40
Units: patients with enthesisits	9	16	5	6

Statistical analyses

Statistical analysis title	Patients with enthesitis
Comparison groups	Baseline CRESPA study: Placebo v Baseline CRESPA study: Golimumab 50mg (Simponi®) v CRESPA study: Placebo v CRESPA study: Golimumab 50mg (Simponi®)
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.48
Method	Fisher exact

Secondary: Patients achieving Peripheral Spondyloarthritis Response Criteria pSpARC 40 at week 12

End point title	Patients achieving Peripheral Spondyloarthritis Response Criteria pSpARC 40 at week 12
End point description:	

End point type	Secondary

End point timeframe: At week 12

End point values	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	40		
Units: number (n)	4	23		

Statistical analyses

Statistical analysis title	pSpARC 40%
Comparison groups	CRESPA study: Golimumab 50mg (Simponi®) v CRESPA study: Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007
Method	Fisher exact

Secondary: Patients achieving Peripheral Spondyloarthritis Response Criteria pSpARC 50 at week 12

End point title	Patients achieving Peripheral Spondyloarthritis Response Criteria pSpARC 50 at week 12
End point description:	
End point type	Secondary
End point timeframe: At week 12	

End point values	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	40		
Units: number (n)	4	22		

Statistical analyses

Statistical analysis title	pSpARC 50%
Comparison groups	CRESPA study: Placebo v CRESPA study: Golimumab 50mg (Simponi®)
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.013
Method	Fisher exact

Secondary: Patients achieving Peripheral Spondyloarthritis Response Criteria pSpARC 70 at week 12

End point title	Patients achieving Peripheral Spondyloarthritis Response Criteria pSpARC 70 at week 12

End point description:

End point type	Secondary

End point timeframe:

At week 12

End point values	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	40		
Units: pSpARC 70%	3	20		

Statistical analyses

Statistical analysis title	pSpARC 70%
Comparison groups	CRESPA study: Placebo v CRESPA study: Golimumab 50mg (Simponi®)
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011
Method	Fisher exact

Secondary: Bath AS Disease Activity Index (BASDAI) 50% response

End point title	Bath AS Disease Activity Index (BASDAI) 50% response

End point description:

End point type	Secondary

End point timeframe:
At 24 weeks

End point values	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	40		
Units: percentage of patients	3	29		

Statistical analyses

Statistical analysis title	BASDAI 50% response
Comparison groups	CRESPA study: Placebo v CRESPA study: Golimumab 50mg (Simponi®)
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Fisher exact

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Overall study	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	CRESPA study: Placebo
Reporting group description: -	
Reporting group title	CRESPA study: Golimumab 50mg (Simponi®)
Reporting group description: -	

Serious adverse events	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	4 / 40 (10.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Papillar carcinoma of the thyroidgland			
subjects affected / exposed	0 / 20 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Flare of peripheral spondyloarthritis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Worsening of artritis			
subjects affected / exposed	0 / 20 (0.00%)	2 / 40 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicula fracture			

