Clinical trial results:
Efficacy of golimumab in early axial spondyloarthritis (axSpA) in relation to gut inflammation, an early remission induction study (GO GUT).

Summary

EudraCT number	2017-001728-23
Trial protocol	BE
Global end of trial date	14 December 2023

Results information

Result version number	v1 (current)
This version publication date	20 July 2024
First version publication date	20 July 2024

Trial information

Trial identification

Sponsor protocol code	AGO/2017/004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03270501
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Department of Rheumatology, Gent University Hospital
Sponsor organisation address	Corneel Heymanslaan 10, Gent, Belgium, 9000
Public contact	Health, Innovation & Research Institute, Gent University Hospital, +32 9332 05 00, hiruz.ctu@uzgent.be
Scientific contact	Health, Innovation & Research Institute, Gent University Hospital, +32 9332 05 00, 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	31 May 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 December 2023
Global end of trial reached?	Yes
Global end of trial date	14 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To describe and confirm the relationship between subclinical gut inflammation and axSpA.
- To evaluate whether there is a higher need of anti-tumor necrosis factor α (anti-TNFα) treatment in axSpA patients with (subclinical) gut inflammation compared to those without.

Protection of trial subjects:

Tight-control, treat-to-target therapy according to the current international recommendations for the management of axial spondyloarthritis

Background therapy: -

Evidence for comparator:

The study has a single arm, no comparators are used

Actual start date of recruitment	08 November 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	Belgium: 64
Worldwide total number of subjects	64
EEA total number of subjects	64

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)	64
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients diagnosed with axial spondyloarthritis, fulfilling the trial's inclusion criteria were recruited across 3 rheumatology centres in Belgium, i.e. Gent University Hospital, Imelda Hospital in Bonheiden and Jessa Hospital in Hasselt between November 2017 and December 2022.

Pre-assignment

Screening details:

Main inclusion criteria were: expert diagnosis of axial spondyloarthritis, fulfillinf the ASAS classification criteria; treatment-naive status; symptom duration of less than 1 year; high disease activity and signs of inflammation at inclusion (positive MRI of the sacroiliac joints, elevated CRP).

Pre-assignment period milestones

Number of subjects started	64
Number of subjects completed	64

Period 1

Period 1 title	Pre-treatment period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Single arm study, no blinding implemented.

Arms

Arm title	NSAIDs With Possible Step-up to Golimumab

Arm description: -

Arm type	Experimental
Investigational medicinal product name	NSAIDs with possible step up to Golimumab (Simponi s.c. 50mg 1x/4 weeks)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Solution for injection in pre-filled pen
Routes of administration	Injection , Oral use

Dosage and administration details:

NSAIDs: All patients fulfilling the inclusion criteria will be treated according to the current recommendations for the management of axial spondyloarthritis, i.e. with 2 courses of NSAIDs in maximum tolerated anti-inflammatory dose. Specific NSAIDs and form of admonistration is chosen individually by the patient and treating rheumatologist. If sufficient response is acheived, the patients will continue receiving NSAIDs and after sustained remission, the therapy will be stopped. If therapy with NSAIDs provides insufficient control of disease activity, switch to therapy with Golimumab will be made.
Golimumab: Patients who did not have a good treatment response to 2 NSAIDs, will be treated with golimumab adminiostered subcutanously (Simponi pre-filled pens 50mg/4 weeks). After sustained remission, the therapy will be stopped.

Number of subjects in period 1	NSAIDs With Possible Step-up to Golimumab
Started	64
Completed	58
Not completed	6
Protocol deviation	6

Period 2

Period 2 title	Treatment period
Is this the baseline period?	Yes[1]
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Single arm study protocol - no blinding implemented.

Arms

Arm title	NSAIDs With Possible Step-up to Golimumab

Arm description:

NSAIDs: All patients fulfilling the inclusion criteria will be treated according to the current recommendations for the management of axial spondyloarthritis, i.e. with 2 courses of NSAIDs. If sufficient response is acheived, the patients will continue receiving NSAIDs and after sustained remission, the therapy will be stopped. If therapy with NSAIDs provides insufficient control of disease activity, switch to therapy with Golimumab will be made.
Golimumab: Patients who did not have a good treatment response to 2 NSAIDs, will be treated with golimumab sc 50mg/4 weeks. After sustained remission, the therapy will be stopped.
All patients will undergo a ileocoloscopy at baseline and, if positive, at time of remission.

Arm type	Experimental
Investigational medicinal product name	NSAIDs with possible step up to Golimumab (Simponi s.c. 50mg 1x/4 weeks)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen, Capsule
Routes of administration	Oral use, Injection

Dosage and administration details:

NSAIDs: All patients fulfilling the inclusion criteria will be treated according to the current recommendations for the management of axial spondyloarthritis, i.e. with 2 courses of NSAIDs in maximum tolerated anti-inflammatory dose. Specific NSAIDs and form of admonistration is chosen individually by the patient and treating rheumatologist. If sufficient response is acheived, the patients will continue receiving NSAIDs and after sustained remission, the therapy will be stopped. If therapy with NSAIDs provides insufficient control of disease activity, switch to therapy with Golimumab will be made.
Golimumab: Patients who did not have a good treatment response to 2 NSAIDs, will be treated with golimumab adminiostered subcutanously (Simponi pre-filled pens 50mg/4 weeks). After sustained remission, the therapy will be stopped.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: According to the study protocol, a short period of time was allowed between patient enrollment and the start of the treatment (baseline period). During that time some patients' complaints spontaneously improved. As a result, these patients were no longer eligible to participate in the study.

Number of subjects in period 2[2]	NSAIDs With Possible Step-up to Golimumab
Started	58
Completed	55
Not completed	3
Adverse event, non-fatal	1
Lost to follow-up	2

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The reported worldwide number enrolled in the trial is 64, which is the number of patients who successfully completed the screening visit and received study-specific interventions (eg. biological sample collection). However, in the time between patient enrollment and the start of the treatment (baseline period) some patients' complaints spontaneously improved. As a result, these patients were no longer eligible to participate in the study.

Baseline characteristics

Reporting groups

Reporting group title	Treatment period

Reporting group description: -

Reporting group values	Treatment period	Total	
Number of subjects	58	58	
Age categorical			
Adult patients between 18 and 64 years of age			
Units: Subjects			
Adults (18-64 years)	58	58	
Age continuous			
Mean age of patients included in the trial			
Units: years			
arithmetic mean	28.2		
standard deviation	± 6.3	-	
Gender categorical			
Units: Subjects			
Female	24	24	
Male	34	34	
Ethnicity (NIH/OMB)			
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	56	56	
Unknown or Not Reported	2	2	
HLA-B27			
Positive for HLA-B27 (%)			
Units: Subjects			
Positive	50	50	
Negative	8	8	
Assessment of SpondyloArthritis international Society (ASAS) criteria: Inflammatory Back Pain			
IBP according to experts: four out of five of the following parameters present: (1) age at onset less than 40 years, (2) insidious onset, (3) improvement with exercise, (4) no improvement with rest, (5) pain at night (with improvement upon getting up). (Reference: Ann Rheum Dis 2009;68:777-83)			
Units: Subjects			
Yes	51	51	
No	7	7	
Assessment of SpondyloArthritis international Society (ASAS) criteria: Arthritis			
Documented past or present active synovitis diagnosed by a doctor.			
Units: Subjects			
Yes	5	5	
No	53	53	
Assessment of SpondyloArthritis international Society (ASAS) criteria: Heel enthesitis			

Measure Description: Heel enthesitis: past or present spontaneous pain or tenderness at examination at the site of the insertion of the Achilles tendon or plantar fascia at the calcaneus. (Reference: Ann Rheum Dis 2009;68:777-83)			
Units: Subjects			
Yes	3	3	
No	55	55	
Assessment of SpondyloArthritis international Society (ASAS) criteria: Psoriasis			
Documented past or present psoriatic skin or nail lesions diagnosed by a doctor.			
Units: Subjects			
Yes	0	0	
No	58	58	
Assessment of SpondyloArthritis international Society (ASAS) criteria: Uveitis			
Documented past or present anterior uveitis, diagnosed by an ophthalmologist. (Reference: Ann Rheum Dis 2009;68:777-83)			
Units: Subjects			
Yes	0	0	
No	58	58	
Assessment of SpondyloArthritis international Society (ASAS) criteria: Dactylitis			
Documented past or present dactylitis diagnosed by a doctor. (Reference: Ann Rheum Dis 2009;68:777-83)			
Units: Subjects			
Yes	0	0	
No	58	58	
Assessment of SpondyloArthritis international Society (ASAS) criteria: Inflammatory bowel disease			
Documented past or present inflammatory bowel disease diagnosed by a doctor. (Reference: Ann Rheum Dis 2009;68:777-83)			
Units: Subjects			
Yes	1	1	
No	57	57	
Assessment of SpondyloArthritis international Society criteria: Elevated C-reactive protein			
Measured within 3 months priort to study inclusoon or at baseline and temporally associated with patient's complaints emergence of CRP above upper normal limit in the presence of back pain, after exclusion of other causes for elevated CRP concentration. (Reference: Ann Rheum Dis 2009;68:777-83)			
Units: Subjects			
Yes	24	24	
No	34	34	
Assessment of SpondyloArthritis international Society criteria: Family history of spondyloarthritis			
Patient reported presence in first-degree or second-degree relatives of any of the following: (a) ankylosing spondylitis, (b) psoriasis, (c) uveitis, (d) reactive arthritis, (e) inflammatory bowel disease. (Reference: Ann Rheum Dis 2009;68:777-83)			
Units: Subjects			
Yes	22	22	
No	36	36	

Ankylosing Spondylitis Disease Activity Score (ASDAS)-CRP			
ASDAS is a composite index to assess disease activity in axSpA. ASDAS parameters: 1) Total back pain 2) Patient global 3) Peripheral pain/swelling 4) Duration of morning stiffness 5) CRP in mg/L: ASDAS calculation: 0.121 × total back pain + 0.110 × patient global + 0.073 × peripheral pain/swelling + 0.058 × duration of morning stiffness + 0.579 × Ln(max(CRP,2)+1). Parameters 1-4 are reported by patients on a visual analogue score ranging from 0 to 10. Data from five variables combine to yield a score (minimum 0.636 to no defined upper limit), higher scores indicate higher disease activity.			
Units: Point on a continuous scale			
arithmetic mean	3.0		
standard deviation	± 0.9	-	
Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)			
BASDAI is a measure of disease activity which was calculated based on 6 separate questionnaire items that were answered by the patients using visual analogue scale scales with range 0-10. A weighted average was performed, where items 5 and 6 had a weight of 0.5 whereas items 1, 2, 3 and 4 had a weight of 1. Range is from 0 to 10, with 10 indicating more severe disease activity.			
Units: Units on a continuous scale			
arithmetic mean	4.5		
standard deviation	± 1.5	-	
Bath Ankylosing Spondylitis Functional index (BASFI)			
BASFI is a measure of physical function which was calculated based on 10 separate questionnaire items that were answered by the patients using visual analogue scales with range 0-10, an average across 10 items was calculated. The range is 0-10 with 10 indicating that the level of physical functioning is more severely affected.			
Units: Units on a continuous scale			
arithmetic mean	3.0		
standard deviation	± 2.2	-	
CRP			
Inflammatory marker			
Units: mg/ml			
arithmetic mean	7.6		
standard deviation	± 11	-	
Body mass index (BMI)			
Units: kg/m2			
arithmetic mean	23.3		
standard deviation	± 4.7	-	
Time from diagnosis			
ime from the first diagnosis of axial spondyloarthritis to enrollment in the trial			
Units: days			
median	37		
standard deviation	± 18	-	

End points

End points reporting groups

Reporting group title	NSAIDs With Possible Step-up to Golimumab
Reporting group description: -	
Reporting group title	NSAIDs With Possible Step-up to Golimumab

Reporting group description:

NSAIDs: All patients fulfilling the inclusion criteria will be treated according to the current recommendations for the management of axial spondyloarthritis, i.e. with 2 courses of NSAIDs. If sufficient response is acheived, the patients will continue receiving NSAIDs and after sustained remission, the therapy will be stopped. If therapy with NSAIDs provides insufficient control of disease activity, switch to therapy with Golimumab will be made.
Golimumab: Patients who did not have a good treatment response to 2 NSAIDs, will be treated with golimumab sc 50mg/4 weeks. After sustained remission, the therapy will be stopped.
All patients will undergo a ileocoloscopy at baseline and, if positive, at time of remission.

Primary: Sustained clinical remission

End point title	Sustained clinical remission[1]

End point description:

The primary endpoint of the study was achieving sustained clinical remission, defined as disease activity outcome measure ASDAS-CRP <1.3 at two consequtive study visits with at least 12 week interval between them.

End point type	Primary

End point timeframe:

From the initiation of the treatment protocol (=baseline) to week 52 visit of the trial.

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 trial has a single arm, therefore no comparative analyses are possible. The primary study endpoint - sustained clinical remission - is reported as percentage of patients achieving the endpoint.

End point values	NSAIDs With Possible Step-up to Golimumab			
Subject group type	Reporting group			
Number of subjects analysed	55[2]			
Units: Patients achieving remission	34			

Notes:

[2] - Number of patients who completed the study.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events data was collected between the first dose administration of trial medication and the last trial related activity. Medical events that occured between signing of the Informed Consent and the first intake of trial medication were documented a

Adverse event reporting additional description:

All adverse events and serious adverse events were recorded in the patient's file and in the Case Report Form. Adverse Events were defined as any untoward medical occurrence in a patient administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Included patients

Reporting group description:

Patients included in the trial, for whom the treatment protocol was initiated.

Serious adverse events	Included patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 58 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Included patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 58 (32.76%)		
Infections and infestations			
Nasopharyngitis	Additional description: Viral or bacterial upper respiratory tract infection, including confirmed SARS-CoV-2 infections.		
subjects affected / exposed	14 / 58 (24.14%)		
occurrences (all)	16		
Gastroenteritis	Additional description: Gastroenteritis of unspecified origin, self-limiting.		
subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	4		
Otitis media			

subjects affected / exposed occurrences (all)	3 / 58 (5.17%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 September 2017	Clarification of the timing and analysis of stool sample collection.
09 October 2019	New trial center (Center 02) added: Reuma Institute Hasselt.
15 October 2020	Extension of the enrollment period.
19 January 2021	New trial center (Center 03) added: Imelda hospital Bonheiden. Additional medical examination in case if the baseline visit takes place more than 4 weeks after the screening visit.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The trial included 64 of initially anticipated 147 patients, what impacts downstream analyses powered for a larger group. The baseline prevalence of gut inflammation was lower than anticipated, therefore the primary objective could not be assessed.

Notes: