Clinical trial results:
Multicenter, Double-Blind, Randomized, 2-Arm, Parallel-Group, Equivalence Study Evaluating Efficacy and Safety Similarity of Mylan Adalimumab (MYL-1401A) Compared With Humira® in Subjects With Moderate-to-Severe Chronic Plaque Psoriasis

Summary

EudraCT number	2014-003420-46
Trial protocol	HU DE EE BG
Global end of trial date	06 March 2017

Results information

Result version number	v1 (current)
This version publication date	08 March 2018
First version publication date	08 March 2018

Trial information

Trial identification

Sponsor protocol code	MYL-1401A-3001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02714322
WHO universal trial number (UTN)	U1111-1164-6368

Notes:

Sponsors

Sponsor organisation name	Mylan GmbH
Sponsor organisation address	Thurgauerstrasse 40 , Zürich , Switzerland, 8050
Public contact	Clinical Development Lead, Mylan GmbH , +91 80 66728952 , PrasannaC.Ganapathi@mylan.in
Scientific contact	Clinical Development Lead, Mylan GmbH , +91 80 66728952 , PrasannaC.Ganapathi@mylan.in

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	05 April 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 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 assess the equivalence of MYL-1401A to Humira® with regards to efficacy at Week 12 in subjects with moderate-to-severe chronic plaque psoriasis.

Protection of trial subjects:

The study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki, ICH E6(R1) guidelines and all applicable regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 May 2015
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: 143
Country: Number of subjects enrolled	Bulgaria: 16
Country: Number of subjects enrolled	Estonia: 88
Country: Number of subjects enrolled	Hungary: 20
Country: Number of subjects enrolled	Russian Federation: 10
Country: Number of subjects enrolled	Ukraine: 17
Worldwide total number of subjects	294
EEA total number of subjects	267

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)	278

From 65 to 84 years	16
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

- Age: 18 to 75 years, inclusive
- Gender: male or female
- Body surface area (BSA) ≥10%, PASI ≥12, and sPGA ≥3 (moderate)

Pre-assignment

Screening details:

Three hundred sixty-three (363) patients were screened for the study, and 294 patients were randomized to study treatment.

Period 1

Period 1 title	Active Treatment Phase (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Humira®

Arm description:

Humira®

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

Dosage and administration details:

Initial dose of 80 mg, followed by 40 mg given every other week starting 1 week after initial dose

Arm title	MYL-1401A

Arm description:

Mylan's Adalimumab

Arm type	Experimental
Investigational medicinal product name	Adalimumab
Investigational medicinal product code	MYL-1401A
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Initial dose of 80 mg, followed by 40 mg given every other week starting 1 week after initial dose

Number of subjects in period 1	Humira®	MYL-1401A
Started	98	196
Week 12	96	194
Completed	86	172
Not completed	12	24
Consent withdrawn by subject	4	10
Physician decision	-	3
Adverse event, non-fatal	1	3
Other	1	2
Lost to follow-up	-	2
Missing	1	-
Lack of efficacy	5	4

Baseline characteristics

Reporting groups	
Reporting group title	Humira®
Reporting group description: Humira®	
Reporting group title	MYL-1401A
Reporting group description: Mylan's Adalimumab	

Reporting group values	Humira®	MYL-1401A	Total
Number of subjects	98	196	294
Age categorical Units: Subjects			
< 45 years	62	98	160
>= 45 years	36	98	134
Age continuous Units: years			
arithmetic mean	41.2	44.7	
standard deviation	± 12.53	± 12.52	-
Gender categorical Units: Subjects			
Female	24	65	89
Male	74	131	205
Race Units: Subjects			
White	98	196	294
Presence of Psoriatic Arthritis Units: Subjects			
Yes	35	73	108
No	63	123	186
Baseline PASI Score Units: Subjects			
12 to 20	28	67	95
> 20	70	129	199
Baseline SPGA Score Units: Subjects			
3 (moderate)	60	122	182
4 or 5 (severe to very severe)	38	74	112
Baseline BSA Involvement Units: Subjects			
10% to 30%	43	85	128
> 30%	52	106	158
Missing	3	5	8

End points

End points reporting groups

Reporting group title	Humira®
Reporting group description:	
Humira®	
Reporting group title	MYL-1401A
Reporting group description:	
Mylan's Adalimumab	
Subject analysis set title	ITT Population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients who were randomly assigned to study treatment. Patients in the ITT set were categorized to the treatment randomly assigned.	

Primary: Psoriasis Area and Severity Index Percent Improvement From Baseline to Week 12

End point title	Psoriasis Area and Severity Index Percent Improvement From Baseline to Week 12
End point description:	
End point type	Primary
End point timeframe:	
12 weeks	

End point values	Humira®	MYL-1401A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	196		
Units: percent				
arithmetic mean (standard deviation)	86.563 (± 13.8650)	85.498 (± 16.1182)		

Statistical analyses

Statistical analysis title	Analysis of covariance
Comparison groups	Humira® v MYL-1401A
Number of subjects included in analysis	293
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	LS mean difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	2.9

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 60 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	Humira
Reporting group description: Humira	
Reporting group title	MYL-1401A
Reporting group description: Mylan's Adalimumab	

Serious adverse events	Humira	MYL-1401A	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 97 (5.15%)	4 / 196 (2.04%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Postoperative respiratory failure			
subjects affected / exposed	0 / 97 (0.00%)	1 / 196 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	1 / 97 (1.03%)	0 / 196 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 97 (1.03%)	0 / 196 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Sarcoidosis			

subjects affected / exposed	0 / 97 (0.00%)	1 / 196 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastric ulcer perforation			
subjects affected / exposed	0 / 97 (0.00%)	1 / 196 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal polyp			
subjects affected / exposed	0 / 97 (0.00%)	1 / 196 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 97 (0.00%)	1 / 196 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	1 / 97 (1.03%)	0 / 196 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriasis			
subjects affected / exposed	1 / 97 (1.03%)	0 / 196 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Psoriatic arthropathy			
subjects affected / exposed	1 / 97 (1.03%)	0 / 196 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Chronic tonsillitis			

subjects affected / exposed	1 / 97 (1.03%)	0 / 196 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 97 (0.00%)	1 / 196 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Humira	MYL-1401A	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 97 (19.59%)	33 / 196 (16.84%)	
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	7 / 97 (7.22%)	8 / 196 (4.08%)	
occurrences (all)	7	9	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 97 (3.09%)	15 / 196 (7.65%)	
occurrences (all)	3	20	
Pharyngitis			
subjects affected / exposed	6 / 97 (6.19%)	9 / 196 (4.59%)	
occurrences (all)	6	9	
Tonsillitis			
subjects affected / exposed	5 / 97 (5.15%)	2 / 196 (1.02%)	
occurrences (all)	5	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 March 2016	Amendment was based on regulatory interactions and scientific advice from the European Medicines Agency and resulted in changes to the primary objective.
06 May 2016	Amendment was based on scientific advice from the United States Food and Drug Administration received on March 8, 2016. An assessment of safety and immunogenicity following a single transition from the reference product to the proposed biosimilar product was requested in the planned 351(k) Biologics License Application submission to support the safe use of MYL-140A in nontreatment naïve patients.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported