Clinical trial results:
Efficacy, Safety, and Immunogenicity of BI 695501 versus Humira® in Patients with Moderate to Severe Chronic Plaque Psoriasis: A Randomized, Double-Blind, Parallel-Arm, Multiple-Dose, Active Comparator Trial

Summary

EudraCT number	2016-000613-79
Trial protocol	DE CZ SK PL
Global end of trial date	17 January 2018

Results information

Result version number	v1 (current)
This version publication date	01 February 2019
First version publication date	01 February 2019

Trial information

Trial identification

Sponsor protocol code	1297.12

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02850965
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, Ingelheim am Rhein, Germany, 55216
Public contact	QRPE Processes and Systems Coordination, Clinical Trial Information Disclosure, Boehringer Ingelheim, 001 8002430127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	QRPE Processes and Systems Coordination, Clinical Trial Information Disclosure, Boehringer Ingelheim, 001 8002430127, clintriage.rdg@boehringer-ingelheim.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	06 February 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial was to establish equivalence in efficacy between BI 695501 and US-licensed Humira® at Week 16 in patients with active moderate to severe chronic plaque psoriasis.

Protection of trial subjects:

Only patients that met all the study inclusion and none of the exclusion criteria were to be randomized in the study. All patients were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all patients was adhered to throughout the trial conduct.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 September 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 109
Country: Number of subjects enrolled	Czech Republic: 32
Country: Number of subjects enrolled	Estonia: 3
Country: Number of subjects enrolled	Germany: 32
Country: Number of subjects enrolled	Poland: 81
Country: Number of subjects enrolled	Russian Federation: 66
Country: Number of subjects enrolled	Slovakia: 11
Country: Number of subjects enrolled	Ukraine: 90
Worldwide total number of subjects	424
EEA total number of subjects	159

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)	395
From 65 to 84 years	29
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Phase III, multinational, randomized, double-blind, parallel-arm, multiple-dose, active-comparator trial of BI 695501 and US-licensed Humira with a 24-week treatment period and 10 weeks of safety follow up, in patients with moderate to severe chronic plaque psoriasis.

Pre-assignment

Screening details:

All patients were screened for eligibility to participate in the trial. Patients attended a specialist sites which ensured that they (the patients) met all strictly implemented inclusion/exclusion criteria. Patients were not to be entered to trial treatment if any one of the specific entry criteria was violated.

Period 1

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

Blinding implementation details:

This was a double-blind trial.

Arms

Are arms mutually exclusive?	Yes
Arm title	BI 695501

Arm description:

Patients were administered with BI 695501 via subcutaneous (SC) injection 80 milligram (mg) on Day 1 and 40 milligram (mg) on every other week from Week 1 to Week 23.

Arm type	Experimental
Investigational medicinal product name	BI 695501
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Patients were administered with BI 695501 via subcutaneous (SC) injection 80 milligram (mg) on Day 1 and 40 milligram (mg) on every other week from Week 1 to Week 23.

Arm title	US-licensed Humira

Arm description:

Patients were administered US-licensed Humira via subcutaneous (SC) injection 80 mg on Day 1 and 40 milligram on every other week from Week 1 to Week 23.

Arm type	Active comparator
Investigational medicinal product name	US-licensed Humira
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Patients were administered US-licensed Humira via subcutaneous (SC) injection 80 mg on Day 1 and 40 milligram on every other week from Week 1 to Week 23.

Number of subjects in period 1[1]	BI 695501	US-licensed Humira
Started	159	158
Completed	141	134
Not completed	18	24
Consent withdrawn by subject	3	4
Physician decision	-	1
Adverse event, non-fatal	3	2
Lost to follow-up	5	3
Other than listed	3	4
Lack of efficacy	4	8
Protocol deviation	-	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Baseline characteristics are based on patients who were randomised after successfully completing the screening period and received at least one dose of the trial medication.

Baseline characteristics

Reporting groups	
Reporting group title	BI 695501
Reporting group description:	
Patients were administered with BI 695501 via subcutaneous (SC) injection 80 milligram (mg) on Day 1 and 40 milligram (mg) on every other week from Week 1 to Week 23.	
Reporting group title	US-licensed Humira
Reporting group description:	
Patients were administered US-licensed Humira via subcutaneous (SC) injection 80 mg on Day 1 and 40 milligram on every other week from Week 1 to Week 23.	

Reporting group values	BI 695501	US-licensed Humira	Total
Number of subjects	159	158	317
Age categorical			
Units: Subjects			

Age Continuous			
Safety Analysis Set (SAF): The SAF contained all patients who provided signed informed consent, who were randomized, and who received at least one dose of trial medication.			
Units: years			
arithmetic mean	42.1	44.7	
standard deviation	± 12.79	± 13.92	-
Sex: Female, Male			
SAF			
Units: Subjects			
Female	58	56	114
Male	101	102	203
Race (NIH/OMB)			
SAF			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	1	1
Black or African American	1	1	2
White	157	156	313
More than one race	0	0	0
Unknown or Not Reported	1	0	1
Ethnicity (NIH/OMB)			
SAF			
Units: Subjects			
Hispanic or Latino	12	10	22
Not Hispanic or Latino	147	146	293
Unknown or Not Reported	0	2	2

End points

End points reporting groups

Reporting group title	BI 695501
Reporting group description:	
Patients were administered with BI 695501 via subcutaneous (SC) injection 80 milligram (mg) on Day 1 and 40 milligram (mg) on every other week from Week 1 to Week 23.	
Reporting group title	US-licensed Humira
Reporting group description:	
Patients were administered US-licensed Humira via subcutaneous (SC) injection 80 mg on Day 1 and 40 milligram on every other week from Week 1 to Week 23.	

Primary: The percentage of patients with at least 75% reduction in Psoriasis Area and Severity Index (PASI 75) response at Week 16

End point title	The percentage of patients with at least 75% reduction in Psoriasis Area and Severity Index (PASI 75) response at Week 16
End point description:	
PASI tool provides numeric scoring for a patient's overall psoriasis disease state, ranging from 0 to 72. Head(h),trunk(t),upper extremities(u) and lower extremities(l) areas were assessed; correspond to 10,30,20and40% of the total body area. Lesions were assessed using numeric scale of 0 to 4 where 0 was complete lack of cutaneous involvement and 4 was severest possible involvement. Area of psoriatic involvement of areas (Ah, At, Au, and Al) was given a numerical value: 0 = no involvement, 1=<10%, 2=10 to <30%, 3=30 to <50%, 4=50 to <70%, 5=70 to <90%, and 6=90 to 100%involvement.PASI=0.1(Eh+Ih+Dh)Ah+0.3(Et+It+Dt)At+0.2(Eu+Iu+Du)Au+0.4(El+Il+Dl)Al. Percentage=least squares means per treatment groups back transformed using inverse logit function. Full Analysis Set(FAS) contained all randomized patients who received at least one dose of trial medication, and had all efficacy measures relevant for the PASI 75,measured at baseline and at least once post-baseline (prior to or on Week16).	
End point type	Primary
End point timeframe:	
Week 16	

End point values	BI 695501	US-licensed Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158[1]	157[2]		
Units: Percentage (%)				
number (not applicable)	68.2	70.4		

Notes:

[1] - FAS

[2] - FAS

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Week16 confidence interval for estimated difference in percentage are produced using cumulative distribution function method of Reeve. Statistical model: Logit (response to treatment at Week16)=Treatment+Baseline PASI+Prior exposure to a biologic agent+random error. Model included fixed, categorical effects of treatment (BI 695501 vs US-licensed Humira) and prior exposure to a biologic	

agent (yes/no), continuous effect of baseline PASI. The random error was assumed to be binomially distributed.

Comparison groups	BI 695501 v US-licensed Humira
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	equivalence[3]
Method	Regression, Logistic
Parameter estimate	Difference in PASI 75 Response Rate
Point estimate	-2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.4
upper limit	8.7

Notes:

[3] - Protocol defined margins are: [-18.0%, +18.0%] for Week 16, 95% confidence interval. Between-imputation variance is zero. Confidence interval is based on one imputed set. Difference in PASI 75 Response Rate = (BI 695501 – US-licensed Humira, %)

Secondary: The percentage of patients with a PASI 75 response at Week 24

End point title	The percentage of patients with a PASI 75 response at Week 24

End point description:

The PASI tool provides numeric scoring for a patient's overall psoriasis disease state, ranging from 0 to 72. Head (h), trunk (t), upper extremities (u) and lower extremities (l) areas were assessed; correspond to 10, 30, 20, and 40% of the total body area, respectively. The signs of severity, erythema (E), induration (I) and desquamation (D) of lesions were assessed using a numeric scale of 0 to 4 where 0 was a complete lack of cutaneous involvement and 4 was the severest possible involvement. The area of psoriatic involvement of these areas (Ah, At, Au, and Al) was given a numerical value: 0 = no involvement, 1 = <10%, 2 = 10 to <30%, 3 = 30 to <50%, 4 = 50 to <70%, 5 = 70 to <90%, and 6 = 90 to 100% involvement. PASI = 0.1(Eh+Ih+Dh)Ah + 0.3(Et+It+Dt)At + 0.2(Eu+Iu+Du)Au + 0.4(El+Il+Dl)Al. Percentage = least squares means per treatment groups back transformed using inverse logit function.

End point type	Secondary

End point timeframe:

Week 24

End point values	BI 695501	US-licensed Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158[4]	157[5]		
Units: Percentage (%)				
number (not applicable)	75.3	72.4		

Notes:

[4] - FAS

[5] - FAS

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Week 24 confidence interval for estimated difference in percentage are produced using cumulative distribution function method of Reeve. Statistical model: Logit (response to treatment at Week 24)=Treatment+Baseline PASI+Prior exposure to a biologic agent+random error. Model included fixed,

categorical effects of treatment (BI 695501 vs US-licensed Humira) and prior exposure to biologic agent (yes/no), continuous effect of baseline PASI. The random error was assumed to be binomially distributed.

Comparison groups	BI 695501 v US-licensed Humira
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	other[6]
Method	Regression, Logistic
Parameter estimate	Difference in PASI 75 Response Rate
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.5
upper limit	12.6

Notes:

[6] - Missing PASI 75 at Week 24 data were imputed using a combination of non-responder imputation (NRI) and last observed carried forward (LOCF). Difference in PASI 75 Response Rate = (BI 695501 – US-licensed Humira, %).

Secondary: The mean percentage improvement in PASI at Week 16

End point title	The mean percentage improvement in PASI at Week 16

End point description:

The PASI tool provides numeric scoring for a patient's overall psoriasis disease state, ranging from 0 to 72. Head (h), trunk (t), upper extremities (u) and lower extremities (l) areas were assessed; correspond to 10, 30, 20, and 40% of the total body area, respectively. The signs of severity, erythema (E), induration (I) and desquamation (D) of lesions were assessed using a numeric scale of 0 to 4 where 0 was a complete lack of cutaneous involvement and 4 was the severest possible involvement. The area of psoriatic involvement of these areas (Ah, At, Au, and Al) was given a numerical value: 0 = no involvement, 1 =<10%, 2 =10 to <30%, 3 =30 to <50%, 4 =50 to <70%, 5 =70 to <90%, and 6 =90 to 100% involvement. PASI = 0.1(Eh+Ih+Dh)Ah + 0.3(Et+It+Dt)At + 0.2(Eu+Iu+Du)Au + 0.4(El+Il+Dl)Al. Results based on PASI mean percentage improvement from Baseline after 16 weeks of treatment = overall mean + treatment group + Baseline PASI + prior exposure to a biological agent + random error.

End point type	Secondary

End point timeframe:

Week 16

End point values	BI 695501	US-licensed Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149[7]	149[8]		
Units: Percentage (%)				
least squares mean (confidence interval 95%)	83.7 (80.2 to 87.2)	82.1 (78.6 to 85.6)		

Notes:

[7] - FAS

[8] - FAS

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis of covariance (ANCOVA) was performed based on the following model: PASI percentage

improvement from baseline at Week 16= Treatment + Baseline PASI +Prior exposure to a biologic agent + random error.

Comparison groups	BI 695501 v US-licensed Humira
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other[9]
Method	ANCOVA
Parameter estimate	Difference of Least Squares Means (LSM)
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	6

Notes:

[9] - Difference of LSM = LSM of (BI 695501 – Humira)

Secondary: The percentage of patients with a Static Physician's Global Assessment (sPGA) ≤1 (clear or almost clear) at Week 16

End point title	The percentage of patients with a Static Physician's Global Assessment (sPGA) ≤1 (clear or almost clear) at Week 16

End point description:

The Static Physician's Global Assessment (sPGA) is a 5-point score ranging from 0 to 4, based on the physician's assessment of the average thickness, erythema, and scaling of all psoriatic lesions. The assessment was considered "static", which referred to the patient's disease state at the time of the assessment, without comparison to any of the patient's previous disease states (dynamic), whether at Baseline or at a previous visit. A lower score indicated less body coverage, with 0 being clear, 1 being almost clear, and 4 being. Percentage = least squares means per treatment groups back transformed using inverse logit function.

End point type	Secondary

End point timeframe:

Week 16

End point values	BI 695501	US-licensed Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158[10]	157[11]		
Units: Percentage (%)				
number (not applicable)	59.6	52.1		

Notes:

[10] - FAS

[11] - FAS

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Week16 confidence interval for the estimated difference in percentage are produced using the cumulative distribution function method of Reeve. Statistical model: Logit (response to treatment at Week16)=Treatment+Baseline PASI+Prior exposure to a biologic agent+random error. Model included fixed, categorical effects of treatment (BI 695501 vs US-licensed Humira) and prior exposure to a biologic agent (yes/no), continuous effect of baseline PASI.

Comparison groups	BI 695501 v US-licensed Humira

Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	other[12]
Method	Regression, Logistic
Parameter estimate	Difference in sPGA <= 1 Response Rate
Point estimate	7.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	19.1

Notes:

[12] - Missing sPGA at Week 16 data were imputed using a combination of non-responder imputation (NRI) and last observed carried forward (LOCF). Difference in sPGA <= 1 Response Rate = (BI 695501 – US-licensed Humira, %).

Secondary: The percentage of patients achieving a Dermatology Life Quality Index (DLQI) of 0 or 1 at Week 16

End point title	The percentage of patients achieving a Dermatology Life Quality Index (DLQI) of 0 or 1 at Week 16

End point description:

The DLQI is a subject-administered, 10-question, that covers 6 domains including symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. It has a 1-week recall period. Every item score ranges from 0 (not relevant/not at all) to 3 (very much). Question 7 is a "yes/no" question where "yes" is scored as 3. The DLQI total score was calculated by summing the scores of each question resulting in a range of 0 to 30 where 0-1 = no effect on subject's life, 2-5 = small effect, 6-10 = moderate effect, 11-20 = very large effect, and 21-30 = extremely large effect on the subject's life. The higher the score, the more the quality of life is impaired. If the answer to 1 question in a domain was missing, that domain was treated as missing. If 2 or more questions were left unanswered (missing), DLQI total score was treated as missing. Percentage = least squares means per treatment groups back transformed using inverse logit function.

End point type	Secondary

End point timeframe:

Week 16

End point values	BI 695501	US-licensed Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158[13]	157[14]		
Units: Percentage (%)				
number (not applicable)	67.2	66.8		

Notes:

[13] - FAS

[14] - FAS

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Week16 confidence interval for estimated difference in percentage are produced using cumulative distribution function method of Reeve. Statistical model: Logit (response to treatment at Week16)=Treatment+Baseline PASI+Prior exposure to a biologic agent+random error. Model included fixed, categorical effects of treatment (BI 695501 vs US-licensed Humira) and prior exposure to a biologic agent (yes/no), continuous effect of baseline PASI.

Comparison groups	BI 695501 v US-licensed Humira
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	other[15]
Method	Regression, Logistic
Parameter estimate	Difference in DLQI Response Rate
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.7
upper limit	11.3

Notes:

[15] - Missing DLQI at Week 16 data were imputed using a combination of non-responder imputation (NRI) and last observed carried forward (LOCF). Difference in DLQI (0, 1) Response Rate = (BI 695501 – US-licensed Humira, %).

Secondary: The percentage of patients with drug-related adverse events (AEs)

End point title	The percentage of patients with drug-related adverse events (AEs)

End point description:

The secondary safety endpoint was defined as the percentage of patients with drug-related adverse events (AEs). Safety Analysis Set (SAF): The SAF contained all patients who provided signed informed consent, who were randomized, and who received at least one dose of trial medication.

End point type	Secondary

End point timeframe:

From first drug administration until 10 weeks after last drug administration, up to 33 weeks.

End point values	BI 695501	US-licensed Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159[16]	158[17]		
Units: Percentage of patients (%)				
number (not applicable)	13.2	20.3		

Notes:

[16] - SAF

[17] - SAF

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first drug administration until 10 weeks after last drug administration, up to 33 weeks.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	BI 695501

Reporting group description:

Patients were administered with BI 695501 via subcutaneous (SC) injection 80 milligram (mg) on Day 1 and 40 milligram (mg) on every other week from Week 1 to Week 23.

Reporting group title	US-licensed Humira

Reporting group description:

Patients were administered US-licensed Humira via subcutaneous (SC) injection 80 mg on Day 1 and 40 milligram on every other week from Week 1 to Week 23.

Serious adverse events	BI 695501	US-licensed Humira	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 159 (3.14%)	7 / 158 (4.43%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Congestive cardiomyopathy			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Pancreatitis chronic			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis toxic			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Exostosis			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot deformity			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Furuncle			

subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral herpes			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	0 / 159 (0.00%)	1 / 158 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 159 (0.63%)	0 / 158 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	BI 695501	US-licensed Humira	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 159 (10.69%)	24 / 158 (15.19%)	
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	3 / 159 (1.89%)	10 / 158 (6.33%)	
occurrences (all)	3	29	
Injection site erythema			
subjects affected / exposed	5 / 159 (3.14%)	10 / 158 (6.33%)	
occurrences (all)	10	24	
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	12 / 159 (7.55%) 14	7 / 158 (4.43%) 7	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported