Clinical trial results:
A Double-Blind, Randomized, Parallel-Group, Active-Control Study to Compare the Efficacy and Safety of CHS-1420 Versus Humira® in Subjects With Chronic Plaque Psoriasis (PsOsim)

Summary

EudraCT number	2015-000632-15
Trial protocol	LV IT SK EE PL HR
Global end of trial date	13 March 2017

Results information

Result version number	v1 (current)
This version publication date	07 August 2019
First version publication date	07 August 2019

Trial information

Trial identification

Sponsor protocol code	CHS-1420-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	IND Number: 119540

Notes:

Sponsors

Sponsor organisation name	Coherus BioSciences, Inc.
Sponsor organisation address	333 Twin Dolphin Drive, Suit 600, Redwood City, CA, United States, 94065
Public contact	Barbara K. Finck, MD Chief Clinical Advisor, Coherus BioSciences, Inc., 001 650649-3530, clinicaltrialregistries@coherus.com
Scientific contact	Barbara K. Finck, MD Chief Clinical Advisor, Coherus BioSciences, Inc., 001 650649-3530, clinicaltrialregistries@coherus.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	27 August 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 May 2016
Global end of trial reached?	Yes
Global end of trial date	13 March 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to compare the efficacy (measured by the Psoriasis Area and Severity Index [PASI]) and safety of CHS-1420 and Humira at 12 weeks in subjects with moderate to severe chronic psoriasis .

Protection of trial subjects:

The study was conducted in accordance with the International Conference on Harmonisation, Good Clinical Practice, the Declaration of Helsinki, and with all applicable laws and regulations of the sites and countries where the study was conducted.
The rationale of the study, procedural details, and investigational goals were explained to each subject, along with potential risks and benefits. Each subject was assured of his/her right to withdraw from the study at any time for any reason. Prior to the initiation of any study procedures, each subject signed and dated an approved ICF. The original was kept on file by the Investigator with the subject's records, and a copy was given to each subject.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 August 2015
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	Poland: 125
Country: Number of subjects enrolled	Slovakia: 5
Country: Number of subjects enrolled	Croatia: 5
Country: Number of subjects enrolled	Bulgaria: 4
Country: Number of subjects enrolled	Estonia: 10
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Latvia: 21
Country: Number of subjects enrolled	Georgia: 18
Country: Number of subjects enrolled	Israel: 8
Country: Number of subjects enrolled	Moldova, Republic of: 9
Country: Number of subjects enrolled	Canada: 30
Country: Number of subjects enrolled	Chile: 9
Country: Number of subjects enrolled	Russian Federation: 13
Country: Number of subjects enrolled	South Africa: 41
Country: Number of subjects enrolled	Ukraine: 122
Country: Number of subjects enrolled	United States: 120

Worldwide total number of subjects	545
EEA total number of subjects	175

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)	507
From 65 to 84 years	38
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects with a diagnosis of chronic PsO for at least 6 months prior to Screening and must have moderate to severe chronic PsO as defined at Screening by PASI score of ≥12; Physician's Static Global Assessment (PSGA) score ≥3 (based on a scale of 0 to 5); and body surface area affected by chronic PsO of ≥10%.

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

Blinding implementation details:

Subjects, Investigators, sites staff and all personnel involved in the conduct of the study remained blinded to the subjects' treatment assignment until all subjects completed the blinded portion of the study and the database was locked. Individual subject treatment assignment could be unblinded in the case of an unexpected SAE that required knowledge of the study drug received by the subject in order to provide appropriate treatment or management of the adverse event.

Arms

Are arms mutually exclusive?	Yes
Arm title	CHS-1420

Arm description:

Subjects randomized to receive CHS-1420 in Treatment Period 1 after meeting the inclusion/exclusion criteria.

Arm type	Experimental
Investigational medicinal product name	CHS-1420
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received 2 subcutaneous (SC) injections (2 prefilled syringes [80 mg]) of CHS-1420 on Week 0/Day 0 followed by a single SC injection (1 prefilled syringe [40 mg]) of CHS-1420 every other week from Week 1/Day 7 through Week 15/Day 105.

Arm title	Humira

Arm description:

Subjects randomized to receive Humira in Treatment Period 1 after meeting the inclusion/exclusion criteria..

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

Dosage and administration details:

Two SC injections (2 prefilled syringes [80 mg]) of Humira were administered on Week 0/Day 0. From Week 1/Day 7 through up to Week 47/Day 329, 1 SC injection (1 prefilled syringe [40 mg]) of Humira was administered QOW.

Number of subjects in period 1	CHS-1420	Humira
Started	274	271
Completed	259	257
Not completed	15	14
Sponsor's decision	2	-
Investigator's decision	1	-
Consent withdrawn by subject	8	9
Adverse event, non-fatal	1	-
Other	1	1
Disease progression requiring additional therapy	1	1
Lost to follow-up	1	3

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

Blinding implementation details:

Subjects, Investigators, sites staff and all personnel involved in the conduct of the study remained blinded to the subjects' treatment assignment until all subjects completed the blinded portion of the study and the database was locked. Individual subject treatment assignment could be unblinded in the case of an unexpected SAE that required knowledge of the study drug received by the subject in order to provide appropriate treatment or management of the adverse event.

Arms

Are arms mutually exclusive?	Yes
Arm title	CHS-1420

Arm description:

In Treatment Period 2, half of the subjects assigned to Humira in Treatment Period 1 were assigned to receive CHS-1420, subjects assigned to CHS-1420 in Treatment Period 1 will continue to receive CHS-1420 and the reminder of the subjects continued on Humira.

Arm type	Experimental
Investigational medicinal product name	CHS-1420
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

1 SC injection (1 prefilled syringe [40 mg]) of CHS-1420 was administered QOW.

Arm title	Humira/CHS-1420/CHS-1420

Arm description:

Half of the subjects assigned to Humira in Treatment Period 1 continued on Humira in Period 2, or were switched from Humira to CHS-1420 and continued to receive single SC injections of study drug QOW from Week 17/Day 119 through Week 23/Day 161.

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

Dosage and administration details:

1 SC injection (1 prefilled syringe [40 mg]) of Adalimumab was administered QOW from Week 17/Day 119 through Week 23/Day 161.

Investigational medicinal product name	CHS-1420
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

1 SC injection (1 prefilled syringe [40 mg]) of CHS-1420 was administered QOW from Week 17/Day 119 through Week 23/Day 161.

Arm title	Humira/Humira/CHS-1420

Arm description:

Half of the subjects assigned to Humira in Treatment Period 1 continued on Humira in Period 2, or were switched from Humira to CHS-1420 and continued to receive single SC injections of study drug QOW from Week 17/Day 119 through Week 23/Day 161.

Arm type	Active comparator/Active comparator/Exprimental
Investigational medicinal product name	Adalimumab
Investigational medicinal product code	
Other name	Humira
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

1 SC injection (1 prefilled syringe [40 mg]) of Adalimumab was administered QOW from Week 17/Day 119 through Week 23/Day 161.

Investigational medicinal product name	CHS-1420
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

1 SC injection (1 prefilled syringe [40 mg]) of CHS-1420 was administered QOW.

Number of subjects in period 2	CHS-1420	Humira/CHS-1420/CHS-1420	Humira/Humira/CHS-1420
Started	259	128	129
Completed	235	115	125
Not completed	24	13	4
Sponsor's decision	2	1	-
Consent withdrawn by subject	7	3	1

Active TB or a positive QuantiFERON-TB Gold	1	-	-
Disease progression	1	-	-
Failure to complete visits or follow-up visits	-	1	-
Adverse event, non-fatal	1	-	-
Medical treatment excluded by protocol	1	-	-
Other	9	8	3
Lost to follow-up	2	-	-

Period 3

Period 3 title	Treatment Period 3
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	CHS-1420

Arm description:

All subjects who completed Treatment Periods 1+2 and achieved at least a 50% improvement in PASI (PASI-50) score at Week 24.

Arm type	Experimental
Investigational medicinal product name	CHS-1420
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

All subjects received 23 weeks of open-label CHS-1420 administered QOW from Week 25/Day 185 through Week 47/Day 329.

Number of subjects in period 3	CHS-1420
Started	475
Completed	438
Not completed	37
Consent withdrawn by subject	17
Active TB or a positive QuantiFERON-TB Gold	6
Failure to complete visits or follow-up visits	2
Adverse event, non-fatal	3
Other	1

Disease progression requiring additional therapy	2
Required medical treatment excluded by protocol	1
Lost to follow-up	5

Baseline characteristics

Reporting groups	
Reporting group title	CHS-1420
Reporting group description:	
Subjects randomized to receive CHS-1420 in Treatment Period 1 after meeting the inclusion/exclusion criteria.	
Reporting group title	Humira
Reporting group description:	
Subjects randomized to receive Humira in Treatment Period 1 after meeting the inclusion/exclusion criteria..	

Reporting group values	CHS-1420	Humira	Total
Number of subjects	274	271	545
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)	256	251	507
From 65-84 years	18	20	38
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	82	69	151
Male	192	202	394

End points

End points reporting groups

Reporting group title	CHS-1420
Reporting group description:	
Subjects randomized to receive CHS-1420 in Treatment Period 1 after meeting the inclusion/exclusion criteria.	
Reporting group title	Humira
Reporting group description:	
Subjects randomized to receive Humira in Treatment Period 1 after meeting the inclusion/exclusion criteria..	
Reporting group title	CHS-1420
Reporting group description:	
In Treatment Period 2, half of the subjects assigned to Humira in Treatment Period 1 were assigned to receive CHS-1420, subjects assigned to CHS-1420 in Treatment Period 1 will continue to receive CHS-1420 and the reminder of the subjects continued on Humira.	
Reporting group title	Humira/CHS-1420/CHS-1420
Reporting group description:	
Half of the subjects assigned to Humira in Treatment Period 1 continued on Humira in Period 2, or were switched from Humira to CHS-1420 and continued to receive single SC injections of study drug QOW from Week 17/Day 119 through Week 23/Day 161.	
Reporting group title	Humira/Humira/CHS-1420
Reporting group description:	
Half of the subjects assigned to Humira in Treatment Period 1 continued on Humira in Period 2, or were switched from Humira to CHS-1420 and continued to receive single SC injections of study drug QOW from Week 17/Day 119 through Week 23/Day 161.	
Reporting group title	CHS-1420
Reporting group description:	
All subjects who completed Treatment Periods 1+2 and achieved at least a 50% improvement in PASI (PASI-50) score at Week 24.	

Primary: Improvement of 75% in PASI (PASI-75) at Week 12 relative to baseline.

End point title	Improvement of 75% in PASI (PASI-75) at Week 12 relative to baseline.
End point description:	
The primary efficacy endpoint was PASI-75 at Week 12 relative to baseline, where baseline was the last assessment prior to beginning study drug. The efficacy success criterion was the equivalence between CHS-1420 and Humira at Week 12. Equivalence was based upon 2-sided 95% confidence interval (CI) for the difference between the proportions of subjects in the CHS-1420 and Humira groups achieving PASI-75 at Week 12. If the 95% CI lay entirely within the interval (-15%, 15%), equivalence was established.	
End point type	Primary
End point timeframe:	
12 weeks	

End point values	CHS-1420	Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	271		
Units: Patients	259	257		

Statistical analyses

Statistical analysis title	Equivalence between CHS-1420 and Humira at Week 12
Comparison groups	CHS-1420 v Humira
Number of subjects included in analysis	545
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Mean difference (net)
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.75
upper limit	9.21

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from Period 1 Week 0 Day 0 through the study until the end of Period 3 Week 47 Day 329.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	CHS-1420/CHS-1420/CHS-1420
Reporting group description:	
Treatment Periods 1+2+3 combined.	
Reporting group title	Humira/CHS-1420/ CHS-1420
Reporting group description:	
Treatment Periods 1+2+3 combined.	
Reporting group title	Humira/Humira/ CHS-1420
Reporting group description:	
Treatment Periods 1+2+3 combined.	

Serious adverse events	CHS-1420/CHS-1420/CHS-1420	Humira/CHS-1420/ CHS-1420	Humira/Humira/ CHS-1420
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 274 (3.28%)	9 / 134 (6.72%)	2 / 137 (1.46%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Glioblastoma multiforme			
subjects affected / exposed	0 / 274 (0.00%)	1 / 134 (0.75%)	0 / 137 (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
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	1 / 274 (0.36%)	0 / 134 (0.00%)	0 / 137 (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
Foot fracture			

subjects affected / exposed	0 / 274 (0.00%)	1 / 134 (0.75%)	0 / 137 (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
Vascular disorders			
Shock			
subjects affected / exposed	1 / 274 (0.36%)	0 / 134 (0.00%)	0 / 137 (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
Congenital, familial and genetic disorders			
Congenital cystic kidney disease			
subjects affected / exposed	0 / 274 (0.00%)	1 / 134 (0.75%)	0 / 137 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 274 (0.36%)	0 / 134 (0.00%)	0 / 137 (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
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	1 / 274 (0.36%)	0 / 134 (0.00%)	0 / 137 (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
Inguinal hernia			
subjects affected / exposed	1 / 274 (0.36%)	0 / 134 (0.00%)	0 / 137 (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
Anal fistula			
subjects affected / exposed	0 / 274 (0.00%)	1 / 134 (0.75%)	0 / 137 (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
Diarrhoea			

subjects affected / exposed	0 / 274 (0.00%)	0 / 134 (0.00%)	1 / 137 (0.73%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 274 (0.00%)	1 / 134 (0.75%)	0 / 137 (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
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	1 / 274 (0.36%)	0 / 134 (0.00%)	0 / 137 (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
Renal and urinary disorders			
Calculus urethral			
subjects affected / exposed	0 / 274 (0.00%)	1 / 134 (0.75%)	0 / 137 (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
Renal failure chronic			
subjects affected / exposed	0 / 274 (0.00%)	1 / 134 (0.75%)	0 / 137 (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
Musculoskeletal and connective tissue disorders			
Psoriatic arthropathy			
subjects affected / exposed	1 / 274 (0.36%)	0 / 134 (0.00%)	0 / 137 (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
Rotator cuff syndrome			
subjects affected / exposed	1 / 274 (0.36%)	0 / 134 (0.00%)	0 / 137 (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
Infections and infestations			
Bronchitis			

subjects affected / exposed	0 / 274 (0.00%)	1 / 134 (0.75%)	0 / 137 (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
Pneumonia			
subjects affected / exposed	0 / 274 (0.00%)	1 / 134 (0.75%)	1 / 137 (0.73%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 274 (0.00%)	1 / 134 (0.75%)	0 / 137 (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
Tuberculosis			
subjects affected / exposed	0 / 274 (0.00%)	0 / 134 (0.00%)	1 / 137 (0.73%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 274 (0.00%)	1 / 134 (0.75%)	0 / 137 (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
Lobar pneumonia			
subjects affected / exposed	0 / 274 (0.00%)	1 / 134 (0.75%)	1 / 137 (0.73%)
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			
Obesity			
subjects affected / exposed	1 / 274 (0.36%)	0 / 134 (0.00%)	0 / 137 (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
Dehydration			
subjects affected / exposed	0 / 274 (0.00%)	1 / 134 (0.75%)	0 / 137 (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
Diabetic ketoacidosis			

subjects affected / exposed	0 / 274 (0.00%)	1 / 134 (0.75%)	0 / 137 (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

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

Non-serious adverse events	CHS-1420/CHS-1420/CHS-1420	Humira/CHS-1420/CHS-1420	Humira/Humira/CHS-1420
Total subjects affected by non-serious adverse events			
subjects affected / exposed	139 / 274 (50.73%)	67 / 134 (50.00%)	76 / 137 (55.47%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	10 / 274 (3.65%)	5 / 134 (3.73%)	6 / 137 (4.38%)
occurrences (all)	10	6	6
Aspartate aminotransferase increased			
subjects affected / exposed	8 / 274 (2.92%)	3 / 134 (2.24%)	7 / 137 (5.11%)
occurrences (all)	8	3	8
Blood creatine phosphokinase increased			
subjects affected / exposed	12 / 274 (4.38%)	5 / 134 (3.73%)	8 / 137 (5.84%)
occurrences (all)	12	6	9
Hepatic enzyme increased			
subjects affected / exposed	4 / 274 (1.46%)	0 / 134 (0.00%)	4 / 137 (2.92%)
occurrences (all)	4	0	4
Interferon gamma release assay positive			
subjects affected / exposed	8 / 274 (2.92%)	4 / 134 (2.99%)	0 / 137 (0.00%)
occurrences (all)	8	4	0
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 274 (2.19%)	0 / 134 (0.00%)	3 / 137 (2.19%)
occurrences (all)	6	0	3
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 274 (5.11%)	7 / 134 (5.22%)	8 / 137 (5.84%)
occurrences (all)	22	7	10
General disorders and administration site conditions			

Injection site reaction			
subjects affected / exposed	12 / 274 (4.38%)	5 / 134 (3.73%)	6 / 137 (4.38%)
occurrences (all)	15	5	18
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 274 (1.09%)	3 / 134 (2.24%)	2 / 137 (1.46%)
occurrences (all)	3	3	2
Diarrhoea			
subjects affected / exposed	4 / 274 (1.46%)	3 / 134 (2.24%)	2 / 137 (1.46%)
occurrences (all)	5	3	2
Nausea			
subjects affected / exposed	1 / 274 (0.36%)	4 / 134 (2.99%)	0 / 137 (0.00%)
occurrences (all)	1	4	0
Vomiting			
subjects affected / exposed	1 / 274 (0.36%)	2 / 134 (1.49%)	3 / 137 (2.19%)
occurrences (all)	1	2	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 274 (2.92%)	1 / 134 (0.75%)	0 / 137 (0.00%)
occurrences (all)	9	1	0
Oropharyngeal pain			
subjects affected / exposed	7 / 274 (2.55%)	3 / 134 (2.24%)	4 / 137 (2.92%)
occurrences (all)	8	3	5
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	7 / 274 (2.55%)	2 / 134 (1.49%)	3 / 137 (2.19%)
occurrences (all)	8	2	3
Psoriasis			
subjects affected / exposed	9 / 274 (3.28%)	8 / 134 (5.97%)	10 / 137 (7.30%)
occurrences (all)	13	11	11
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	10 / 274 (3.65%)	2 / 134 (1.49%)	2 / 137 (1.46%)
occurrences (all)	13	2	2
Back pain			

subjects affected / exposed	4 / 274 (1.46%)	5 / 134 (3.73%)	5 / 137 (3.65%)
occurrences (all)	6	5	6
Pain in extremity			
subjects affected / exposed	0 / 274 (0.00%)	2 / 134 (1.49%)	4 / 137 (2.92%)
occurrences (all)	0	2	4
Infections and infestations			
Bronchitis			
subjects affected / exposed	7 / 274 (2.55%)	2 / 134 (1.49%)	3 / 137 (2.19%)
occurrences (all)	7	3	3
Gastroenteritis			
subjects affected / exposed	2 / 274 (0.73%)	3 / 134 (2.24%)	1 / 137 (0.73%)
occurrences (all)	2	3	1
Influenza			
subjects affected / exposed	9 / 274 (3.28%)	5 / 134 (3.73%)	7 / 137 (5.11%)
occurrences (all)	9	5	8
Nasopharyngitis			
subjects affected / exposed	35 / 274 (12.77%)	17 / 134 (12.69%)	17 / 137 (12.41%)
occurrences (all)	46	21	20
Pharyngitis			
subjects affected / exposed	6 / 274 (2.19%)	4 / 134 (2.99%)	1 / 137 (0.73%)
occurrences (all)	6	4	1
Respiratory tract infection viral			
subjects affected / exposed	5 / 274 (1.82%)	5 / 134 (3.73%)	4 / 137 (2.92%)
occurrences (all)	9	5	4
Rhinitis			
subjects affected / exposed	6 / 274 (2.19%)	2 / 134 (1.49%)	4 / 137 (2.92%)
occurrences (all)	6	2	7
Sinusitis			
subjects affected / exposed	5 / 274 (1.82%)	4 / 134 (2.99%)	1 / 137 (0.73%)
occurrences (all)	5	4	1
Upper respiratory tract infection			
subjects affected / exposed	23 / 274 (8.39%)	6 / 134 (4.48%)	13 / 137 (9.49%)
occurrences (all)	36	6	14
Urinary tract infection			
subjects affected / exposed	11 / 274 (4.01%)	3 / 134 (2.24%)	5 / 137 (3.65%)
occurrences (all)	13	7	7

Metabolism and nutrition disorders Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 274 (0.00%) 0	1 / 134 (0.75%) 1	3 / 137 (2.19%) 3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 July 2015	Amendment - 1 -The primary reason for the protocol amendment was to add a 24-week Open-Label Extension Study (Treatment Period 3) after a subject successfully completed the original double-blind 24-week study (Treatment Periods 1+2). Text related to Treatment Period 3 was added in several places in the amended protocol, including objectives, description of the treatment period, criteria to enter, time points, procedures, and safety analysis. The study design figure was also modified to include Treatment Period 3. - Added restriction to biologics and added laser treatment in inclusion criteria. - Changed abstinence from heterosexual intercourse from 8 weeks to 5 months after taking last dose of study drug, to match EU recommendations in inclusion criteria. - Removed branded or marketed names from excluded medication names to avoid confusion between regions. - Added exclusion criteria about live vaccines to ensure that prohibited medications were in agreement with guidelines for administration of Humira. - Added percentages to clarify compliance. - Added clarification to ensure that a CXR was obtained if results were not available. - Modified adverse event outcomes to match database design. - Added text to clarify that the Sponsor would remain blinded to treatment assignments and would be informed of top line results. Apart from these, various edits were made to address administrative errors, typos, and omissions, and to improve clarity, internal document consistency, etc.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported