



## Clinical trial results:

### A Phase 2 Multicenter, Randomized, Double-Blinded, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of CC-99677 in Subjects with Active Ankylosing Spondylitis

#### Summary

EudraCT number	2019-004108-37
Trial protocol	DE CZ PL RO
Global end of trial date	21 February 2023

#### Results information

Result version number	v1 (current)
This version publication date	08 March 2024
First version publication date	08 March 2024

#### Trial information

##### Trial identification

Sponsor protocol code	CC-99677-AS-001
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##### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com

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	16 May 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	21 February 2023
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

Evaluate the Efficacy and Safety of CC-99677 in Subjects with Active Ankylosing Spondylitis

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 August 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	China: 1
Country: Number of subjects enrolled	Czechia: 45
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Poland: 90
Country: Number of subjects enrolled	Romania: 1
Country: Number of subjects enrolled	Spain: 15
Country: Number of subjects enrolled	Türkiye: 7
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	167
EEA total number of subjects	156

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)	166
From 65 to 84 years	1
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

167 participants treated

### Period 1

Period 1 title	Week 0 - Week 12 (Placebo-Controlled)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer

### Arms

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	Placebo Biologic Naive
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Arm description:

Placebo Biologic Naive QD PO from week 0 - 12. At week 12, participants rerandomized to CC-99677 (150 mg or 60 mg PO QD) through Week 64 or until early discontinuation

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

QD PO

<b>Arm title</b>	CC-99677 60 mg Biologic Naive
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Arm description:

CC-99677 60 mg Biologic Naive QD PO

Arm type	Experimental
Investigational medicinal product name	CC-99677
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

60 mg QD PO

<b>Arm title</b>	CC-99677 150 mg Biologic Naive
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Arm description:

CC-99677 150 mg Biologic Naive QD PO

Arm type	Experimental
Investigational medicinal product name	CC-99677
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

150 mg QD PO

<b>Arm title</b>	Placebo Biologic Failure
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Arm description:

Placebo Biologic Failure QD PO from week 0 - 12. At week 12, participants rerandomized to CC-99677 (150 mg or 60 mg PO QD) through Week 64 or until early discontinuation

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

QD PO

<b>Arm title</b>	CC-99677 60 mg Biologic Failure
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Arm description:

CC-99677 60 mg Biologic Failure QD PO

Arm type	Experimental
Investigational medicinal product name	CC-99677
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

60 mg QD PO

<b>Arm title</b>	CC-99677 150 mg Biologic Failure
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Arm description:

CC-99677 150 mg Biologic Failure QD PO

Arm type	Experimental
Investigational medicinal product name	CC-99677
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

150 mg QD PO

<b>Number of subjects in period 1</b>	Placebo Biologic Naive	CC-99677 60 mg Biologic Naive	CC-99677 150 mg Biologic Naive
Started	49	49	49
Completed	42	42	39
Not completed	7	7	10
Consent withdrawn by subject	1	1	2
Protocol Deviation	1	-	-

Adverse event, non-fatal	-	-	-
Study terminated by sponsor	5	6	7
Other reasons	-	-	1

Number of subjects in period 1	Placebo Biologic Failure	CC-99677 60 mg Biologic Failure	CC-99677 150 mg Biologic Failure
Started	5	7	8
Completed	3	5	7
Not completed	2	2	1
Consent withdrawn by subject	-	2	-
Protocol Deviation	-	-	-
Adverse event, non-fatal	1	-	-
Study terminated by sponsor	1	-	1
Other reasons	-	-	-

## Period 2

Period 2 title	Week 12 - Week 52 (Long-Term Extension)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer

## Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Placebo Biologic Naive

Arm description:

Placebo Biologic Naive QD PO

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

QD PO

<b>Arm title</b>	CC-99677 60 mg Biologic Naive
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Arm description:

CC-99677 60 mg Biologic Naive QD PO

Arm type	Experimental
Investigational medicinal product name	CC-99677
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

60 mg QD PO

<b>Arm title</b>	CC-99677 150 mg Biologic Naive
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Arm description:

CC-99677 150 mg Biologic Naive QD PO

Arm type	Experimental
Investigational medicinal product name	CC-99677
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

150 mg QD PO

<b>Arm title</b>	Placebo Biologic Failure
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Arm description:

Placebo Biologic Failure QD PO

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

QD PO

<b>Arm title</b>	CC-99677 60 mg Biologic Failure
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Arm description:

CC-99677 60 mg Biologic Failure QD PO

Arm type	Experimental
Investigational medicinal product name	CC-99677
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

60 mg QD PO

<b>Arm title</b>	CC-99677 150 mg Biologic Failure
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Arm description:

CC-99677 150 mg Biologic Failure QD PO

Arm type	Experimental
Investigational medicinal product name	CC-99677
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

150 mg QD PO

<b>Number of subjects in period 2</b>	Placebo Biologic Naive	CC-99677 60 mg Biologic Naive	CC-99677 150 mg Biologic Naive
Started	42	42	39
Re-randomized to CC-99677 60 mg	21	0	0 <sup>[1]</sup>
Re-randomized to CC-99677 150 mg	21	0	0 <sup>[2]</sup>
Completed	1	0	1
Not completed	41	42	38
Adverse event, serious fatal	1	-	-
Consent withdrawn by subject	2	1	3
Adverse event, non-fatal	-	1	-
Study terminated by sponsor	34	35	30
Other reasons	3	5	5
Lost to follow-up	1	-	-

<b>Number of subjects in period 2</b>	Placebo Biologic Failure	CC-99677 60 mg Biologic Failure	CC-99677 150 mg Biologic Failure
Started	3	5	7
Re-randomized to CC-99677 60 mg	2	0	0
Re-randomized to CC-99677 150 mg	1	0	0
Completed	0	0	0
Not completed	3	5	7
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	1	1	2
Adverse event, non-fatal	-	-	1
Study terminated by sponsor	1	4	4
Other reasons	1	-	-
Lost to follow-up	-	-	-

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Only participants from the placebo group are re-randomized

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Only participants from the placebo group are re-randomized



## Baseline characteristics

### Reporting groups

Reporting group title	Placebo Biologic Naive
Reporting group description: Placebo Biologic Naive QD PO from week 0 - 12. At week 12, participants rerandomized to CC-99677 (150 mg or 60 mg PO QD) through Week 64 or until early discontinuation	
Reporting group title	CC-99677 60 mg Biologic Naive
Reporting group description: CC-99677 60 mg Biologic Naive QD PO	
Reporting group title	CC-99677 150 mg Biologic Naive
Reporting group description: CC-99677 150 mg Biologic Naive QD PO	
Reporting group title	Placebo Biologic Failure
Reporting group description: Placebo Biologic Failure QD PO from week 0 - 12. At week 12, participants rerandomized to CC-99677 (150 mg or 60 mg PO QD) through Week 64 or until early discontinuation	
Reporting group title	CC-99677 60 mg Biologic Failure
Reporting group description: CC-99677 60 mg Biologic Failure QD PO	
Reporting group title	CC-99677 150 mg Biologic Failure
Reporting group description: CC-99677 150 mg Biologic Failure QD PO	

Reporting group values	Placebo Biologic Naive	CC-99677 60 mg Biologic Naive	CC-99677 150 mg Biologic Naive
Number of subjects	49	49	49
Age categorical Units:			

Age Continuous Units: years			
arithmetic mean	44.1	40.5	40.4
standard deviation	± 10.27	± 11.78	± 9.75
Sex: Female, Male Units: Participants			
Female	8	6	12
Male	41	43	37
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	1	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	48	48	48
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			

Hispanic or Latino	2	2	0
Not Hispanic or Latino	47	47	49
Unknown or Not Reported	0	0	0

Reporting group values	Placebo Biologic Failure	CC-99677 60 mg Biologic Failure	CC-99677 150 mg Biologic Failure
Number of subjects	5	7	8
Age categorical Units:			

Age Continuous Units: years arithmetic mean standard deviation	43.8 ± 7.16	44.4 ± 10.06	42.5 ± 9.46
Sex: Female, Male Units: Participants			
Female	1	1	0
Male	4	6	8
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	5	7	8
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	5	7	8
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	167		
Age categorical Units:			

Age Continuous Units: years arithmetic mean standard deviation	-		
Sex: Female, Male Units: Participants			
Female	28		
Male	139		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1		
Asian	2		

Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	164		
More than one race	0		
Unknown or Not Reported	0		
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	4		
Not Hispanic or Latino	163		
Unknown or Not Reported	0		

## End points

### End points reporting groups

Reporting group title	Placebo Biologic Naive
Reporting group description: Placebo Biologic Naive QD PO from week 0 - 12. At week 12, participants rerandomized to CC-99677 (150 mg or 60 mg PO QD) through Week 64 or until early discontinuation	
Reporting group title	CC-99677 60 mg Biologic Naive
Reporting group description: CC-99677 60 mg Biologic Naive QD PO	
Reporting group title	CC-99677 150 mg Biologic Naive
Reporting group description: CC-99677 150 mg Biologic Naive QD PO	
Reporting group title	Placebo Biologic Failure
Reporting group description: Placebo Biologic Failure QD PO from week 0 - 12. At week 12, participants rerandomized to CC-99677 (150 mg or 60 mg PO QD) through Week 64 or until early discontinuation	
Reporting group title	CC-99677 60 mg Biologic Failure
Reporting group description: CC-99677 60 mg Biologic Failure QD PO	
Reporting group title	CC-99677 150 mg Biologic Failure
Reporting group description: CC-99677 150 mg Biologic Failure QD PO	
Reporting group title	Placebo Biologic Naive
Reporting group description: Placebo Biologic Naive QD PO	
Reporting group title	CC-99677 60 mg Biologic Naive
Reporting group description: CC-99677 60 mg Biologic Naive QD PO	
Reporting group title	CC-99677 150 mg Biologic Naive
Reporting group description: CC-99677 150 mg Biologic Naive QD PO	
Reporting group title	Placebo Biologic Failure
Reporting group description: Placebo Biologic Failure QD PO	
Reporting group title	CC-99677 60 mg Biologic Failure
Reporting group description: CC-99677 60 mg Biologic Failure QD PO	
Reporting group title	CC-99677 150 mg Biologic Failure
Reporting group description: CC-99677 150 mg Biologic Failure QD PO	

### Primary: Percentage of Participants who Achieve ASAS 20 at Week 12

End point title	Percentage of Participants who Achieve ASAS 20 at Week 12
End point description: Percentage of participants who achieve an improvement in disease activity from baseline of $\geq 20\%$ and $\geq 1$ unit in at least 3 of the 4 SpondyloArthritis International Society (ASAS) domains on a scale of 0 to 10, and no worsening from baseline of $\geq 20\%$ and $\geq 1$ unit in the remaining domain on a scale of 0 to 10. Baseline is the last non-missing value on or before the date of the first dose of investigational product. The four ASAS Domains are:	

- Patient Global Assessment of Disease (0 to 10 unit Numerical Rating Scale [NRS]);
- Total Back Pain NRS;
- Function (the Bath Ankylosing Spondylitis Functional Index [BASFI] score NRS);
- Inflammation (mean of Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] NRS Questions #5 and #6 for morning stiffness).

End point type	Primary
End point timeframe:	
Week 12	

End point values	Placebo Biologic Naive	CC-99677 60 mg Biologic Naive	CC-99677 150 mg Biologic Naive	Placebo Biologic Failure
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	43	41	3
Units: Percentage of Participants				
number (not applicable)	48.8	51.2	56.1	66.7

End point values	CC-99677 60 mg Biologic Failure	CC-99677 150 mg Biologic Failure		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	7		
Units: Percentage of Participants				
number (not applicable)	83.3	57.1		

### Statistical analyses

Statistical analysis title	CC-99677 150 mg - Placebo
Comparison groups	Placebo Biologic Naive v CC-99677 150 mg Biologic Naive
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.512
Method	Cochran-Mantel-Haenszel
Parameter estimate	Stratified difference
Point estimate	7.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.8
upper limit	27.5

Statistical analysis title	CC-99677 60 mg - Placebo
Comparison groups	Placebo Biologic Naive v CC-99677 60 mg Biologic Naive

Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.829
Method	Cochran-Mantel-Haenszel
Parameter estimate	Stratified difference
Point estimate	2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.2
upper limit	22.7

## Secondary: Percentage of Participants who Achieve ASAS 40 at Week 12

End point title	Percentage of Participants who Achieve ASAS 40 at Week 12
End point description:	
<p>Percentage of participants who achieve an improvement in disease activity from baseline of <math>\geq 40\%</math> and <math>\geq 2</math> unit in at least 3 of the 4 SpondyloArthritis International Society (ASAS) domains on a scale of 0 to 10, and no worsening at all from baseline in the remaining domain. Baseline is the last non-missing value on or before the date of the first dose of investigational product. The four ASAS Domains are:</p> <ul style="list-style-type: none"> <li>- Patient Global Assessment of Disease (0 to 10 unit Numerical Rating Scale [NRS]);</li> <li>- Total Back Pain NRS;</li> <li>- Function (the Bath Ankylosing Spondylitis Functional Index [BASFI] score NRS);</li> <li>- Inflammation (mean of Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] NRS Questions #5 and #6 for morning stiffness).</li> </ul>	
End point type	Secondary
End point timeframe:	
Week 12	

End point values	Placebo Biologic Naïve	CC-99677 60 mg Biologic Naïve	CC-99677 150 mg Biologic Naïve	Placebo Biologic Failure
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	43	41	3
Units: Percentage of Participants				
number (not applicable)	22.0	25.6	34.1	33.3

End point values	CC-99677 60 mg Biologic Failure	CC-99677 150 mg Biologic Failure		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	7		
Units: Percentage of Participants				
number (not applicable)	50.0	28.6		

## Statistical analyses

<b>Statistical analysis title</b>	CC-99677 150 mg - Placebo
Comparison groups	Placebo Biologic Naive v CC-99677 150 mg Biologic Naive
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.219
Method	Cochran-Mantel-Haenszel
Parameter estimate	Stratified difference
Point estimate	12.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.2
upper limit	30.5

<b>Statistical analysis title</b>	CC-99677 60 mg - Placebo
Comparison groups	Placebo Biologic Naive v CC-99677 60 mg Biologic Naive
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.725
Method	Cochran-Mantel-Haenszel
Parameter estimate	Stratified difference
Point estimate	3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.9
upper limit	21

## Secondary: Change from Baseline in Ankylosing Spondylitis Disease Activity Score with CRP (ASDAS-CRP) at Week 12

End point title	Change from Baseline in Ankylosing Spondylitis Disease Activity Score with CRP (ASDAS-CRP) at Week 12
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### End point description:

ASDAS-CRP is a score of disease activity that combines patient reported assessments of back pain (Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] question 2), duration of morning stiffness (BASDAI question 6), peripheral joint pain and/or swelling (BASDAI question 3), general wellbeing, and CRP in a weighted manner. The cut-off values for disease activity states and improvement scores are defined as follows: <1.3 inactive disease,  $\geq 1.3$  and <2.1 low disease activity,  $\geq 2.1$  and  $\leq 3.5$  high

disease activity and 3.5 very high disease activity. The minimum clinically important difference (MCID) are defined as: change of at least 1.1 unit for 'clinically important improvement' and change of at least 2.0 units for 'major improvement'. Baseline is the last non-missing value on or before the date of the first dose of investigational product. ASDAS-CRP Formula:  $0.12 \times \text{Back Pain} + 0.06 \times \text{Duration of Morning Stiffness} + 0.11 \times \text{Patient Global} + 0.07 \times \text{Peripheral Pain/Swelling} + 0.58 \times \ln(\text{CRP} + 1)$

End point type	Secondary
End point timeframe:	
Baseline and Week 12	

End point values	Placebo Biologic Naive	CC-99677 60 mg Biologic Naive	CC-99677 150 mg Biologic Naive	Placebo Biologic Failure
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	43	41	3
Units: Units on a scale				
arithmetic mean (standard deviation)	-0.69 (± 0.856)	-0.87 (± 0.681)	-0.80 (± 0.869)	-0.84 (± 0.621)

End point values	CC-99677 60 mg Biologic Failure	CC-99677 150 mg Biologic Failure		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	7		
Units: Units on a scale				
arithmetic mean (standard deviation)	-1.02 (± 0.464)	-0.44 (± 0.323)		

## Statistical analyses

Statistical analysis title	CC-99677 150 mg - Placebo
Comparison groups	Placebo Biologic Naive v CC-99677 150 mg Biologic Naive
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.488
Method	Longitudinal data analysis model
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	0.22
Variability estimate	Standard error of the mean
Dispersion value	0.168



<b>Statistical analysis title</b>	CC-99677 60 mg - Placebo
Comparison groups	Placebo Biologic Naive v CC-99677 60 mg Biologic Naive
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.299
Method	Longitudinal data analysis model
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.16
Variability estimate	Standard error of the mean
Dispersion value	0.167

### Secondary: Change from Baseline in BASDAI at Week 12

End point title	Change from Baseline in BASDAI at Week 12
End point description:	
<p>Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) is a composite score based on a self-administered survey of six questions using a 0 to 10 unit numerical rating scale (NRS) that assesses five major symptoms of AS during the last week: 1) fatigue; 2) spinal pain; 3) peripheral joint pain/swelling; 4) areas of localized tenderness; 5a) morning stiffness severity upon waking; 5b) morning stiffness duration upon waking. To give each of the five symptoms equal weighting, the mean of the two scores relating to morning stiffness is taken. The resulting 0 to 50 score is divided by 5 to give a final 0 to 10 BASDAI score. A BASDAI score of 4 or greater is considered to be indicative of active AS disease. Baseline is the last non-missing value on or before the date of the first dose of investigational product.</p>	
End point type	Secondary
End point timeframe:	
Baseline and Week 12	

End point values	Placebo Biologic Naive	CC-99677 60 mg Biologic Naive	CC-99677 150 mg Biologic Naive	Placebo Biologic Failure
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	43	41	3
Units: Units on a scale				
arithmetic mean (standard deviation)	-1.88 (± 1.862)	-1.96 (± 1.494)	-2.03 (± 2.080)	-1.63 (± 0.651)

End point values	CC-99677 60 mg Biologic	CC-99677 150 mg Biologic		
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	Failure	Failure		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	7		
Units: Units on a scale				
arithmetic mean (standard deviation)	-2.20 (± 1.394)	-1.43 (± 1.517)		

## Statistical analyses

<b>Statistical analysis title</b>	CC-99677 150 mg - Placebo
Comparison groups	Placebo Biologic Naive v CC-99677 150 mg Biologic Naive
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.668
Method	Longitudinal data analysis model
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.95
upper limit	0.61
Variability estimate	Standard error of the mean
Dispersion value	0.393

<b>Statistical analysis title</b>	CC-99677 60 mg - Placebo
Comparison groups	Placebo Biologic Naive v CC-99677 60 mg Biologic Naive
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.97
Method	Longitudinal data analysis model
Parameter estimate	Difference in Adjusted Means
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	0.79
Variability estimate	Standard error of the mean
Dispersion value	0.391

## Secondary: Change from Baseline in BASFI at Week 12

End point title	Change from Baseline in BASFI at Week 12
End point description:	
Bath Ankylosing Spondylitis Functional Index (BASFI) is a composite score based on a self administered survey of ten questions using a 0 to 10 unit numerical rating scale (NRS) that assesses degree of mobility and functional ability during the last week. The questionnaire consists of eight questions regarding function in AS and the two last questions reflecting ability to cope with everyday life. The left-hand box of 0 represents "easy," and the right-hand box represents "impossible." The resulting 0 to 100 score is divided by 10 to give a final 0 to 10 BASFI score. A higher BASFI score correlates to reduced functional ability. Baseline is the last non-missing value on or before the date of the first dose of investigational product.	
End point type	Secondary
End point timeframe:	
Baseline and Week 12	

End point values	Placebo Biologic Naive	CC-99677 60 mg Biologic Naive	CC-99677 150 mg Biologic Naive	Placebo Biologic Failure
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	43	41	3
Units: Units on a scale				
arithmetic mean (standard deviation)	-1.22 (± 1.727)	-1.33 (± 1.985)	-1.28 (± 2.542)	-1.77 (± 0.850)

End point values	CC-99677 60 mg Biologic Failure	CC-99677 150 mg Biologic Failure		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	7		
Units: Units on a scale				
arithmetic mean (standard deviation)	-1.47 (± 1.841)	-1.29 (± 0.703)		

## Statistical analyses

Statistical analysis title	CC-99677 150 mg - Placebo
Comparison groups	Placebo Biologic Naive v CC-99677 150 mg Biologic Naive
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.545
Method	Longitudinal data analysis model
Parameter estimate	Difference in Adjusted Means
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	1.08

Variability estimate	Standard error of the mean
Dispersion value	0.417

<b>Statistical analysis title</b>	CC-99677 60 mg - Placebo
Comparison groups	Placebo Biologic Naive v CC-99677 60 mg Biologic Naive
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.89
Method	Longitudinal data analysis model
Parameter estimate	Difference in Adjusted Means
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.77
upper limit	0.88
Variability estimate	Standard error of the mean
Dispersion value	0.416

## Secondary: Change from Baseline in the SPARCC SI Joint Score at Week 12

End point title	Change from Baseline in the SPARCC SI Joint Score at Week 12
End point description:	
Change from Baseline in the Spondyloarthritis Research Consortium of Canada (SPARCC) scores of the sacroiliac joints. The SPARCC assesses 16 sites for enthesitis using a score of "0" for no activity or "1" for activity. Sites assessed include Medial epicondyle (left/right [L/R]), Lateral epicondyle (L/R), Supraspinatus insertion into greater tuberosity of humerus (L/R), Greater trochanter (L/R), Quadriceps insertion into superior border of patella (L/R), Patellar ligament insertion into inferior pole of patella or tibial tubercle (L/R), Achilles tendon insertion into calcaneum (L/R), and Plantar fascia insertion into calcaneum (L/R). The SPARCC is the sum of all site scores (range 0 to 16). Higher scores indicate more severe enthesitis. Baseline is the last non-missing value on or before the date of the first dose of investigational product.	
End point type	Secondary
End point timeframe:	
Baseline and Week 12	

End point values	Placebo Biologic Naive	CC-99677 60 mg Biologic Naive	CC-99677 150 mg Biologic Naive	Placebo Biologic Failure
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	43	39	3
Units: Units on a scale				
arithmetic mean (standard deviation)	0.25 (± 3.168)	-0.81 (± 5.453)	-1.72 (± 6.084)	-0.17 (± 1.258)

<b>End point values</b>	CC-99677 60 mg Biologic Failure	CC-99677 150 mg Biologic Failure		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	7		
Units: Units on a scale				
arithmetic mean (standard deviation)	-3.00 (± 7.608)	-3.00 (± 4.093)		

## Statistical analyses

<b>Statistical analysis title</b>	CC-99677 150 mg - Placebo
Comparison groups	Placebo Biologic Naive v CC-99677 150 mg Biologic Naive
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.33
Method	Longitudinal data analysis model
Parameter estimate	Difference in Adjusted Means
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.02
upper limit	1.03
Variability estimate	Standard error of the mean
Dispersion value	1.022

<b>Statistical analysis title</b>	CC-99677 60 mg - Placebo
Comparison groups	Placebo Biologic Naive v CC-99677 60 mg Biologic Naive
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.778
Method	Longitudinal data analysis model
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.26
upper limit	1.7
Variability estimate	Standard error of the mean
Dispersion value	0.999

## Secondary: Change from Baseline in the SPARCC Spine Score at Week 12

End point title	Change from Baseline in the SPARCC Spine Score at Week 12
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End point description:

Change from Baseline in the Spondyloarthritis Research Consortium of Canada (SPARCC) scores of the total spine. All 23 disco-vertebral units (DVU) of the spine (from C2 to S1) were scored for bone marrow edema. A single DVU has 18 scoring units, and each has score of 0 or 1, bringing the maximum total score to 414, the sum ranges from 0 to 414 with higher scores reflecting worse disease.

Baseline is the last non-missing value on or before the date of the first dose of investigational product.

End point type	Secondary
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End point timeframe:

Baseline and Week 12

End point values	Placebo Biologic Naive	CC-99677 60 mg Biologic Naive	CC-99677 150 mg Biologic Naive	Placebo Biologic Failure
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	43	39	3
Units: Units on a scale				
arithmetic mean (standard deviation)	-0.92 (± 7.557)	-1.53 (± 8.331)	-1.86 (± 7.081)	-8.17 (± 7.371)

End point values	CC-99677 60 mg Biologic Failure	CC-99677 150 mg Biologic Failure		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	7		
Units: Units on a scale				
arithmetic mean (standard deviation)	-2.40 (± 5.128)	-2.71 (± 8.640)		

## Statistical analyses

Statistical analysis title	CC-99677 60 mg - Placebo
Comparison groups	Placebo Biologic Naive v CC-99677 60 mg Biologic Naive
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6
Method	Longitudinal data analysis model
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.82

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.93
upper limit	2.28
Variability estimate	Standard error of the mean
Dispersion value	1.567

<b>Statistical analysis title</b>	CC-99677 150 mg - Placebo
Comparison groups	Placebo Biologic Naive v CC-99677 150 mg Biologic Naive
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.416
Method	Longitudinal data analysis model
Parameter estimate	Difference in Adjusted Means
Point estimate	-1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.49
upper limit	1.87
Variability estimate	Standard error of the mean
Dispersion value	1.605

### Secondary: Percent Change from Baseline in hsCRP at Week 12

End point title	Percent Change from Baseline in hsCRP at Week 12
End point description:	
Percent change from baseline in high-sensitivity C-reactive protein (hsCRP). Baseline is the last non-missing value on or before the date of the first dose of investigational product.	
End point type	Secondary
End point timeframe:	
Baseline and Week 12	

End point values	Placebo Biologic Naive	CC-99677 60 mg Biologic Naive	CC-99677 150 mg Biologic Naive	Placebo Biologic Failure
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	43	41	3
Units: mg/L				
arithmetic mean (standard deviation)	72.83 (± 474.199)	-1.43 (± 64.157)	20.88 (± 130.181)	-13.68 (± 55.618)

<b>End point values</b>	CC-99677 60 mg Biologic Failure	CC-99677 150 mg Biologic Failure		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	7		
Units: mg/L				
arithmetic mean (standard deviation)	8.52 (± 66.057)	452.34 (± 1226.664)		

### Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Participants were assessed for deaths (all-causes) from their first dose to their study completion (Up to approximately 17 months). SAEs and NSAEs were assessed from first dose up to 28 days post last dose (Up to approximately 4 months).

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.1
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### Reporting groups

Reporting group title	CC-99677 150 mg Biologic Naive
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Reporting group description:

CC-99677 150 mg Biologic Naive QD PO only

Reporting group title	CC-99677 60 mg Biologic Naive
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Reporting group description:

CC-99677 60 mg Biologic Naive QD PO only

Reporting group title	Placebo Biologic Naive
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Reporting group description:

Placebo Biologic Naive QD PO only

Reporting group title	Placebo to CC-99677 150 mg Biologic Naive
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Reporting group description:

Placebo Biologic Naive QD PO from week 0 - 12. At week 12, participants rerandomized to CC-99677 150 mg PO QD through Week 64 or until early discontinuation

Reporting group title	Placebo to CC-99677 60 mg Biologic Failure
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Reporting group description:

Placebo Biologic Failure QD PO from week 0 - 12. At week 12, participants rerandomized to CC-99677 60 mg PO QD through Week 64 or until early discontinuation

Reporting group title	CC-99677 150 mg Biologic Failure
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Reporting group description:

CC-99677 150 mg Biologic Failure QD PO

Reporting group title	CC-99677 60 mg Biologic Failure
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Reporting group description:

CC-99677 60 mg Biologic Failure QD PO

Reporting group title	Placebo Biologic Failure
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Reporting group description:

Placebo Biologic Failure QD PO

Reporting group title	Placebo to CC-99677 150 mg Biologic Failure
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Reporting group description:

Placebo Biologic Failure QD PO from week 0 - 12. At week 12, participants rerandomized to CC-99677 150 mg PO QD through Week 64 or until early discontinuation

Reporting group title	Placebo to CC-99677 60 mg Biologic Naive
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Reporting group description:

Placebo Biologic Naive QD PO from week 0 - 12. At week 12, participants rerandomized to CC-99677 60 mg PO QD through Week 64 or until early discontinuation

<b>Serious adverse events</b>	CC-99677 150 mg Biologic Naive	CC-99677 60 mg Biologic Naive	Placebo Biologic Naive
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	1 / 7 (14.29%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to peritoneum			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Colitis ulcerative			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Oral candidiasis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Placebo to CC-99677 150 mg Biologic Naive	Placebo to CC-99677 60 mg Biologic Failure	CC-99677 150 mg Biologic Failure
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 21 (14.29%)	0 / 2 (0.00%)	3 / 8 (37.50%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to peritoneum			
subjects affected / exposed	1 / 21 (4.76%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	1 / 21 (4.76%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 21 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Concussion			
subjects affected / exposed	0 / 21 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 21 (4.76%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	0 / 21 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	0 / 21 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Oral candidiasis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Serious adverse events</b>	CC-99677 60 mg Biologic Failure	Placebo Biologic Failure	Placebo to CC-99677 150 mg Biologic Failure
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to peritoneum			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			

Psychotic disorder			
subjects affected / exposed	0 / 7 (0.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Oral candidiasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Placebo to CC-99677 60 mg Biologic Naive		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to peritoneum			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Concussion			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			

Myocardial infarction subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 21 (0.00%) 0 / 0 0 / 0		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 21 (0.00%) 0 / 0 0 / 0		
Gastrointestinal disorders Colitis ulcerative subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 21 (0.00%) 0 / 0 0 / 0		
Psychiatric disorders Psychotic disorder subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 21 (0.00%) 0 / 0 0 / 0		
Infections and infestations Oral candidiasis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 21 (0.00%) 0 / 0 0 / 0		

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

<b>Non-serious adverse events</b>	CC-99677 150 mg Biologic Naive	CC-99677 60 mg Biologic Naive	Placebo Biologic Naive
Total subjects affected by non-serious adverse events subjects affected / exposed	11 / 49 (22.45%)	26 / 49 (53.06%)	0 / 7 (0.00%)
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)  Blood creatine phosphokinase increased	0 / 49 (0.00%) 0	2 / 49 (4.08%) 2	0 / 7 (0.00%) 0

subjects affected / exposed	1 / 49 (2.04%)	3 / 49 (6.12%)	0 / 7 (0.00%)
occurrences (all)	1	3	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 49 (0.00%)	1 / 49 (2.04%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Transaminases increased			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 49 (2.04%)	1 / 49 (2.04%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Radiculopathy			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 49 (4.08%)	3 / 49 (6.12%)	0 / 7 (0.00%)
occurrences (all)	2	3	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 49 (0.00%)	1 / 49 (2.04%)	0 / 7 (0.00%)
occurrences (all)	0	1	0



Eye disorders			
Swelling of eyelid			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Iridocyclitis			
subjects affected / exposed	0 / 49 (0.00%)	3 / 49 (6.12%)	0 / 7 (0.00%)
occurrences (all)	0	4	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Aphthous ulcer			
subjects affected / exposed	0 / 49 (0.00%)	1 / 49 (2.04%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	0 / 49 (0.00%)	1 / 49 (2.04%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
subjects affected / exposed	0 / 49 (0.00%)	2 / 49 (4.08%)	0 / 7 (0.00%)
occurrences (all)	0	3	0
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 49 (4.08%)	8 / 49 (16.33%)	0 / 7 (0.00%)
occurrences (all)	2	8	0

Genital candidiasis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 49 (0.00%)	1 / 49 (2.04%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Laryngitis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	4 / 49 (8.16%)	3 / 49 (6.12%)	0 / 7 (0.00%)
occurrences (all)	5	3	0
Oral candidiasis			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	2 / 49 (4.08%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 49 (0.00%)	1 / 49 (2.04%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Pulpitis dental			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	2 / 49 (4.08%)	1 / 49 (2.04%)	0 / 7 (0.00%)
occurrences (all)	4	1	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 49 (0.00%)	0 / 49 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	1 / 49 (2.04%)	1 / 49 (2.04%)	0 / 7 (0.00%)
occurrences (all)	1	1	0

Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 49 (0.00%) 0	6 / 49 (12.24%) 7	0 / 7 (0.00%) 0
Tonsillitis subjects affected / exposed occurrences (all)	0 / 49 (0.00%) 0	0 / 49 (0.00%) 0	0 / 7 (0.00%) 0

<b>Non-serious adverse events</b>	Placebo to CC-99677 150 mg Biologic Naive	Placebo to CC-99677 60 mg Biologic Failure	CC-99677 150 mg Biologic Failure
Total subjects affected by non-serious adverse events subjects affected / exposed	8 / 21 (38.10%)	1 / 2 (50.00%)	6 / 8 (75.00%)
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Electrocardiogram QT prolonged subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Hepatic enzyme increased subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Transaminases increased subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 2	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Injury, poisoning and procedural complications			
Head injury subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Rib fracture subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Nervous system disorders			

Dizziness subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Radiculopathy subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Headache subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Eye disorders Swelling of eyelid subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Iridocyclitis subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Aphthous ulcer subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 2
Diarrhoea subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			

Pneumothorax subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Renal and urinary disorders Renal colic subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 5
Psychiatric disorders Depressed mood subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Musculoskeletal and connective tissue disorders Ankylosing spondylitis subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	0 / 2 (0.00%) 0	2 / 8 (25.00%) 2
Genital candidiasis subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Gingivitis subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	0 / 2 (0.00%) 0	0 / 8 (0.00%) 0
Laryngitis subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Oral candidiasis subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	0 / 2 (0.00%) 0	1 / 8 (12.50%) 1
Otitis media			

subjects affected / exposed	0 / 21 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 2 (50.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Pulpitis dental			
subjects affected / exposed	0 / 21 (0.00%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	2 / 21 (9.52%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	1 / 21 (4.76%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 21 (9.52%)	0 / 2 (0.00%)	1 / 8 (12.50%)
occurrences (all)	3	0	1
Tonsillitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 2 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0

<b>Non-serious adverse events</b>	CC-99677 60 mg Biologic Failure	Placebo Biologic Failure	Placebo to CC-99677 150 mg Biologic Failure
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 7 (57.14%)	1 / 2 (50.00%)	1 / 1 (100.00%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Blood creatine phosphokinase increased			

subjects affected / exposed	0 / 7 (0.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Radiculopathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0

Eye disorders			
Swelling of eyelid			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Iridocyclitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Aphthous ulcer			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	0 / 7 (0.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1



Genital candidiasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Laryngitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pulpitis dental			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Viral infection			
subjects affected / exposed	2 / 7 (28.57%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0

Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0
Tonsillitis subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 2 (0.00%) 0	0 / 1 (0.00%) 0

<b>Non-serious adverse events</b>	Placebo to CC-99677 60 mg Biologic Naive		
Total subjects affected by non-serious adverse events subjects affected / exposed	7 / 21 (33.33%)		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Electrocardiogram QT prolonged subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Hepatic enzyme increased subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Transaminases increased subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Injury, poisoning and procedural complications Head injury subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Rib fracture subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Nervous system disorders			

Dizziness subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Radiculopathy subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Headache subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Eye disorders Swelling of eyelid subjects affected / exposed occurrences (all)  Iridocyclitis subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0  0 / 21 (0.00%) 0		
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all)  Aphthous ulcer subjects affected / exposed occurrences (all)  Diarrhoea subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0  0 / 21 (0.00%) 0  2 / 21 (9.52%) 2		
Respiratory, thoracic and mediastinal disorders			

Pneumothorax subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Renal and urinary disorders Renal colic subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Psychiatric disorders Depressed mood subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Musculoskeletal and connective tissue disorders Ankylosing spondylitis subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	4 / 21 (19.05%) 4		
Genital candidiasis subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Gingivitis subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Laryngitis subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Oral candidiasis subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Otitis media			

subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Respiratory tract infection			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Pulpitis dental			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Viral infection			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Tonsillitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		

**More information**

**Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 November 2020	Objectives and study design update
16 June 2021	Study design and endpoints update
21 September 2022	Endpoints and contact information update

Notes:

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**Interruptions (globally)**

Were there any global interruptions to the trial? No

**Limitations and caveats**

None reported