Clinical trial results:
Comparison of the effect of treatment with NSAIDs added to anti-TNF therapy versus anti-TNF therapy alone on progression of structural damage in the spine over two years in patients with ankylosing spondylitis: a randomized controlled multicentre trial (CONSUL)

Summary

EudraCT number	2016-000615-33
Trial protocol	DE
Global end of trial date	25 February 2021

Results information

Result version number	v1 (current)
This version publication date	31 July 2022
First version publication date	31 July 2022

Trial information

Trial identification

Sponsor protocol code	CONSUL2016

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02758782
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Charité Universitätsmedizin Berlin
Sponsor organisation address	Charitéplatz 1, Berlin, Germany, 10117
Public contact	Rheumatology at Campus B Franklin, Charite Universitaetsmedizin, +49 3084454144, denis.poddubnyy@charite.de
Scientific contact	Rheumatology at Campus B Franklin, Charite Universitaetsmedizin, +49 3084454144, denis.poddubnyy@charite.de

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	25 February 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 February 2021
Global end of trial reached?	Yes
Global end of trial date	25 February 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the impact of treatment with a non-steroidal anti-inflammatory drug (NSAID) – Celecoxib – when added to anti-tumour necrosis factor (TNF) therapy – Golimumab – as compared to anti-TNF therapy (Golimumab) alone on progression of structural damage in the spine over two years in patients with AS (Absolute progression of the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) over two years of therapy (weeks 12-108) in the Phase II (core phase) of the trial)

Protection of trial subjects:

The study was conducted according to the ethical principles of the Declaration of Helsinki (JAMA. 2013;310(20):2191-2194).
The study protocol and all amendments were reviewed by the Independent Ethics Commission of the State of Berlin (Ethik-Kommission des Landes Berlin) and Independent Ethics Committees for each center. All patients provided a written informed consent prior to randomization. The International Conference of Harmonisation Good Clinical Practice
guidelines and the German drug law (Arzneimittelgesetz).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 June 2016
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	Germany: 128
Worldwide total number of subjects	128
EEA total number of subjects	128

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)	128
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Start of recruitment was on September 19th 2016 and was finished on December 12th in 2018. Recruitment was conducted at 16 study centres in Germany.

Pre-assignment

Screening details:

157 patients were screened 6 week prior run-in phase(treatment with Golimumab); 130 fulfilled the inclusion and exclusion criteria. 2 patients withdrew their informed consent
remaining n=128 patients were enrolled into the run-in phase. Run-in phase was 12 weeks. 19 Patientes were non responders and were excluded.

Pre-assignment period milestones

Number of subjects started	128
Number of subjects completed	109

Pre-assignment subject non-completion reasons

Reason: Number of subjects	non responders: 19

Period 1

Period 1 title	core phase (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Golimumab & celecoxib
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Golimumab
Investigational medicinal product code	
Other name	Simponi
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details: Golimumab 50mg s.c. per Month	
Investigational medicinal product name	Celebrex
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details: a daily dose of 400 mg/day	
Arm title	Golimumab alone
Arm description: -	
Arm type	Active comparator

Investigational medicinal product name	Golimumab
Investigational medicinal product code	
Other name	Simponi
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

golimumab 50 mg subcutaneously every 4 weeks alone

Number of subjects in period 1[1]	Golimumab & celecoxib	Golimumab alone
Started	54	55
Completed	45	52
Not completed	9	3
Adverse event, non-fatal	4	1
Lack of efficacy	2	1
Protocol deviation	3	1

Notes:

[1] - 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: 109 patients fulfilled the BASDAI response criterion at week 12 and were randomized with 54 patients in the combination arm with Golimumab + Celecoxib and 55 patients in the monotherapy with Golimumab arm.

Baseline characteristics

Reporting groups	
Reporting group title	Golimumab & celecoxib
Reporting group description: -	
Reporting group title	Golimumab alone
Reporting group description: -	

Reporting group values	Golimumab & celecoxib	Golimumab alone	Total
Number of subjects	54	55	109
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	39.9	37.5	
full range (min-max)	21 to 59	19 to 63	-
Gender categorical Units: Subjects			
Female	14	14	28
Male	40	41	81

End points

End points reporting groups

Reporting group title	Golimumab & celecoxib
Reporting group description: -	
Reporting group title	Golimumab alone
Reporting group description: -	

Primary: mSASSS progression and mSASSS at year 2

End point title	mSASSS progression and mSASSS at year 2
End point description:	
The percentage of patients with radiographic progression (mSASSS >=2) was only slightly higher in the golimumab alone group (27.2% vs 23.6%) (Similar in the case of (mSASSS > 0: 59.7% vs. 56.3%).	
End point type	Primary
End point timeframe:	
108 weeks	

End point values	Golimumab & celecoxib	Golimumab alone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	55		
Units: Score				
arithmetic mean (standard deviation)				
mSASSS change	1.1 (± 3)	1.7 (± 3.5)		
mSASSS year 2	12.9 (± 17.9)	12.4 (± 14.5)		

Statistical analyses

Statistical analysis title	The radiographic progression
Comparison groups	Golimumab alone v Golimumab & celecoxib
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05 [1]
Method	Wilcoxon (Mann-Whitney)

Notes:

[1] - The difference in mSASSS progression did not achieve statistical significance (p=0.79, Mann-Whitney U-test).

Secondary: Change Bath Ankylosing Spondylitis

End point title	Change Bath Ankylosing Spondylitis
End point description:	
End point type	Secondary

End point timeframe:

108 weeks

End point values	Golimumab & celecoxib	Golimumab alone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	52		
Units: Score				
arithmetic mean (standard deviation)				
BASDAI	6.2 (± 1)	6.2 (± 1.2)		
BASFI	5.6 (± 1.4)	4.6 (± 1.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: CRP

End point title	CRP

End point description:

End point type	Secondary

End point timeframe:

108 weeks

End point values	Golimumab & celecoxib	Golimumab alone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	52		
Units: milligram(s)/cubic metre				
arithmetic mean (full range (min-max))	9.1 (0.4 to 115.5)	9.1 (0.5 to 146.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: New syndesmophytes, growth of syndesmophytes

End point title	New syndesmophytes, growth of syndesmophytes

End point description:

patients with development of new syndesmophytes and of growth of syndesmophytes and combination of both scored by >= 2 readers or three readers

End point type	Secondary

End point timeframe:
108 Weeks

End point values	Golimumab & celecoxib	Golimumab alone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	52		
Units: Subjects				
New syndesm. >=2reader	13	17		
New syndesm. 3 reader	5	13		
Growth of synd. >=2reader	4	8		
Growth of synd. 3 reader	1	4		
New/ growth of synd. >=2reader	15	18		
New/ growth of synd. 3 reader	5	14		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 108 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups	
Reporting group title	golimumab + celecoxib
Reporting group description: -	
Reporting group title	golimumab alone
Reporting group description: -	

Serious adverse events	golimumab + celecoxib	golimumab alone	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 54 (12.96%)	5 / 55 (9.09%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Electric injury			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Meniscus operation			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Chronic focal encephalitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial nerve paresis			

subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Meniscopathy			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Erysipelas			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon infection			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute gastroenteritis			

subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
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: 1.5 %

Non-serious adverse events	golimumab + celecoxib	golimumab alone	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 54 (94.44%)	48 / 55 (87.27%)	
Investigations			
Transaminases increased			
subjects affected / exposed	10 / 54 (18.52%)	9 / 55 (16.36%)	
occurrences (all)	11	12	
Injury, poisoning and procedural complications			
Injection site reaction			
subjects affected / exposed	1 / 54 (1.85%)	1 / 55 (1.82%)	
occurrences (all)	7	1	
Vascular disorders			
Arterial hypertension			
subjects affected / exposed	7 / 54 (12.96%)	5 / 55 (9.09%)	
occurrences (all)	8	7	
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 54 (9.26%)	7 / 55 (12.73%)	
occurrences (all)	6	7	
Immune system disorders			
Axial spondyloarthritis			
subjects affected / exposed	5 / 54 (9.26%)	4 / 55 (7.27%)	
occurrences (all)	5	5	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	1 / 54 (1.85%)	5 / 55 (9.09%)	
occurrences (all)	1	6	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 54 (7.41%)	5 / 55 (9.09%)	
occurrences (all)	5	5	

Diarrhoea			
subjects affected / exposed	6 / 54 (11.11%)	4 / 55 (7.27%)	
occurrences (all)	7	4	
Gastroenteritis			
subjects affected / exposed	5 / 54 (9.26%)	7 / 55 (12.73%)	
occurrences (all)	7	7	
Skin and subcutaneous tissue disorders			
Atopic eczema			
subjects affected / exposed	3 / 54 (5.56%)	0 / 55 (0.00%)	
occurrences (all)	8	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 54 (1.85%)	5 / 55 (9.09%)	
occurrences (all)	1	6	
Joint pain			
subjects affected / exposed	0 / 54 (0.00%)	6 / 55 (10.91%)	
occurrences (all)	0	7	
Infections and infestations			
Herpes labialis			
subjects affected / exposed	3 / 54 (5.56%)	5 / 55 (9.09%)	
occurrences (all)	11	6	
Pharyngitis			
subjects affected / exposed	5 / 54 (9.26%)	0 / 55 (0.00%)	
occurrences (all)	8	0	
Rhinitis			
subjects affected / exposed	5 / 54 (9.26%)	6 / 55 (10.91%)	
occurrences (all)	8	8	
Sinusitis			
subjects affected / exposed	6 / 54 (11.11%)	7 / 55 (12.73%)	
occurrences (all)	8	8	
Tonsillitis			
subjects affected / exposed	5 / 54 (9.26%)	1 / 55 (1.82%)	
occurrences (all)	7	2	
Urinary tract infection			
subjects affected / exposed	2 / 54 (3.70%)	3 / 55 (5.45%)	
occurrences (all)	8	6	

Acute upper respiratory tract infection			
subjects affected / exposed	35 / 54 (64.81%)	38 / 55 (69.09%)	
occurrences (all)	73	92	
Bronchitis			
subjects affected / exposed	8 / 54 (14.81%)	4 / 55 (7.27%)	
occurrences (all)	10	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 March 2017	Protocol clarifications concerning inclusion and exclusion criteria, safety assessment and specification of study related procedures

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/28601821