Clinical trial results:
A Multicenter, Double-blind, Randomized, Parallel-group Study to Compare the Efficacy and Safety of BAT2506 Versus Simponi® in Participants with Active Psoriatic Arthritis

Summary

EudraCT number	2020-002004-39
Trial protocol	CZ BG
Global end of trial date	06 October 2023

Results information

Result version number	v1 (current)
This version publication date	04 August 2024
First version publication date	04 August 2024

Trial information

Trial identification

Sponsor protocol code	BAT-2506-002-CR

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05046431
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bio-Thera Solutions, Ltd.
Sponsor organisation address	Floor 5, Building A6, 11 Kai-Yuan Blvd, Huangpu District,, Guangzhou, China, 510530
Public contact	Clinical Development Department, Bio-Thera Solutions, Ltd., +86 17665187738, CT_Registration@bio-thera.com
Scientific contact	Clinical Development Department, Bio-Thera Solutions, Ltd., +86 17665187738, CT_Registration@bio-thera.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	17 January 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 October 2023
Global end of trial reached?	Yes
Global end of trial date	06 October 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to demonstrate the equivalence of BAT2506 and Simponi® on the efficacy parameter, American College of Rheumatology (ACR) 20 response, in participants with active PsA.

Protection of trial subjects:

The clinical study protocol, protocol amendments, informed consent forms (ICFs), and any other appropriate study-related documents were reviewed and approved by independent ethics committees (IECs) and institutional review boards (IRBs) for each study center. Before entering the study, the investigator (or designee) explained to each subject (or their legally acceptable representatives, if applicable) the nature of the study, its purpose, procedures, expected duration, alternative therapy available, and the benefits and risks involved in study participation. Subjects were given written information about the study, and, before any study procedures were performed, each subject voluntarily signed and dated the ICF. This was to be done during the Screening Period (Days -1 to -28). The master ICF and country-specific and site-specific versions are available upon request.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 April 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 425
Country: Number of subjects enrolled	Bulgaria: 38
Country: Number of subjects enrolled	Czechia: 137
Country: Number of subjects enrolled	China: 92
Country: Number of subjects enrolled	Ukraine: 12
Worldwide total number of subjects	704
EEA total number of subjects	600

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)	664
From 65 to 84 years	40
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

852 subjects were screened, and 704 subjects were enrolled by 11 Aug 2022, with 38 subjects enrolled in Bulgaria, 425 subjects in Poland, 137 subjects in Czech Republic, 12 subjects in Ukraine, and 92 subjects in China.

Pre-assignment

Screening details:

Subjects with active PsA were screened in this study. A total of 852 subjects were screened and 704 subjects were randomized. Investigators completed the protocol defined screening procedures during ≤28-day screening period.

Period 1

Period 1 title	Treatment period 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The investigators, site staff assessing the safety and efficacy, other related study staff (including contract research organization and sponsor), all subjects, and central laboratories would remain blinded to the study treatment assignment throughout this study. The unblinded site staff who were not involved in any study assessment were responsible for IMP storage, transfer and administration.The treatment assignment was not disclosed to any blinded personnel during the study.

Arms

Are arms mutually exclusive?	Yes
Arm title	BAT2506 Arm

Arm description:

Subjects randomized to the BAT2506 Arm at baseline received 13 doses of BAT2506 during the study (6 doses in treatment period 1 and 7 doses in treatment period 2).

Arm type	Experimental
Investigational medicinal product name	BAT2506
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Study treatment was administered at the study site, 50mg SC injection every 4 weeks.

Arm title	Simponi Arm

Arm description:

Subjects randomized to Simponi Arm at baseline received 6 doses of Simponi in treatment period 1, followed by either 7 doses of Simponi or 7 doses of BAT2506 in treatment period 2.

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

Dosage and administration details:

Study treatment was administered at the study site, 50mg SC injection every 4 weeks.

Number of subjects in period 1	BAT2506 Arm	Simponi Arm
Started	351	353
Completed	347	341
Not completed	4	12
Consent withdrawn by subject	2	6
Adverse event, non-fatal	1	5
due to other reason	1	1

Period 2

Period 2 title	Treatment period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The investigators, site staff assessing the safety and efficacy, other related study staff (including contract research organization and sponsor), all subjects, and central laboratories would remain blinded to the study treatment assignment throughout this study. The unblinded site staff who were not involved in any study assessment were responsible for IMP storage, transfer and administration. The treatment assignment was not disclosed to any blinded personnel during study.

Arms

Are arms mutually exclusive?	Yes
Arm title	BAT2506 Arm

Arm description:

Subjects randomized to the BAT2506 Arm at baseline received 13 doses of BAT2506 during the study (6 doses in treatment period 1 and 7 doses in treatment period 2).

Arm type	Experimental
Investigational medicinal product name	BAT2506
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Study treatment was administered at the study site, 50mg SC injection every 4 weeks.

Arm title	Simponi Arm

Arm description:

Subjects randomized to Simponi Arm at baseline received 6 doses of Simponi in treatment period 1, followed by 7 doses of Simponi in treatment period 2.

Arm type	Active comparator

Investigational medicinal product name	Simponi
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Study treatment was administered at the study site, 50mg SC injection every 4 weeks.

Arm title	Simponi BAT2506 Arm

Arm description:

Subjects randomized to RoActemra Arm at baseline received 6 doses of Sinponi in treatment period 1, followed by 7 doses of BAT2506 in treatment period 2.

Arm type	Experimental
Investigational medicinal product name	Simponi
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Study treatment was administered at the study site, 50mg SC injection every 4 weeks.

Number of subjects in period 2[1]	BAT2506 Arm	Simponi Arm	Simponi BAT2506 Arm
Started	341	172	166
Completed	315	159	154
Not completed	26	13	12
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	8	5	4
Adverse event, non-fatal	2	1	-
due to other reason	2	-	2
did not complete the safety follow-up visit	11	5	6
Lost to follow-up	-	1	-
Lack of efficacy	1	-	-
Protocol deviation	2	-	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: A subject completed TP1 was defined as those who received study drug administration at or after week 20. A subject entered TP2 was defined as those who received the study drug administration at or after week 24. In this study, there are some subjects – 9 subjects in total - who completed TP1 but did not enter in TP2 (subjects didn't receive dose at week 24 and early terminated at week 24).

Baseline characteristics

Reporting groups	
Reporting group title	BAT2506 Arm
Reporting group description:	
Subjects randomized to the BAT2506 Arm at baseline received 13 doses of BAT2506 during the study (6 doses in treatment period 1 and 7 doses in treatment period 2).	
Reporting group title	Simponi Arm
Reporting group description:	
Subjects randomized to Simponi Arm at baseline received 6 doses of Simponi in treatment period 1, followed by either 7 doses of Simponi or 7 doses of BAT2506 in treatment period 2.	

Reporting group values	BAT2506 Arm	Simponi Arm	Total
Number of subjects	351	353	704
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	328	336	664
From 65-84 years	23	17	40
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	46.6	45	
standard deviation	± 11.8	± 12.4	-
Gender categorical Units: Subjects			
Female	171	175	346
Male	180	178	358
Region Units: Subjects			
Asia	44	48	92
Europe	307	305	612
Concomitant use of MTX Units: Subjects			
Concomitant use of MTX(yes)	155	156	311
Concomitant use of MTX(no)	196	197	393
Plaque Psoriatic Involvement Units: Subjects			
Mild (<12)	287	296	583
Moderate and Severe (≥12)	64	57	121
Body Weight Group Units: Subjects			
≤84 kg	204	205	409

>84 kg	147	148	295

Body Weight			
Units: Kg			
arithmetic mean	81.92	81.60	
standard deviation	± 17.01	± 19.06	-
Height			
Units: cm			
arithmetic mean	171.1	170.5	
standard deviation	± 9.8	± 9.0	-
BMI			
Units: kg/m2			
arithmetic mean	27.8794	27.9943	
standard deviation	± 4.9330	± 5.8360	-

Subject analysis sets

Subject analysis set title	Full Analysis Set for TP1
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set 1 comprised all subjects randomized to a study treatment arm.

Subject analysis set title	Safety Analysis Set for TP1 (SAF1)
Subject analysis set type	Safety analysis

Subject analysis set description:

The SAF1 comprised all subjects in the FAS1 who received at least one dose of study drug during TP1.

Subject analysis set title	Per PK Analysis Set for TP1 (PKS1)
Subject analysis set type	Safety analysis

Subject analysis set description:

The PKS1 consisted of all subjects in the SAF who had at least one quantifiable PK concentration during TP1, excluding observations after relevant ICEs that might impact PK evaluations. Subjects in the PKS1 were analyzed under the treatment as actually received. The PKS1 was used for analyses of PK during TP1.

Reporting group values	Full Analysis Set for TP1	Safety Analysis Set for TP1 (SAF1)	Per PK Analysis Set for TP1 (PKS1)
Number of subjects	704	704	704
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	664	664	664
From 65-84 years	40	40	40
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	45.8	45.8	45.8

standard deviation	± 12.1	± 12.1	± 12.1

Gender categorical Units: Subjects			
Female	346	346	346
Male	358	358	358
Region Units: Subjects			
Asia	92	92	92
Europe	612	612	612
Concomitant use of MTX Units: Subjects			
Concomitant use of MTX(yes)	311	311	311
Concomitant use of MTX(no)	393	393	393
Plaque Psoriatic Involvement Units: Subjects			
Mild (<12)	583	583	583
Moderate and Severe (≥12)	121	121	121
Body Weight Group Units: Subjects			
≤84 kg	409	409	409
>84 kg	295	295	295
Body Weight Units: Kg			
arithmetic mean	81.76	81.76	81.76
standard deviation	± 18.05	± 18.05	± 18.05
Height Units: cm			
arithmetic mean	170.8	170.8	170.8
standard deviation	± 9.4	± 9.4	± 9.4
BMI Units: kg/m2			
arithmetic mean	27.9369	27.9369	27.9369
standard deviation	± 5.4005	± 5.4005	± 5.4005

End points

End points reporting groups

Reporting group title	BAT2506 Arm
Reporting group description:	
Subjects randomized to the BAT2506 Arm at baseline received 13 doses of BAT2506 during the study (6 doses in treatment period 1 and 7 doses in treatment period 2).	
Reporting group title	Simponi Arm
Reporting group description:	
Subjects randomized to Simponi Arm at baseline received 6 doses of Simponi in treatment period 1, followed by either 7 doses of Simponi or 7 doses of BAT2506 in treatment period 2.	
Reporting group title	BAT2506 Arm
Reporting group description:	
Subjects randomized to the BAT2506 Arm at baseline received 13 doses of BAT2506 during the study (6 doses in treatment period 1 and 7 doses in treatment period 2).	
Reporting group title	Simponi Arm
Reporting group description:	
Subjects randomized to Simponi Arm at baseline received 6 doses of Simponi in treatment period 1, followed by 7 doses of Simponi in treatment period 2.	
Reporting group title	Simponi BAT2506 Arm
Reporting group description:	
Subjects randomized to RoActemra Arm at baseline received 6 doses of Sinponi in treatment period 1, followed by 7 doses of BAT2506 in treatment period 2.	
Subject analysis set title	Full Analysis Set for TP1
Subject analysis set type	Full analysis
Subject analysis set description:	
Full Analysis Set 1 comprised all subjects randomized to a study treatment arm.	
Subject analysis set title	Safety Analysis Set for TP1 (SAF1)
Subject analysis set type	Safety analysis
Subject analysis set description:	
The SAF1 comprised all subjects in the FAS1 who received at least one dose of study drug during TP1.	
Subject analysis set title	Per PK Analysis Set for TP1 (PKS1)
Subject analysis set type	Safety analysis
Subject analysis set description:	
The PKS1 consisted of all subjects in the SAF who had at least one quantifiable PK concentration during TP1, excluding observations after relevant ICEs that might impact PK evaluations. Subjects in the PKS1 were analyzed under the treatment as actually received. The PKS1 was used for analyses of PK during TP1.	

Primary: Percentage of subjects achieving ACR 20 response at Week 8

End point title	Percentage of subjects achieving ACR 20 response at Week 8
End point description:	
End point type	Primary
End point timeframe:	
baseline to week 8	

End point values	BAT2506 Arm	Simponi Arm	Full Analysis Set for TP1	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	351	353	704	
Units: Proportion of Subjects				
number (not applicable)	74.53	63.41	68.95	

Statistical analyses

Statistical analysis title	ACR20 analysis for week 8 (Full Analysis Set 1)
Comparison groups	BAT2506 Arm v Simponi Arm v Full Analysis Set for TP1
Number of subjects included in analysis	1408
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Risk difference (RD)
Point estimate	11.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.4
upper limit	18.25

Primary: Percentage of subjects achieving ACR 20 response at Week 14	
End point title	Percentage of subjects achieving ACR 20 response at Week 14
End point description:	
End point type	Primary
End point timeframe: baseline to week 14	

End point values	BAT2506 Arm	Simponi Arm	Full Analysis Set for TP1	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	351	353	704	
Units: Proportion of subjects				
number (not applicable)	79.26	77.08	78.17	

Statistical analyses

Statistical analysis title	ACR20 analysis for week 14 (Full Analysis Set 1)
Comparison groups	BAT2506 Arm v Simponi Arm

Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Risk difference (RD)
Point estimate	2.36
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.91
upper limit	7.63

Statistical analysis title	ACR20 analysis for week 14 (Full Analysis Set 1)
Comparison groups	BAT2506 Arm v Simponi Arm
Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Risk difference (RD)
Point estimate	2.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.92
upper limit	8.64

Secondary: Percentage of subjects achieving ACR 50 response at Week 8	
End point title	Percentage of subjects achieving ACR 50 response at Week 8
End point description:	

End point type	Secondary
End point timeframe:	
baseline to week 8	

End point values	BAT2506 Arm	Simponi Arm	Full Analysis Set for TP1	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	351	353	704	
Units: Proportion of Subjects				
number (not applicable)	36.03	34.05	35.04	

Statistical analyses

Statistical analysis title	ACR50 analysis for Week 8 (Full Analysis Set 1)
Comparison groups	BAT2506 Arm v Simponi Arm
Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Risk difference (RD)
Point estimate	2.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.98
upper limit	9.35

Secondary: Percentage of subjects achieving ACR 50 response at Week 14	
End point title	Percentage of subjects achieving ACR 50 response at Week 14
End point description:	
End point type	Secondary
End point timeframe: baseline to week 14	

End point values	BAT2506 Arm	Simponi Arm	Full Analysis Set for TP1	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	351	353	704	
Units: Percentage of subjects				
number (not applicable)	49.29	50.10	49.70	

Statistical analyses

Statistical analysis title	ACR50 analysis for Week 14 (Full Analysis Set 1)
Comparison groups	BAT2506 Arm v Simponi Arm
Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Risk difference (RD)
Point estimate	-0.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.02
upper limit	5.62

Statistical analysis title	ACR50 analysis for Week 14 (Full Analysis Set 1)
Comparison groups	BAT2506 Arm v Simponi Arm
Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Risk difference (RD)
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.23
upper limit	6.84

Secondary: Percentage of subjects achieving ACR 70 response at Week 8	
End point title	Percentage of subjects achieving ACR 70 response at Week 8
End point description:	
End point type	Secondary
End point timeframe:	
baseline to week 8	

End point values	BAT2506 Arm	Simponi Arm	Full Analysis Set for TP1	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	351	353	704	
Units: Proportion of Subjects				
number (not applicable)	16.21	14.67	15.44	

Statistical analyses

Statistical analysis title	ACR70 analysis at Week 8 (Full Analysis Set 1)
Comparison groups	BAT2506 Arm v Simponi Arm
Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Risk difference (RD)
Point estimate	1.76

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.61
upper limit	7.13

Secondary: Percentage of subjects achieving ACR 70 response at Week 14

End point title	Percentage of subjects achieving ACR 70 response at Week 14
End point description:	

End point type	Secondary
End point timeframe:	
baseline to week 14	

End point values	BAT2506 Arm	Simponi Arm	Full Analysis Set for TP1	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	351	353	704	
Units: Proportion of Subjects				
number (not applicable)	29.06	23.13	26.09	

Statistical analyses

Statistical analysis title	ACR70 analysis at Week 14 (Full Analysis Set 1)
Comparison groups	BAT2506 Arm v Simponi Arm
Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Risk difference (RD)
Point estimate	6.08
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.57
upper limit	11.59

Statistical analysis title	ACR70 analysis at Week 14 (Full Analysis Set 1)
Comparison groups	BAT2506 Arm v Simponi Arm

Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Risk difference (RD)
Point estimate	6.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	12.64

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs occuring during the study (from the time of receiving written informed consent to 12 weeks after the last dose of IMP) must be collected and documented on the relevant eCRF pages.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	BAT2506 Arm
Reporting group description: -	
Reporting group title	Simponi Arm
Reporting group description: -	
Reporting group title	Simponi BAT2506 Arm

Reporting group description: -

Serious adverse events	BAT2506 Arm	Simponi Arm	Simponi BAT2506 Arm
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 351 (5.41%)	8 / 187 (4.28%)	5 / 166 (3.01%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	1 / 351 (0.28%)	0 / 187 (0.00%)	0 / 166 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	2 / 351 (0.57%)	0 / 187 (0.00%)	1 / 166 (0.60%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic cancer			
subjects affected / exposed	0 / 351 (0.00%)	1 / 187 (0.53%)	0 / 166 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal proliferative breast lesion			

subjects affected / exposed	0 / 351 (0.00%)	1 / 187 (0.53%)	0 / 166 (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
Cerebral infarction			
subjects affected / exposed	1 / 351 (0.28%)	0 / 187 (0.00%)	0 / 166 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Foetal growth restriction			
subjects affected / exposed	0 / 351 (0.00%)	1 / 187 (0.53%)	0 / 166 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Sudden death			
subjects affected / exposed	0 / 351 (0.00%)	1 / 187 (0.53%)	0 / 166 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	0 / 351 (0.00%)	1 / 187 (0.53%)	0 / 166 (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
Cervical polyp			
subjects affected / exposed	1 / 351 (0.28%)	0 / 187 (0.00%)	0 / 166 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Adenoidal hypertrophy			
subjects affected / exposed	1 / 351 (0.28%)	0 / 187 (0.00%)	0 / 166 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Femur fracture			
subjects affected / exposed	1 / 351 (0.28%)	0 / 187 (0.00%)	0 / 166 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	1 / 351 (0.28%)	1 / 187 (0.53%)	0 / 166 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 351 (0.28%)	0 / 187 (0.00%)	0 / 166 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 351 (0.28%)	0 / 187 (0.00%)	1 / 166 (0.60%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Anal fissure			
subjects affected / exposed	0 / 351 (0.00%)	0 / 187 (0.00%)	1 / 166 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	1 / 351 (0.28%)	0 / 187 (0.00%)	0 / 166 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteonecrosis			
subjects affected / exposed	1 / 351 (0.28%)	0 / 187 (0.00%)	0 / 166 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis			

subjects affected / exposed	1 / 351 (0.28%)	0 / 187 (0.00%)	0 / 166 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 351 (0.00%)	1 / 187 (0.53%)	0 / 166 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 351 (0.28%)	0 / 187 (0.00%)	0 / 166 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	1 / 351 (0.28%)	0 / 187 (0.00%)	1 / 166 (0.60%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 351 (0.28%)	0 / 187 (0.00%)	0 / 166 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 351 (0.28%)	0 / 187 (0.00%)	1 / 166 (0.60%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 351 (0.00%)	1 / 187 (0.53%)	0 / 166 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 351 (0.28%)	0 / 187 (0.00%)	0 / 166 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			

subjects affected / exposed	1 / 351 (0.28%)	0 / 187 (0.00%)	0 / 166 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	BAT2506 Arm	Simponi Arm	Simponi BAT2506 Arm
Total subjects affected by non-serious adverse events			
subjects affected / exposed	291 / 351 (82.91%)	152 / 187 (81.28%)	134 / 166 (80.72%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	28 / 351 (7.98%)	12 / 187 (6.42%)	12 / 166 (7.23%)
occurrences (all)	43	16	18
Aspartate aminotransferase increased			
subjects affected / exposed	16 / 351 (4.56%)	4 / 187 (2.14%)	12 / 166 (7.23%)
occurrences (all)	21	4	16
Low density lipoprotein increased			
subjects affected / exposed	9 / 351 (2.56%)	2 / 187 (1.07%)	9 / 166 (5.42%)
occurrences (all)	16	4	18
Weight increased			
subjects affected / exposed	7 / 351 (1.99%)	0 / 187 (0.00%)	3 / 166 (1.81%)
occurrences (all)	9	0	3
Blood cholesterol increased			
subjects affected / exposed	6 / 351 (1.71%)	3 / 187 (1.60%)	6 / 166 (3.61%)
occurrences (all)	8	4	8
Blood alkaline phosphatase increased			
subjects affected / exposed	4 / 351 (1.14%)	0 / 187 (0.00%)	6 / 166 (3.61%)
occurrences (all)	5	0	7
SARS-CoV-2 test positive			
subjects affected / exposed	3 / 351 (0.85%)	5 / 187 (2.67%)	2 / 166 (1.20%)
occurrences (all)	3	5	2
Vascular disorders			
Hypertension			
subjects affected / exposed	18 / 351 (5.13%)	3 / 187 (1.60%)	3 / 166 (1.81%)
occurrences (all)	19	3	3

Nervous system disorders			
Headache			
subjects affected / exposed	15 / 351 (4.27%)	12 / 187 (6.42%)	8 / 166 (4.82%)
occurrences (all)	17	13	8
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	4 / 351 (1.14%)	1 / 187 (0.53%)	4 / 166 (2.41%)
occurrences (all)	7	1	8
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 351 (1.14%)	4 / 187 (2.14%)	2 / 166 (1.20%)
occurrences (all)	5	4	2
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	17 / 351 (4.84%)	12 / 187 (6.42%)	10 / 166 (6.02%)
occurrences (all)	17	12	11
Nausea			
subjects affected / exposed	5 / 351 (1.42%)	4 / 187 (2.14%)	1 / 166 (0.60%)
occurrences (all)	5	4	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 351 (1.99%)	6 / 187 (3.21%)	1 / 166 (0.60%)
occurrences (all)	7	6	1
Rhinorrhoea			
subjects affected / exposed	4 / 351 (1.14%)	2 / 187 (1.07%)	4 / 166 (2.41%)
occurrences (all)	4	2	4
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	11 / 351 (3.13%)	5 / 187 (2.67%)	3 / 166 (1.81%)
occurrences (all)	13	5	4
Musculoskeletal and connective tissue disorders			
Psoriatic arthropathy			
subjects affected / exposed	27 / 351 (7.69%)	7 / 187 (3.74%)	7 / 166 (4.22%)
occurrences (all)	40	8	8
Arthralgia			

subjects affected / exposed	5 / 351 (1.42%)	2 / 187 (1.07%)	4 / 166 (2.41%)
occurrences (all)	6	2	4
Back pain			
subjects affected / exposed	5 / 351 (1.42%)	5 / 187 (2.67%)	3 / 166 (1.81%)
occurrences (all)	5	5	3
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	61 / 351 (17.38%)	29 / 187 (15.51%)	43 / 166 (25.90%)
occurrences (all)	78	40	52
Nasopharyngitis			
subjects affected / exposed	56 / 351 (15.95%)	27 / 187 (14.44%)	25 / 166 (15.06%)
occurrences (all)	71	37	32
COVID-19			
subjects affected / exposed	49 / 351 (13.96%)	16 / 187 (8.56%)	19 / 166 (11.45%)
occurrences (all)	51	16	20
Tonsillitis			
subjects affected / exposed	18 / 351 (5.13%)	5 / 187 (2.67%)	6 / 166 (3.61%)
occurrences (all)	19	5	6
Pharyngitis			
subjects affected / exposed	17 / 351 (4.84%)	7 / 187 (3.74%)	7 / 166 (4.22%)
occurrences (all)	18	9	7
Urinary tract infection			
subjects affected / exposed	16 / 351 (4.56%)	12 / 187 (6.42%)	8 / 166 (4.82%)
occurrences (all)	19	13	11
Sinusitis			
subjects affected / exposed	11 / 351 (3.13%)	7 / 187 (3.74%)	3 / 166 (1.81%)
occurrences (all)	14	8	3
Bronchitis			
subjects affected / exposed	9 / 351 (2.56%)	4 / 187 (2.14%)	5 / 166 (3.01%)
occurrences (all)	10	4	7
Oral herpes			
subjects affected / exposed	8 / 351 (2.28%)	4 / 187 (2.14%)	5 / 166 (3.01%)
occurrences (all)	11	4	5
Respiratory tract infection			
subjects affected / exposed	8 / 351 (2.28%)	5 / 187 (2.67%)	7 / 166 (4.22%)
occurrences (all)	10	5	7

Gastroenteritis			
subjects affected / exposed	7 / 351 (1.99%)	7 / 187 (3.74%)	1 / 166 (0.60%)
occurrences (all)	7	7	1
Rhinitis			
subjects affected / exposed	6 / 351 (1.71%)	6 / 187 (3.21%)	2 / 166 (1.20%)
occurrences (all)	10	6	2
Acute sinusitis			
subjects affected / exposed	3 / 351 (0.85%)	4 / 187 (2.14%)	0 / 166 (0.00%)
occurrences (all)	3	4	0
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	20 / 351 (5.70%)	7 / 187 (3.74%)	12 / 166 (7.23%)
occurrences (all)	30	9	20
Hypertriglyceridaemia			
subjects affected / exposed	14 / 351 (3.99%)	4 / 187 (2.14%)	8 / 166 (4.82%)
occurrences (all)	24	8	16
Hyperlipidaemia			
subjects affected / exposed	7 / 351 (1.99%)	10 / 187 (5.35%)	4 / 166 (2.41%)
occurrences (all)	8	14	5
Hyperuricaemia			
subjects affected / exposed	7 / 351 (1.99%)	4 / 187 (2.14%)	4 / 166 (2.41%)
occurrences (all)	16	9	6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 November 2020	1)Update primary endpoint to percentage of participants achieving ACR 20 response at Week 8 for studies conducted under the EMA and at Week 14 for studies conducted under other regulatory agencies. Delete key secondary endpoint. Add study data from GO-REVEAL study in Appendix 8. 2) Update protocol to clarify what concomitant medications are prohibited during the study. Add section regarding the use of rescue medicine. 3)Add plaque psoriatic involvement as stratification factor for randomization. Add that the percentage of participants using MTX concomitantly should not exceed 60%. 4)Include 3 additional PK sampling time points and added more parameters to be assessed for other secondary endpoints. 5)Update equivalence margin from 15% to 13.8%. 6)Delete % Reticulocytes as parameters for hematology assessment. 7)Minor administrative updates.
15 November 2021	1)Update the statistical analyses with estimand framework. 2)Update that the percentage of participants using MTX concomitantly should not exceed 50%. 3)Add one more Safety Follow up Visit (SFU2) to Week60. Include 1 additional PK and 2 additional ADA sampling time points. 4)Update the follow up period for participants who discontinue the study treatment early: they will be followed till W24 or 12 weeks post last dose (following the longer period)if they withdraw before dosing of W24, or they will be followed till W60. 5)Update sample size to 700. Update equivalence margin for FDA to [-12.6, +15%]. 6)Update the interim Analyses to Week36. 7)Adding Urea and Urine leukocyte/other indicatiors for Urine white cell detection. Change “Nonfasting Glucose ” to “ Glucose”. 8)Minor administrative updates.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

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

Notes: