



Clinical trial results:

Disease activity-guided tapering of biologics in patients with rheumatoid arthritis, psoriatic arthritis or axial spondyloarthritis: The pragmatic, multi-centre, randomized, open-label, equivalence BIOlogical Dose OPTimisation (BIODOPT) trial

Summary

EudraCT number	2017-001970-41
Trial protocol	DK
Global end of trial date	19 January 2025

Results information

Result version number	v1 (current)
This version publication date	10 December 2025
First version publication date	10 December 2025

Trial information

Trial identification

Sponsor protocol code	20170508
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Aalborg University Hospital, Department of Rheumatology
Sponsor organisation address	Reberbangade 15, Aalborg, Denmark, 9000
Public contact	MD, PhD Line Uhrenholt, Aalborg University Hospital, Department of Rheumatology, +45 21707727, l.uhrenholt@rn.dk
Scientific contact	MD, PhD Line Uhrenholt, Aalborg University Hospital, Department of Rheumatology, +45 21707727, l.uhrenholt@rn.dk
Sponsor organisation name	Aalborg University Hospital, Department of Rheumatology
Sponsor organisation address	Reberbangade 15, Aalborg, Denmark, 9000
Public contact	MD, PhD Salome Kristensen, Aalborg University Hospital, Department of Rheumatology, +45 97664015, sakr@rn.dk
Scientific contact	MD, PhD Salome Kristensen, Aalborg University Hospital, Department of Rheumatology, +45 97664015, sakr@rn.dk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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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	20 January 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 January 2025
Global end of trial reached?	Yes
Global end of trial date	19 January 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The BIODOPT trial compares a disease activity-guided tapering algorithm to continuation of biologics as usual care in patients with inflammatory arthritis in sustained low disease activity. The co-primary objective was met if superiority in the proportion of patients achieving $\geq 50\%$ biologic reduction at 18 months was demonstrated while mean disease activity remained equivalent, an equivalence margin of ± 0.5 disease activity points was pre-specified.

Protection of trial subjects:

Trial subjects were monitored at the rheumatology out patient clinic at baseline, month 4, month 8, month 12, month 18, and month 24. Furthermore, a long-term assessment at year 5 was conducted. Between year 2 and year 5, patients were monitored in accordance with national guidelines i.e., yearly or after the treating rheumatologist discretion.

Background therapy:

At baseline, concomitant csDMARDs were used by 43% of the tapering group and 47% of the control group - the majority was MTX (42% vs 43%, respectively).

Evidence for comparator:

Biological therapies and disease activity-guided monitoring have improved the management of patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and axial spondyloarthritis (axSpA), as large proportions of patients reach low disease activity (LDA). But increasing evidence suggest that patients can maintain disease control even if the biological therapies are tapered. In clinical trials, biologic tapering is done by either a fixed dose reduction, often in one step, e.g. 50% interval prolongation/dose reduction, or disease activity-guided tapering after an algorithm until flare or withdrawal. Disease activity-guided tapering of biologics is generally the more aggressive approach as it allows maximal tapering. Evidence on disease activity-guided tapering of biologics vs continuation of biologics as usual care is limited to a few randomized controlled trials.

Actual start date of recruitment	17 May 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 142
Worldwide total number of subjects	142
EEA total number of subjects	142

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)	103
From 65 to 84 years	39
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Eligible patients received information about the trial at routine visits in the Rheumatology outpatient clinic. Patients who wished to participate were enrolled after written informed consent was provided. The inclusion period started in May 2018 and ended pre-maturely in April 2020 because of the national implications of the COVID-19 pandemic.

Pre-assignment

Screening details:

Eligible patients were adults diagnosed with RA, PsA, or axSpA in LDA and treated with abatacept, adalimumab, certolizumab-pegol, etanercept, golimumab, infliximab, or tocilizumab, including biosimilars, on a stable dosage for ≥ 12 months. Glucocorticoids (oral, intramuscular, or intraarticular) within the past 12 months were not allowed.

Period 1

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

Blinding implementation details:

The interventions in this trial were not blinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	The tapering group

Arm description:

The tapering group followed a disease activity-guided tapering strategy for the biological therapy, i.e., the biologic dosing interval was prolonged by approximately 25% every 4 months until flare or complete biological withdrawal. However, due to the longer dosing interval for infliximab, it was decided to space the infliximab dosing interval by 2 weeks at each infusion.

Arm type	Experimental
Investigational medicinal product name	Abatacept
Investigational medicinal product code	L04AA24
Other name	
Pharmaceutical forms	Concentrate and solvent for dispersion for injection, Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Injection , Concentrate for solution for infusion

Dosage and administration details:

Subcutaneous injections: 125 mg every week

Intravenous infusions:

- Weight < 60 kg: 500 mg every 4 weeks
- Weight 60-100 kg: 750 mg every 4 weeks
- Weight > 100 kg: 1000 mg every 4 week

Investigational medicinal product name	Adalimumab
Investigational medicinal product code	L04AB04
Other name	
Pharmaceutical forms	Concentrate and solvent for dispersion for injection
Routes of administration	Injection

Dosage and administration details:

Subcutaneous: 40 mg every 2 weeks

Investigational medicinal product name	Certolizumab-pegol
Investigational medicinal product code	L04AB05
Other name	
Pharmaceutical forms	Concentrate and solvent for dispersion for injection
Routes of administration	Injection
Dosage and administration details:	
Subcutaneous:	
- 200 mg subcutaneous every 2 weeks	
OR	
- 400 mg subcutaneous every 4 week	
Investigational medicinal product name	Etanercept
Investigational medicinal product code	L04AB01
Other name	
Pharmaceutical forms	Concentrate and solvent for dispersion for injection
Routes of administration	Injection
Dosage and administration details:	
Subcutaneous: 50 mg every week	
Investigational medicinal product name	Golimumab
Investigational medicinal product code	L04AB06
Other name	
Pharmaceutical forms	Concentrate and solvent for dispersion for injection
Routes of administration	Injection
Dosage and administration details:	
Subcutaneous: 50 mg every 4 weeks	
Investigational medicinal product name	Infliximab
Investigational medicinal product code	L04AB02
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Infusion
Dosage and administration details:	
- RA: 6 mg/kg intravenous every 8 weeks	
- PsA: 5 mg/kg intravenous every 8 weeks	
- AxSpA: 5 mg/kg intravenous every 6 weeks	
Investigational medicinal product name	Tocilizumab
Investigational medicinal product code	L04AC07
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion, Concentrate and solvent for dispersion for injection
Routes of administration	Infusion , Injection
Dosage and administration details:	
- Subcutaneous: 162 mg every week	
- Intravenous: 8 mg/kg every 4 weeks	
Arm title	The Control group
Arm description:	
A pragmatic usual care practice was applied to the control group, i.e. the control group continued their baseline biological dosing interval unchanged but, if requested by the patient, a small increase of the dosing interval was allowed.	
Arm type	Active comparator
Investigational medicinal product name	Abatacept
Investigational medicinal product code	L04AA24
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion, Concentrate and solvent for dispersion for injection
Routes of administration	Concentrate for solution for infusion , Injection

Dosage and administration details:

Subcutaneous injections: 125 mg every week

Intravenous infusions:

- Weight < 60 kg: 500 mg every 4 weeks
- Weight 60-100 kg: 750 mg every 4 weeks
- Weight > 100 kg: 1000 mg every 4 week

Investigational medicinal product name	Adalimumab
Investigational medicinal product code	L04AB04
Other name	
Pharmaceutical forms	Concentrate and solvent for dispersion for injection
Routes of administration	Injection

Dosage and administration details:

Subcutaneous: 40 mg every 2 weeks

Investigational medicinal product name	Certolizumab-pegol
Investigational medicinal product code	L04AB05
Other name	
Pharmaceutical forms	Concentrate and solvent for dispersion for injection
Routes of administration	Injection

Dosage and administration details:**Subcutaneous:**

- 200 mg subcutaneous every 2 weeks

OR

- 400 mg subcutaneous every 4 week

Investigational medicinal product name	Etanercept
Investigational medicinal product code	L04AB01
Other name	
Pharmaceutical forms	Concentrate and solvent for dispersion for injection
Routes of administration	Injection