subjects affected / exposed	0 / 20 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Acute cholecystitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nefrolithiasis en nefritis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infectious bronchitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	CRESPA study: Placebo	CRESPA study: Golimumab 50mg (Simponi®)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 20 (55.00%)	26 / 40 (65.00%)	
Infections and infestations			
Infectious AE			
subjects affected / exposed	11 / 20 (55.00%)	26 / 40 (65.00%)	
occurrences (all)	25	52	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 June 2012	Amendment 2: reasons for the substantial amendment: French ICF and questionnaire
17 April 2013	Amendment 3: Reasons for the substantial amendment: Rescue medication sulfasalazine/corticosteroid injections will be replaced by Golimumab 50 mg sc. Description: Starting at week 12 and until week 20, there will be an option to start rescue medication (in total 6 injections) with Golimumab 50mg sc every 4 weeks if all criteria for starting rescue medication are met. Reasons for the substantial amendment: Rescue medication sulfasalazine/corticosteroid injections will be replaced by Golimumab 50 mg sc. Description: In case of clinical relapse (after having reached "sustained clinical remission" at 2 consecutive visits), patients will have the option to receive open-label treatment with golimumab at a dose of 50 mg SC every 4 weeks. For this "relapse treatment phase" the open-label study medication (6 injections planned for visits week 24-44) will be used. Reasons for the substantial amendment: Visits at week 60 and 72 are extra. Investigators wish to clinically evaluate the patients a while longer.
05 August 2013	Amendment 4: Reasons for the substantial amendment: A 2-year open-label extension study to explore the long-term safety and efficacy of golimumab 50 mg SC every 4 weeks in patients that experienced major improvement of a clinical flare after achieving initial clinical remission. Description: Exploration of TNF-alpha blockade with golimumab in the induction of clinical remission in patients with early peripheral spondyloarthitis (SpA) according to ASAS-criteria. (‘CRESPA’), including a 2-year open-label extension study to explore the long-term safety and efficacy of golimumab 50 mg SC every 4 weeks in patients that experienced major improvement of a clinical flare after achieving initial clinical remission (‘CRESPA-extension’). In the open-label ‘CRESPA-extension’ part of the study, we want to investigate the long-term safety and efficacy of golimumab administered every 4 weeks at a dose of 50 mg subcutaneously (SC). Subjects will be allowed to participate in the ‘CRESPA-Extension’ part of the study if they are considered good candidates for chronic anti-TNF treatment and fulfill one of the following 2 scenarios:

26 February 2015	Amendment 5: reasons for the substantial amendment: Changes in conduct or management of the trial -Patients that are already more than one year in drug-free remission are considered to be in stable sustained remission and will not be entered in the CRESPA extension part of the study anymore. However, for patients that are already in drug-free remission for more than one year at the time of approval of version 6.0 of the protocol, a transitional measure will be applicable which allows them to still enter the CRESPA extension for a period of up to 2 years after reaching initial clinical remission. -Adding of an ultrasound evaluation at the last visit of the CRESPA extension part. -Additional info on labeling for the extension study; The open-label Golimumab syringes will be delivered by Theorem to the Ghent University Hospital Department of Rheumatology (via the Ghent University Hospital Pharmacy) in bulk with a global label. Individual syringes will be labeled study-specific following the hospital law by the Ghent University Hospital Pharmacy before dispensing to the patients.
08 February 2016	Amendment 6 Reasons for the substantial amendment: - Changes in safety or integrity of trial subjects - Changes in interpretation of scientific documents/value of the trial - Changes in conduct or management of the trial Description: - A 12 weeks combination therapy with methotrexate 10-15 mg weekly was added in the open-label CRESPA extension part. - Clarification of the primary analysis: The primary analysis will be a comparison at 24 weeks of the percentage of patients in clinical remissionin the group treated with the TNF-blocking agent versus placebo (for patients who were treated via the open-label Golimumab escape arm, an approach based upon last observation carried forward (LOCF) and non-responder imputation (NRI) will be used). - There will be a comparison at 12 (and if applicable at 24) weeks of the percentage of patients with a PSpARC 40 response in the group treated with the TNF-blocking agent versus placebo. - Changes were made to the secondary endpoints - Three months of follow-up after CRESPA-extension: After receiving 104 weeks of open label monotherapy with golimumab 50 mg SC every 4 weeks in the CRESPA–extension study part, the patients will be offered an additional 12 weeks of open label golimumab 50 mg SC every 4 weeks, but now in combination with methotrexate. After these 12 weeks methotrexate therapy will be continued (if well tolerated), but golimumab will be stopped and the patients will further receive appropriate follow-up according to current best clinical practice guidelines for the treatment of (axial and/or peripheral) spondyloarthritis. As before, clinical evaluations, patient reported outcomes and laboratory evaluations will be recorded in the local registry for spondyloarthritis (Be-GIANT).

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/28213565