Dosage and administration details:

Subcutaneous: 50 mg every week

Investigational medicinal product name	Golimumab
Investigational medicinal product code	L04AB06
Other name	
Pharmaceutical forms	Concentrate and solvent for dispersion for injection
Routes of administration	Injection

Dosage and administration details:

Subcutaneous: 50 mg every 4 weeks

Investigational medicinal product name	Infliximab
Investigational medicinal product code	L04AB02
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

- RA: 6 mg/kg intravenous every 8 weeks
- PsA: 5 mg/kg intravenous every 8 weeks
- AxSpA: 5 mg/kg intravenous every 6 weeks

Investigational medicinal product name	Tocilizumab
Investigational medicinal product code	L04AC07
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion, Concentrate and solvent for dispersion for injection
Routes of administration	Infusion , Injection

Dosage and administration details:

- Subcutaneous: 162 mg every week
- Intravenous: 8 mg/kg every 4 weeks

Number of subjects in period 1	The tapering group	The Control group
Started	95	47
Completed	88	46
Not completed	7	1
Consent withdrawn by subject	4	-
Adverse event, non-fatal	-	1
Non-compliance to visits	2	-
Protocol deviation	1	-

Baseline characteristics

Reporting groups

Reporting group title	The tapering group
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Reporting group description:

The tapering group followed a disease activity-guided tapering strategy for the biological therapy, i.e., the biologic dosing interval was prolonged by approximately 25% every 4 months until flare or complete biological withdrawal. However, due to the longer dosing interval for infliximab, it was decided to space the infliximab dosing interval by 2 weeks at each infusion.

Reporting group title	The Control group
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Reporting group description:

A pragmatic usual care practice was applied to the control group, i.e. the control group continued their baseline biological dosing interval unchanged but, if requested by the patient, a small increase of the dosing interval was allowed.

Reporting group values	The tapering group	The Control group	Total
Number of subjects	95	47	142
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	51.9	52.3	
standard deviation	± 15.4	± 15.9	-
Gender categorical			
Units: Subjects			
Female	52	20	72
Male	43	27	70
Diagnosis			
Units: Subjects			
RA	41	20	61
PsA	18	8	26
AxSpA	36	19	55
Smoking			
Units: Subjects			
Smoking	15	9	24
Not smoking	80	38	118
Disease activity			
Units: Subjects			
In remission	82	40	122
In LDA	13	7	20

On csDMARDs			
Units: Subjects			
On csDMARDs	41	22	63
Not on csDMARDs	54	25	79
On combination csDMARDs			
Units: Subjects			
On combination csDMARDs	2	2	4
Not on combination csDMARDs	93	45	138
On MTX			
Units: Subjects			
On MTX	40	20	60
Not on MTX	55	27	82
Baseline biological therapy			
Units: Subjects			
Abatacept	1	3	4
TNFi	88	41	129
Tocilizumab	6	3	9
Repeated biological failure			
On biological agent number three or higher			
Units: Subjects			
Repeated biological failure	6	3	9
No repeated biological failure	89	44	133
BMI			
Units: kg/m2			
median	25.3	26.6	
inter-quartile range (Q1-Q3)	23.2 to 29.2	23.1 to 29.4	-
Disease duration			
Units: years			
median	11.3	12.4	
inter-quartile range (Q1-Q3)	6.3 to 17.9	6.4 to 19.9	-
HAQ-DI			
Scale: 0.0-3.0			
Units: units			
median	0.13	0.13	
inter-quartile range (Q1-Q3)	0.00 to 0.63	0.00 to 0.50	-
Pain VAS			
Scale: 0-100 mm			
Units: mm			
median	10.0	11.0	
inter-quartile range (Q1-Q3)	2.0 to 17.0	5.0 to 21.0	-
Fatigue VAS			
Scale: 0-100 mm			
Units: mm			
median	16.0	25.0	
inter-quartile range (Q1-Q3)	4.0 to 34.0	10.0 to 42.0	-
Patient Global Health VAS			
Scale: 0-100 mm.			
Units: mm			
median	10.0	14.0	
inter-quartile range (Q1-Q3)	2.0 to 21.0	5.0 to 28.0	-
SF-36 PCS			

Short Form Health Survey 36 Physical Component Summary. Scale: 0-100.			
Units: units median inter-quartile range (Q1-Q3)	52.0 47.4 to 55.1	49.8 44.2 to 52.6	-
Tender joint count			
0-68 joints.			
Units: Joints median inter-quartile range (Q1-Q3)	0.0 0.0 to 0.0	0.0 0.0 to 0.0	-
Swollen joint count			
0-66 joints.			
Units: Joints median inter-quartile range (Q1-Q3)	0.0 0.0 to 0.0	0.0 0.0 to 0.0	-
CRP Units: mg/L median inter-quartile range (Q1-Q3)	2.6 0.8 to 3.9	2.2 0.6 to 3.9	-
Physician Global Health VAS			
Scale: 0-100 mm.			
Units: mm median inter-quartile range (Q1-Q3)	0.0 0.0 to 0.0	0.0 0.0 to 0.0	-
Disease activity score			
Evaluated using mixed model statistics with disease activity evaluated by DAS28-CRP for RA and PsA and ASDAS for axSpA.			
Units: points least squares mean standard deviation	1.47 ± 0.50	1.51 ± 0.50	-
Duration of baseline biological therapy Units: years median inter-quartile range (Q1-Q3)	5.1 2.3 to 8.2	4.2 2.7 to 10.6	-

End points

End points reporting groups

Reporting group title	The tapering group
Reporting group description: The tapering group followed a disease activity-guided tapering strategy for the biological therapy, i.e., the biologic dosing interval was prolonged by approximately 25% every 4 months until flare or complete biological withdrawal. However, due to the longer dosing interval for infliximab, it was decided to space the infliximab dosing interval by 2 weeks at each infusion.	
Reporting group title	The Control group
Reporting group description: A pragmatic usual care practice was applied to the control group, i.e. the control group continued their baseline biological dosing interval unchanged but, if requested by the patient, a small increase of the dosing interval was allowed.	

Primary: Reduced to 50% or less of their baseline biological dosing

End point title	Reduced to 50% or less of their baseline biological dosing
End point description: Part one of the co-primary endpoint was met if superiority in the proportion of patients achieving $\geq 50\%$ biologic reduction at 18 months was demonstrated.	
End point type	Primary
End point timeframe: 18 months	

End point values	The tapering group	The Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	47		
Units: 1				
$\geq 50\%$ biologic reduction	35	1		
$< 50\%$ biologic reduction	60	46		

Statistical analyses

Statistical analysis title	Statistical analysis plan for primary outcome 1A
Statistical analysis description: Analyses were performed and reported in accordance with the prespecified statistical analysis plan and the Consolidated Standards of Reporting Trials (CONSORT) statements. The primary analyses were based on intention to treat, i.e. all randomized patients, independent of protocol deviations. Categorical outcomes were analysed using generalized linear models for binomial data; missing data were handled as trial failures i.e., not achieving a 50% or greater reduction of the biological dose.	
Comparison groups	The tapering group v The Control group

Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Risk difference (RD)
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.24
upper limit	0.45

Primary: Disease activity score

End point title	Disease activity score
End point description:	
Disease activity assessed 18 months from baseline (part two of the co-primary objective)	
End point type	Primary
End point timeframe:	
18 months	

End point values	The tapering group	The Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	47		
Units: 0.1				
least squares mean (standard error)	1.84 (± 0.15)	1.75 (± 0.16)		

Statistical analyses

Statistical analysis title	Statistical analysis plan for primary objective 1B
Statistical analysis description:	
Analysis was performed and reported in accordance with the prespecified statistical analysis plan and the CONSORT statements.	
The primary analyses were based on intention to treat, i.e. all randomized patients, independent of protocol deviations.	
Repeated measures, linear mixed-effects models were applied to evaluate contrasts between groups for continuous outcomes. The fixed factors were group, diagnosis, biologics failure history, centre, time-point, and the interaction (group x time).	
Comparison groups	The tapering group v The Control group
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	equivalence ^[1]
Parameter estimate	Mean difference (final values)
Point estimate	0.08

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.29

Notes:

[1] - The initiating investigators pre-specified a margin of equivalence at ± 0.5 DAS28crp points for patients with RA or PsA and ± 0.5 ASDAS points for patients with axSpA. This margin was determined based on 'less than half of the effect' that would be considered a clinically relevant reduction in DAS28crp level (Δ DAS28crp > 1.2) or ASDAS level (Δ ASDAS > 1.1) corresponding to a clinically unimportant change in arthritis activity.

Secondary: In remission

End point title	In remission
End point description:	
Patients in remission measured by DAS28-CPR (RA and PsA) or ASDAS (axSpA)	
End point type	Secondary
End point timeframe:	
18 months	

End point values	The tapering group	The Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	47		
Units: 1				
In remission	63	33		
Not in remission	32	14		

Statistical analyses

Statistical analysis title	SAP remission
Statistical analysis description:	
Analyses were performed and reported in accordance with the prespecified statistical analysis plan and the Consolidated Standards of Reporting Trials (CONSORT) statements.	
The primary analyses were based on intention to treat, i.e. all randomized patients, independent of protocol deviations.	
Categorical outcomes were analysed using generalized linear models for binomial data; missing data were handled as trial failures i.e., not achieving a 50% or greater reduction of the biological dose.	
Comparison groups	The tapering group v The Control group
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Risk difference (RD)
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.12

Secondary: In low disease activity

End point title	In low disease activity
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End point description:

In LDA evaluated by DAS28-CRP (RA and PsA) or ASDAS (axSpA).

End point type	Secondary
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End point timeframe:

18 months

End point values	The tapering group	The Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	47		
Units: 1				
In LDA	79	41		
Not in LDA	16	6		

Statistical analyses

Statistical analysis title	SAP LDA
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Statistical analysis description:

Analyses were performed and reported in accordance with the prespecified statistical analysis plan and the Consolidated Standards of Reporting Trials (CONSORT) statements.

The primary analyses were based on intention to treat, i.e. all randomized patients, independent of protocol deviations.

Categorical outcomes were analysed using generalized linear models for binomial data; missing data were handled as trial failures i.e., not achieving a 50% or greater reduction of the biological dose.

Comparison groups	The tapering group v The Control group
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Number of subjects included in analysis	142
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Analysis specification	Pre-specified
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Analysis type	superiority
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Parameter estimate	Risk difference (RD)
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Point estimate	-0.04
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Confidence interval

level	95 %
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sides	2-sided
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lower limit	-0.16
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upper limit	0.08
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Secondary: ΔHAQ-DI

End point title	ΔHAQ-DI
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End point description:

Change in HAQ-DI from baseline to month 18

End point type	Secondary
End point timeframe:	
18 months	

End point values	The tapering group	The Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	47		
Units: 0.01				
least squares mean (standard error)	0.06 (\pm 0.06)	0.00 (\pm 0.07)		

Statistical analyses

Statistical analysis title	SAP HAQ-DI
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Statistical analysis description:

Analyses were performed and reported in accordance with the prespecified statistical analysis plan and the CONSORT statements.

The primary analyses were based on intention to treat, i.e. all randomized patients, independent of protocol deviations.

Repeated measures, linear mixed-effects models were applied to evaluate contrasts between groups for continuous outcomes. The fixed factors were group, diagnosis, biologics failure history, centre, time-point, and the interaction (group x time).

Comparison groups	The tapering group v The Control group
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.15

Secondary: Δ Pain VAS

End point title	Δ Pain VAS
End point description:	
Change in pain VAS from baseline to month 18.	
End point type	Secondary
End point timeframe:	
18 months	

End point values	The tapering group	The Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	47		
Units: 0.1				
least squares mean (standard error)	5.6 (\pm 3.2)	1.0 (\pm 3.5)		

Statistical analyses

Statistical analysis title	SAP pain VAS
Statistical analysis description:	
Analyses were performed and reported in accordance with the prespecified statistical analysis plan and the CONSORT statements.	
The primary analyses were based on intention to treat, i.e. all randomized patients, independent of protocol deviations.	
Repeated measures, linear mixed-effects models were applied to evaluate contrasts between groups for continuous outcomes. The fixed factors were group, diagnosis, biologics failure history, centre, time-point, and the interaction (group x time).	
Comparison groups	The tapering group v The Control group
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	4.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	9.3

Secondary: Δ Fatigue VAS

End point title	Δ Fatigue VAS
End point description:	
Change in patient fatigue VAS between baseline and 18 months	
End point type	Secondary
End point timeframe:	
18 months	

End point values	The tapering group	The Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	47		
Units: 0.1				
least squares mean (standard error)	-1.2 (\pm 4.4)	-2.7 (\pm 4.7)		

Statistical analyses

Statistical analysis title	SAP fatigue VAS
Statistical analysis description: Analyses were performed and reported in accordance with the prespecified statistical analysis plan and the CONSORT statements. The primary analyses were based on intention to treat, i.e. all randomized patients, independent of protocol deviations. Repeated measures, linear mixed-effects models were applied to evaluate contrasts between groups for continuous outcomes. The fixed factors were group, diagnosis, biologics failure history, centre, time-point, and the interaction (group x time).	
Comparison groups	The tapering group v The Control group
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.4
upper limit	7.4

Secondary: Δ Patient global health VAS

End point title	Δ Patient global health VAS
End point description: Change in patient global health VAS between baseline and 18 months	
End point type	Secondary
End point timeframe: 18 months	

End point values	The tapering group	The Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	47		
Units: 0.1				
least squares mean (standard error)	2.8 (\pm 3.9)	0.9 (\pm 4.2)		

Statistical analyses

Statistical analysis title	SAP patient global helath VAS
Statistical analysis description:	
Analyses were performed and reported in accordance with the prespecified statistical analysis plan and the Consolidated Standards of Reporting Trials (CONSORT) statements.	
The primary analyses were based on intention to treat, i.e. all randomized patients, independent of protocol deviations.	
Categorical outcomes were analysed using generalized linear models for binomial data; missing data were handled as trial failures i.e., not achieving a 50% or greater reduction of the biological dose.	
Comparison groups	The tapering group v The Control group
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	7.2

Secondary: ΔSF-36 PCS

End point title	ΔSF-36 PCS
End point description:	
Change in SF-36 PCS from baseline to 18 months	
End point type	Secondary
End point timeframe:	
18 months	

End point values	The tapering group	The Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	47		
Units: 0.1				
least squares mean (standard error)	-2.1 (± 1.4)	-2.5 (± 1.5)		

Statistical analyses

Statistical analysis title	SAP SF-36 PCS
Statistical analysis description:	
Analyses were performed and reported in accordance with the prespecified statistical analysis plan and the Consolidated Standards of Reporting Trials (CONSORT) statements.	
The primary analyses were based on intention to treat, i.e. all randomized patients, independent of protocol deviations.	
Categorical outcomes were analysed using generalized linear models for binomial data; missing data were handled as trial failures i.e., not achieving a 50% or greater reduction of the biological dose.	
Comparison groups	The Control group v The tapering group

Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	2.4

Secondary: ΔSF-36 MCS

End point title	ΔSF-36 MCS
End point description:	
Change in SF-36 MCS from baseline to month 18	
End point type	Secondary
End point timeframe:	
18 months	

End point values	The tapering group	The Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	47		
Units: 0.1				
least squares mean (standard error)	-1.6 (± 1.8)	-1.5 (± 1.9)		

Statistical analyses

Statistical analysis title	SAP SF-36 MCS
Statistical analysis description:	
Analyses were performed and reported in accordance with the prespecified statistical analysis plan and the Consolidated Standards of Reporting Trials (CONSORT) statements.	
The primary analyses were based on intention to treat, i.e. all randomized patients, independent of protocol deviations.	
Categorical outcomes were analysed using generalized linear models for binomial data; missing data were handled as trial failures i.e., not achieving a 50% or greater reduction of the biological dose.	
Comparison groups	The Control group v The tapering group
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	2.4

Secondary: Δ Physician global health VAS

End point title	Δ Physician global health VAS
End point description: Change in Physician global health VAS from baseline to month 18.	
End point type	Secondary
End point timeframe: 18 months	

End point values	The tapering group	The Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	47		
Units: 0.1				
least squares mean (standard error)	4.9 (\pm 2.1)	4.1 (\pm 2.3)		

Statistical analyses

Statistical analysis title	SAP physician global health VAS
Statistical analysis description: Analyses were performed and reported in accordance with the prespecified statistical analysis plan and the Consolidated Standards of Reporting Trials (CONSORT) statements. The primary analyses were based on intention to treat, i.e. all randomized patients, independent of protocol deviations. Categorical outcomes were analysed using generalized linear models for binomial data; missing data were handled as trial failures i.e., not achieving a 50% or greater reduction of the biological dose.	
Comparison groups	The tapering group v The Control group
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	3.9

Secondary: ΔTender joint count

End point title	ΔTender joint count
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End point description:

Change in tender joint counts between baseline and month 18

End point type	Secondary
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End point timeframe:

18 months

End point values	The tapering group	The Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	47		
Units: 1				
least squares mean (standard error)	-0.05 (± 0.4)	0.6 (± 0.5)		

Statistical analyses

Statistical analysis title	SAP tender joint count
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Statistical analysis description:

Analyses were performed and reported in accordance with the prespecified statistical analysis plan and the Consolidated Standards of Reporting Trials (CONSORT) statements.

The primary analyses were based on intention to treat, i.e. all randomized patients, independent of protocol deviations.

Categorical outcomes were analysed using generalized linear models for binomial data; missing data were handled as trial failures i.e., not achieving a 50% or greater reduction of the biological dose.

Comparison groups	The tapering group v The Control group
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0

Secondary: ΔSwollen joint count

End point title	ΔSwollen joint count
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End point description:

Change in swollen joint count between baseline and 18 months.

End point type	Secondary
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End point timeframe:

18 months

End point values	The tapering group	The Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	47		
Units: 1				
least squares mean (standard error)	0.3 (\pm 0.2)	0.3 (\pm 0.2)		

Statistical analyses

Statistical analysis title	SAP swollen joints counts
Statistical analysis description:	
Analyses were performed and reported in accordance with the prespecified statistical analysis plan and the Consolidated Standards of Reporting Trials (CONSORT) statements.	
The primary analyses were based on intention to treat, i.e. all randomized patients, independent of protocol deviations.	
Categorical outcomes were analysed using generalized linear models for binomial data; missing data were handled as trial failures i.e., not achieving a 50% or greater reduction of the biological dose.	
Comparison groups	The tapering group v The Control group
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.3

Secondary: ΔCRP

End point title	ΔCRP
End point description:	
Change in CRP between baseline and month 18.	
End point type	Secondary
End point timeframe:	
18 months	

End point values	The tapering group	The Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	47		
Units: 0.1				
least squares mean (standard error)	3.2 (\pm 1.5)	0.7 (\pm 1.6)		

Statistical analyses

Statistical analysis title	SAP CRP
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Statistical analysis description:

Analyses were performed and reported in accordance with the prespecified statistical analysis plan and the Consolidated Standards of Reporting Trials (CONSORT) statements.

The primary analyses were based on intention to treat, i.e. all randomized patients, independent of protocol deviations.

Categorical outcomes were analysed using generalized linear models for binomial data; missing data were handled as trial failures i.e., not achieving a 50% or greater reduction of the biological dose.

Comparison groups	The tapering group v The Control group
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	4.7

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to month 18.

Adverse event reporting additional description:

Safety outcomes: serious adverse events, serious infections, non-serious infections, cardiovascular events, malignancy, death, uveitis flare, skin or nail psoriasis flare, IBD flare, biologic discontinuation due to any adverse event, arthritis flare, and persistent (≥ 12 weeks) arthritis flare.

Assessment type	Systematic
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Dictionary used

Dictionary name	None
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Dictionary version	0
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Reporting groups

Reporting group title	Tapering group
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Reporting group description: -

Reporting group title	Control group
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Reporting group description: -

Serious adverse events	Tapering group	Control group	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 95 (5.26%)	5 / 47 (10.64%)	
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)			
Malignancy	Additional description: Malignancy during the study period (from baseline to month 18).		
subjects affected / exposed	1 / 95 (1.05%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Other serious adverse events	Additional description: Other serious adverse events during the study period (from baseline to month 18).		
subjects affected / exposed	3 / 95 (3.16%)	2 / 47 (4.26%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiovascular events	Additional description: Cardiovascular events through the study period (from baseline to month 18).		

subjects affected / exposed	1 / 95 (1.05%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Serious infections	Additional description: Serious infections during the study period (baseline to 18 months)		
subjects affected / exposed	0 / 95 (0.00%)	2 / 47 (4.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Tapering group	Control group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	77 / 95 (81.05%)	25 / 47 (53.19%)	
Investigations			
Discontinued bDMARD due to any AE	Additional description: Discontinued bDMARD due to any adverse event during the study period (from baseline to month 18).		
subjects affected / exposed	5 / 95 (5.26%)	4 / 47 (8.51%)	
occurrences (all)	5	6	
Fulfil arthritis flare criteria	Additional description: Fulfil the pre-specified arthritis flare criteria during the study period (from baseline to month 18).		
subjects affected / exposed	39 / 95 (41.05%)	10 / 47 (21.28%)	
occurrences (all)	50	16	
Symptoms of arthritis flare	Additional description: Symptoms of arthritis flare but does not fulfil the arthritis flare criteria during the study period (from baseline to month 18).		
subjects affected / exposed	38 / 95 (40.00%)	6 / 47 (12.77%)	
occurrences (all)	78	11	
Eye disorders			
Uveitis flare	Additional description: Uveitis flare during the study period (from baseline to month 18).		
subjects affected / exposed	5 / 95 (5.26%)	3 / 47 (6.38%)	
occurrences (all)	7	4	
Gastrointestinal disorders			
IBD flare	Additional description: Inflammatory bowel disease flare during the study period (from baseline to month 18).		
subjects affected / exposed	3 / 95 (3.16%)	0 / 47 (0.00%)	
occurrences (all)	4	0	
Skin and subcutaneous tissue disorders			

Psoriasis skin flare	Additional description: Psoriasis skin flare during the study period (from baseline to month 18).		
	subjects affected / exposed	4 / 95 (4.21%)	0 / 47 (0.00%)
	occurrences (all)	4	0
Psoriasis nail flare	Additional description: Psoriasis nail flare during the study period (from baseline to month 18).		
	subjects affected / exposed	2 / 95 (2.11%)	0 / 47 (0.00%)
	occurrences (all)	2	0
Infections and infestations			
Non-serious infections	Additional description: Non-serious infections during the study period (from baseline to month 18).		
	subjects affected / exposed	52 / 95 (54.74%)	24 / 47 (51.06%)
	occurrences (all)	103	49

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 March 2019	The eligibility criteria was revised to allow inclusion of patients in sustained low disease activity (LDA) in stead of just sustained remission.
20 March 2020	Due to the national implication of the COVID-19 pandemic to the Danish health care system, remote monitoring by telephone contact was allowed for the following visits: month 4, month 8, month 12, and month 24. The primary endpoint assessment (visit 18 month) was considered to be essential to the patients and the trial; therefore, the visit was conducted as an outpatient consultation in order with the protocol. Similarly, subacute visits due to symptoms of flare were considered to be essential; thus, encouraged to be conducted as an outpatient consultation.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
20 March 2020	Suspension of patient enrolment due to the national implication of the COVID-19 pandemic to the Danish health care system.	20 March 2020
02 April 2020	The inclusion period was closed 1 month before scheduled due to the continued national COVID-19 implication to the Danish health care system	02 April 2020
12 June 2020	Remote monitoring, due to the implication of the COVID-19 pandemic, was lifted; thus, all trial visits were onwards conducted as an outpatient consultation in accordance with the trial protocol.	12 June 2020

Notes:

Limitations and caveats

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

In total, 142 patients out of the planned 180 patients was enrolled before the inclusion period was closed pre-maturely due to the national implications of the COVID-19 pandemic on the Danish health care system.

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/31292181>

<http://www.ncbi.nlm.nih.gov/pubmed/36745114>

<http://www.ncbi.nlm.nih.gov/pubmed/37271939>

