Clinical trial results:
An Open-label Extension Study to Compare the Long-term Efficacy, Safety, Immunogenicity and Pharmacokinetics of FKB327 and Humira® in Patients with Rheumatoid Arthritis on Concomitant Methotrexate

Summary

EudraCT number	2014-000110-61
Trial protocol	DE CZ ES
Global end of trial date	28 January 2018

Results information

Result version number	v1 (current)
This version publication date	03 January 2019
First version publication date	03 January 2019

Trial information

Trial identification

Sponsor protocol code	FKB327-003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02405780
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	FUJIFILM KYOWA KIRIN BIOLOGICS Co., Ltd.
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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	28 January 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 January 2018
Global end of trial reached?	Yes
Global end of trial date	28 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary:
- To compare the safety of long-term treatment with FKB327 and Humira in patients with rheumatoid arthritis (RA).

Secondary:
- To compare the efficacy of long term treatment with FKB327 and Humira.
- To compare the proportions of RA patients developing anti-drug antibodies (ADAs) on long term treatment with FKB327 and Humira.
- To compare the pharmacokinetics (PK) of long term treatment with FKB327 and Humira.
- To evaluate safety, changes in efficacy, changes in PK and immunogenicity in patients switching from Humira in the preceding FKB327-002 double-blind study to FKB327 in the open label extension (OLE) study, and of patients who were switched from FKB327 to Humira, respectively.
- To evaluate safety, changes in efficacy, changes in PK and immunogenicity in patients switching from FKB327 in the preceding FKB327-002 double-blind study to Humira in the OLE study, and then switched back to FKB327 in the second part of the OLE study (from Week 30; double switch).

Protection of trial subjects:

The study was performed in compliance with the European Union (EU) Directives 2001/20/EC and 2015/28/EC and the Declaration of Helsinki (South Africa Revision 1996) Good Manufacturing Practice (GMP) and Good Clinical Practice.

The study protocol, informed consent form, and amendments were reviewed and approved by each Independent Ethics Committee (IEC)/Institutional Review Board (IRB). The study did not start at a given investigational site before the IEC/IRB had given written approval or a favourable opinion.

All subjects provided written informed consent before any study-specific procedures or assessments were performed. Subjects were free to refuse entry into the study and were free to withdraw from the study at any time without prejudice to future treatment.

Background therapy:

FKB327 or Humira 40 mg every other week, as subjects were only eligible for entry to the study if they were currently participating in the double blind study FKB327-002.
Methotrexate (MTX) represents the conventional disease modifying anti-rheumatic drug (DMARD) of choice for Rheumatoid Arthritis (RA) treatment and is thought to act by decreasing the activity of the immune system. MTX was administered with folate therapy to counter down the know adverse effects of MTX treatment.
In line with clinical practice, stable background doses of oral steroids and non-steroidal anti-inflammatory drugs (NSAIDs) were permitted during the study although they were not compulsory.

Evidence for comparator:

Adalimumab is a recombinant human monoclonal antibody against Tumor Necrosing Factor (TNF) α. It neutralises the biological activity of TNF- α by blocking its interaction with TNF- α cell surface receptors. TNF- α is a naturally occurring cytokine produced by many different cell types, including macrophages, mast cells and T-cells. High concentrations of TNF- α lead to inflammation and injury, and TNF- α has been implicated as an important pro-inflammatory cytokine involved in the parthenogenesis of numerous autoimmune diseases, such as RA, psoriasis (Ps), Crohn’s disease (CD) and ulcerative colitis (UC).
Adalimumab was first approved for treatment of RA in September 2003 in the European Union (EU), and was subsequently launched globally under the brand name Humira. Humira is currently indicated in the EU in the adult population for RA, Ps, Psoriatic Arthritis (PsA), Ankylosing Spondylitis (AS) axial

spondyloarthritis (without radiographic evidence of AS), CD, UC, hidradentis suppurativa (HS) and non-infectious uveitis. Approved indication in the paediatric population are polyarticular juvenile idiopathic arthritis in children from 2 years of age, active enthesitis-related arthritis from 6 years of age, severe chronic plaque psoriasis from 4 years of age, moderately to severe CD from 6 years of age and moderate to severe HS in adolescents from 12 years of age.

Actual start date of recruitment	01 June 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: 124
Country: Number of subjects enrolled	Romania: 23
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Czech Republic: 64
Country: Number of subjects enrolled	Germany: 22
Country: Number of subjects enrolled	Chile: 40
Country: Number of subjects enrolled	Peru: 84
Country: Number of subjects enrolled	Russian Federation: 96
Country: Number of subjects enrolled	United States: 71
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Ukraine: 107
Worldwide total number of subjects	645
EEA total number of subjects	242

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)	540
From 65 to 84 years	103
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 92 sites, with 11 countries in Europe, North America, and Rest of World recruiting patients into the study. In total, 645 patients with RA who completed study FKB327-002 and, in the Investigator's opinion, showed a clinical response to treatment during FKB327-002 were screened and entered the FKB327-003 study.

Pre-assignment

Screening details:

Patients who received FKB327 in Study FKB327-002 were re-randomised to FKB327 or Humira in a 2:1 ratio and patients who received Humira in Study FKB327-002 were re-randomised to Humira or FKB327 in a 2:1 ratio.

Period 1

Period 1 title	Period I
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

This was an open-label study throughout.

Arms

Are arms mutually exclusive?	Yes
Arm title	FKB327-FKB327

Arm description:

This arm included patients who were treated with FKB327 in the preceding Study FKB327-002 and were randomised to continue on FKB327 treatment during Period I in Study FKB327-003.

Arm type	Experimental
Investigational medicinal product name	adalimumab (FKB327)
Investigational medicinal product code	FKB327
Other name	Hulio
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

The dose administered was one (1) subcutaneous injection of 40 mg/0.8 mL every other week.

Arm title	Humira-FKB327

Arm description:

This arm included patients who were treated with the reference product Humira in the preceding Study FKB327-002 and were randomised to FKB327 treatment during Period I in Study FKB327-003.

Arm type	Experimental
Investigational medicinal product name	adalimumab (FKB327)
Investigational medicinal product code	FKB327
Other name	Hulio
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

The dose administered was one (1) subcutaneous injection of 40 mg/0.8 mL every other week.

Arm title	FKB327-Humira

Arm description:

This arm included patients who were treated with FKB327 in the preceding Study FKB327-002 and were randomised to the reference product Humira during Period I in Study FKB327-003.

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

Dosage and administration details:

The dose administered was one (1) subcutaneous injection of 40 mg/ 0.8 mL every other week.

Arm title	Humira-Humira

Arm description:

This arm included patients who were treated with the reference product Humira in the preceding Study FKB327-002 and were randomised to continue on Humira during Period I in Study FKB327-003.

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

Dosage and administration details:

The dose administered was one (1) subcutaneous injection of 40 mg/0.8 mL every other week.

Number of subjects in period 1	FKB327-FKB327	Humira-FKB327	FKB327-Humira
Started	216	108	108
Completed	189	93	100
Not completed	27	15	8
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	9	3	1
Screening failure	1	1	-
Adverse event, non-fatal	8	2	-
Medical reason	1	-	1
Protocol deviation	8	8	6

Number of subjects in period 1	Humira-Humira
Started	213
Completed	190
Not completed	23
Adverse event, serious fatal	1
Consent withdrawn by subject	4
Screening failure	-
Adverse event, non-fatal	6
Medical reason	1
Protocol deviation	11

Period 2

Period 2 title	Period II
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	FKB327-FKB327-FKB327

Arm description:

This treatment arm included patients that had been treated with FKB327 in the preceding study FKB327-002 and were continued on FKB327 in Period I of Study FKB327-003. At week 30, patients were transferred to continue on treatment with FKB327 (F-F-F) in Period II of Study FKB327-003.

Arm type	Experimental
Investigational medicinal product name	adalimumab (FKB327)
Investigational medicinal product code	FKB327
Other name	Hulio
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

The dose administered was one (1) subcutaneous injection of 40 mg/0.8 mL every other week using an auto-injector (pre-filled pen) or pre-filled syringe.

Arm title	Humira-FKB327-FKB327

Arm description:

This treatment arm included patients that had been treated with the reference product in the preceding study FKB327-002 and were treated with FKB327 in Period I of Study FKB327-003.
At week 30, patients were transferred to treatment with FKB327 (H-F-F) in Period II of Study FKB327-003.

Arm type	Experimental
Investigational medicinal product name	adalimumab (FKB327)
Investigational medicinal product code	FKB327
Other name	Hulio
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

The dose administered was one (1) subcutaneous injection of 40 mg/0.8 mL every other week using an auto-injector (pre-filled pen) or pre-filled syringe.

Arm title	FKB327-Humira-FKB327

Arm description:

This treatment arm included patients that had been treated with FKB327 in the preceding study FKB327-002 and were treated with the reference product, Humira, in Period I of Study FKB327-003.
At week 30, patients were transferred to treatment with FKB327 (F-H-F) in Period II of Study FKB327-003.

Arm type	Experimental
Investigational medicinal product name	adalimumab (FKB327)
Investigational medicinal product code	FKB327
Other name	Hulio
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

The dose administered was one (1) subcutaneous injection of 40 mg/0.8 mL every other week using an auto-injector (pre-filled pen) or pre-filled syringe.

Arm title	Humira-Humira-FKB327

Arm description:

This treatment arm included patients that had been treated with the reference product Humira in the preceding study FKB327-002 and werecontinued on Humira in Period I of Study FKB327-003.
At week 30, patients were transferred to treatment with FKB327 (H-H-F) in Period II of Study FKB327-003.

Arm type	Experimental
Investigational medicinal product name	adalimumab (FKB327)
Investigational medicinal product code	FKB327
Other name	Hulio
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

The dose administered was one (1) subcutaneous injection of 40 mg/0.8 mL every other week using an auto-injector (pre-filled pen) or pre-filled syringe.

Number of subjects in period 2	FKB327-FKB327-FKB327	Humira-FKB327-FKB327	FKB327-Humira-FKB327
Started	189	93	100
Completed	174	81	88
Not completed	15	12	12
Adverse event, serious fatal	-	2	-
Consent withdrawn by subject	7	-	4
Adverse event, non-fatal	3	2	5
non-compliance with protocol	5	-	-
non-compliance with study procedures	-	7	2
Medical reason	-	-	1
Pregnancy	-	1	-

Number of subjects in period 2	Humira-Humira-FKB327
Started	190
Completed	172
Not completed	18
Adverse event, serious fatal	1
Consent withdrawn by subject	3
Adverse event, non-fatal	10
non-compliance with protocol	-
non-compliance with study procedures	4
Medical reason	-

Pregnancy	-

Baseline characteristics

Reporting groups	
Reporting group title	FKB327-FKB327
Reporting group description:	
This arm included patients who were treated with FKB327 in the preceding Study FKB327-002 and were randomised to continue on FKB327 treatment during Period I in Study FKB327-003.	
Reporting group title	Humira-FKB327
Reporting group description:	
This arm included patients who were treated with the reference product Humira in the preceding Study FKB327-002 and were randomised to FKB327 treatment during Period I in Study FKB327-003.	
Reporting group title	FKB327-Humira
Reporting group description:	
This arm included patients who were treated with FKB327 in the preceding Study FKB327-002 and were randomised to the reference product Humira during Period I in Study FKB327-003.	
Reporting group title	Humira-Humira
Reporting group description:	
This arm included patients who were treated with the reference product Humira in the preceding Study FKB327-002 and were randomised to continue on Humira during Period I in Study FKB327-003.	

Reporting group values	FKB327-FKB327	Humira-FKB327	FKB327-Humira
Number of subjects	216	108	108
Age categorical Units: Subjects			
Adults (18-64 years)	183	96	92
From 65-84 years	32	12	16
85 years and over	1	0	0
Gender categorical Units: Subjects			
Female	162	83	85
Male	54	25	23
Race Units: Subjects			
American Indian or Alaska Native	1	0	0
Asian	1	1	0
Black or African American	1	2	1
White	187	90	90
Other	26	15	17

Reporting group values	Humira-Humira	Total	
Number of subjects	213	645	
Age categorical Units: Subjects			
Adults (18-64 years)	169	540	
From 65-84 years	43	103	
85 years and over	1	2	
Gender categorical Units: Subjects			
Female	171	501	
Male	42	144	

Race Units: Subjects			
American Indian or Alaska Native	1	2	
Asian	0	2	
Black or African American	2	6	
White	185	552	
Other	25	83	

Subject analysis sets

Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Analysis Set comprised all patients who gave consent for this trial and who received at least 1 dose of randomised treatment. The Safety Analysis Set was used for all safety analyses.

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

Subject analysis set description:

The Full Analysis Set (FAS) comprised all patients who received at least 1 dose of the randomised treatment and who had at least 1 evaluable efficacy measurement after their first does of randomised treatment. The FAS was used for all efficacy analysis.

Subject analysis set title	Pharmacokinetic Analysis Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The Pharmacokinetic Analysis Set (PKAS) included all patients who received at least 1 dose of the randomised treatment and had at least 1 serum adalimumab concentration result after receiving randomised treatment in the FKB327-003 study.

Reporting group values	Safety Analysis Set	Full Analysis Set	Pharmacokinetic Analysis Set
Number of subjects	645	645	630
Age categorical Units: Subjects			
Adults (18-64 years)	540	540	530
From 65-84 years	103	103	98
85 years and over	2	2	2
Gender categorical Units: Subjects			
Female	501	501	487
Male	144	144	143
Race Units: Subjects			
American Indian or Alaska Native	2	2	0
Asian	2	2	2
Black or African American	6	6	6
White	552	552	541
Other	83	83	81

End points

End points reporting groups

Reporting group title	FKB327-FKB327

Reporting group description:

This arm included patients who were treated with FKB327 in the preceding Study FKB327-002 and were randomised to continue on FKB327 treatment during Period I in Study FKB327-003.

Reporting group title	Humira-FKB327

Reporting group description:

This arm included patients who were treated with the reference product Humira in the preceding Study FKB327-002 and were randomised to FKB327 treatment during Period I in Study FKB327-003.

Reporting group title	FKB327-Humira

Reporting group description:

This arm included patients who were treated with FKB327 in the preceding Study FKB327-002 and were randomised to the reference product Humira during Period I in Study FKB327-003.

Reporting group title	Humira-Humira

Reporting group description:

This arm included patients who were treated with the reference product Humira in the preceding Study FKB327-002 and were randomised to continue on Humira during Period I in Study FKB327-003.

Reporting group title	FKB327-FKB327-FKB327

Reporting group description:

This treatment arm included patients that had been treated with FKB327 in the preceding study FKB327-002 and were continued on FKB327 in Period I of Study FKB327-003. At week 30, patients were transferred to continue on treatment with FKB327 (F-F-F) in Period II of Study FKB327-003.

Reporting group title	Humira-FKB327-FKB327

Reporting group description:

This treatment arm included patients that had been treated with the reference product in the preceding study FKB327-002 and were treated with FKB327 in Period I of Study FKB327-003.
At week 30, patients were transferred to treatment with FKB327 (H-F-F) in Period II of Study FKB327-003.

Reporting group title	FKB327-Humira-FKB327

Reporting group description:

This treatment arm included patients that had been treated with FKB327 in the preceding study FKB327-002 and were treated with the reference product, Humira, in Period I of Study FKB327-003.
At week 30, patients were transferred to treatment with FKB327 (F-H-F) in Period II of Study FKB327-003.

Reporting group title	Humira-Humira-FKB327

Reporting group description:

This treatment arm included patients that had been treated with the reference product Humira in the preceding study FKB327-002 and werecontinued on Humira in Period I of Study FKB327-003.
At week 30, patients were transferred to treatment with FKB327 (H-H-F) in Period II of Study FKB327-003.

Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Analysis Set comprised all patients who gave consent for this trial and who received at least 1 dose of randomised treatment. The Safety Analysis Set was used for all safety analyses.

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

Subject analysis set description:

The Full Analysis Set (FAS) comprised all patients who received at least 1 dose of the randomised treatment and who had at least 1 evaluable efficacy measurement after their first does of randomised treatment. The FAS was used for all efficacy analysis.

Subject analysis set title	Pharmacokinetic Analysis Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The Pharmacokinetic Analysis Set (PKAS) included all patients who received at least 1 dose of the randomised treatment and had at least 1 serum adalimumab concentration result after receiving randomised treatment in the FKB327-003 study.

Primary: Safety - Summary of Adverse Events; Period I

End point title	Safety - Summary of Adverse Events; Period I[1]

End point description:

Each patient was counted only once within each System Organ Class (SOC) and Preferred Term (PT). A patients may have had multiple events counted. Death is defined as the fatal outcome of an (S) AE. Treatment Emergent Adverse Events (TEAE) defined as AEs that started or increased in severity after the first study medication administration and counted under the treatment arm in which they started.

End point type	Primary

End point timeframe:

Period I: From Baseline visit week 0 through to week 30

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical analysis is provided for this end point. Summary statistics only are presented.

End point values	FKB327-FKB327	Humira-FKB327	FKB327-Humira	Humira-Humira
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	216	108	108	213
Units: number of patients				
number (not applicable)				
Deaths	0	1	0	1
Treatment Emergent Deaths	0	1	0	1
At least 1 TEAE	103	59	59	117
At least 1 severe TEAE	5	3	2	2
At least 1 treatment related TEAE	39	27	21	49
Premature disc. of treatment due to a TEAE	10	4	0	11
Treatment Disc. due to a TESAE	0	0	0	2
Treatment interruption due to a TEAE	19	14	9	20
Treatment interruption due to a TESAE	3	4	2	2
At least 1 TESAE	5	5	7	7
Number of TESAE	7	9	9	7
At leaset 1 SAE	5	5	7	7

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	645			
Units: number of patients				
number (not applicable)				
Deaths	2			
Treatment Emergent Deaths	2			
At least 1 TEAE	338			
At least 1 severe TEAE	12			
At least 1 treatment related TEAE	136			

Premature disc. of treatment due to a TEAE	25			
Treatment Disc. due to a TESAE	2			
Treatment interruption due to a TEAE	62			
Treatment interruption due to a TESAE	11			
At least 1 TESAE	24			
Number of TESAE	32			
At leaset 1 SAE	24			

Statistical analyses

No statistical analyses for this end point

Primary: Vital signs

End point title	Vital signs[2]

End point description:

Vital signs = blood pressure, pulse and temperature measurements forms part of the continuous safety measurements for the study primary safety endpoint.
Blood pressure and pulse rate were measured prior to dosing after the patient had rested in a supine or semi-recumbent position for at least 5 minutes.
Vital signs parameters with change from Baseline_002 were summarised by treatment sequence over the whole study period as well as by treatment for each period (Period I and Period II) for each visit.
Baseline_002 is defined as the last non-missing measurement collected prior to the first study medication administration at Week 0 from FKB327-002.

RESULTS: There were no trends in changes from Baseline/Week 0 for any of the vital signs parameters. TEAEs related to changes in vital signs parameters occurred in a small number of patients, with hypertension/increased blood pressure being the most commonly reported event.

End point type	Primary

End point timeframe:

Weeks 0, 4, 8, 12, 24 and 80/EOT (Period I and II)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical analysis is provided for this end point. Summary statistics only are presented.

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	645			
Units: various	645			

Statistical analyses

No statistical analyses for this end point

Primary: Clinical Laboratory Tests

End point title	Clinical Laboratory Tests[3]

End point description:

RESULTS: There were no clinically relevant changes from Baseline/Week 0 in mean values for any of the haematology, biochemistry or urinalysis parameters. Although there were increases and/or decreases in mean values for several of the laboratory parameters throughout the study, but no clear pattern and the changes were comparable on treatment with FKB327 and Humira.
The most commonly reported laboratory-related TEAE was anaemia, which was experienced by 5 patients receiving FKB327 and 4 patients receiving Humira during Period I and by a further 11 patients receiving FKB327 during Period II. Commonly reported TEAEs related to liver function test abnormalities were experienced by a similar incidence of patients receiving FKB327 and Humira during Period I. Neutropaenia and leukopenia were both experienced by 3 patients receiving FKB327 and 1 patient receiving Humira during Period I.

End point type	Primary

End point timeframe:

Weeks 0, 4, 8, 12, 24, 30 (Period I) and weeks 42, 54, 66, 76 and 80/EOT (Period II).

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical analysis is provided for this end point. Summary statistics only are presented.

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	645			
Units: various	645			

Statistical analyses

No statistical analyses for this end point

Secondary: ACR20; Summary of Response rate over time: Period I

End point title	ACR20; Summary of Response rate over time: Period I

End point description:

The ACR response criteria was derived and used as secondary efficacy variables. These criteria look at improvement in tender joint count (TJC), swollen joint count (SJC) (68/66-joint count) and improvement in at least 3 of the following 5 other specified ACR Core Data Set elements:
- Acute phase reactant (CRP).
- Patient global assessment of disease activity.
- Physician global assessment of disease activity.
- Patient pain scale (VAS).
- Disability/functional questionnaire (patient completed Health Assessment Questionnaire -Disability Index (HAQ-DI))
An ACR20 positive response means that the patient achieved a 20% improvement in tender and swollen joint counts and a 20% improvement in at least 3 of the other 5 Core Data Set elements listed above.

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8, 12 and 24 (Period I)

End point values	FKB327-FKB327	Humira-FKB327	FKB327-Humira	Humira-Humira
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	216[4]	108[5]	108[6]	212[7]
Units: percentage of participants				
number (confidence interval 95%)				
week 0	75.5 (69.2 to 81.0)	75.9 (66.7 to 83.6)	80.6 (71.8 to 87.5)	82.5 (76.8 to 87.4)
week 4	81.4 (75.5 to 86.4)	78.5 (69.5 to 85.9)	79.0 (70.0 to 86.4)	79.3 (73.2 to 84.6)
week 8	78.0 (71.8 to 83.5)	76.0 (66.6 to 83.8)	81.6 (72.7 to 88.5)	84.8 (79.1 to 89.4)
week 12	78.8 (72.5 to 84.2)	79.6 (70.5 to 86.9)	87.3 (79.2 to 93.0)	84.2 (78.5 to 89.0)
week 24	82.2 (76.2 to 87.3)	78.9 (69.4 to 86.6)	83.0 (74.2 to 89.8)	88.9 (83.7 to 92.9)

Notes:

[4] - subjects analysed at w 4 - 210; w 8 - 205; w 12 - 203; w 24 - 197

[5] - subjects analysed at w 4 - 107; w 8 - 104; w 12 - 103; w 24 - 95

[6] - subjects analysed at w 4 - 105; w 8 - 103; w 12 - 102; w 24 - 100

[7] - subjects analysed at w 4 - 208; w 8 - 204; w 12 - 203 - w 24 - 198

End point values	Full Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	644[8]			
Units: percentage of participants				
number (confidence interval 95%)				
week 0	78.7 (75.4 to 81.8)			
week 4	79.8 (76.5 to 82.9)			
week 8	80.5 (77.2 to 83.6)			
week 12	82.2 (78.9 to 85.1)			
week 24	84.1 (80.9 to 86.9)			

Notes:

[8] - subjects analysed at w 4 - 630; w 8 - 616; w 12 - 611; w 24 - 590

Statistical analyses

No statistical analyses for this end point

Secondary: ACR20; Summary of Response rate over time: Period II

End point title	ACR20; Summary of Response rate over time: Period II

End point description:

In period II all patients received FKB327. Long-term efficacy was evaluated up to week 80 and efficacy was evaluated for patients who switched treatment from FKB327 or Humira in Study FKB327-002 to Humira in Study FKB327-003 and back to FKB327 in Period II.
The ACR20 response criteria over time is defined as a 20% improvement in tender joint count, swollen joint count (68/66 joint count) and improvement in at least 3 of the following 5 other specified ACR Core Data Set elements from Baseline (Week 0 of study FKB327-002):

- Acute phase reactant (CRP).
- Patient global assessment of disease activity.
- Physician global assessment of disease activity.

- Patient pain scale.
- Disability/functional questionnaire (patient completed HAQ-DI)

End point type	Secondary

End point timeframe:

Weeks 30, 42, 54, 66, 76, and 80 (Period II)

End point values	FKB327-FKB327-FKB327	Humira-FKB327-FKB327	FKB327-Humira-FKB327	Humira-Humira-FKB327
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	185[9]	92[10]	98[11]	189[12]
Units: percentage of participants				
number (confidence interval 100%)				
week 30	83.2 (77.1 to 88.3)	85.9 (77.0 to 92.3)	83.7 (74.8 to 90.4)	83.6 (77.5 to 88.6)
week 42	84.8 (78.8 to 89.6)	90.0 (81.9 to 95.3)	82.3 (73.2 to 89.3)	87.7 (82.1 to 92.0)
week 54	82.8 (76.5 to 88.0)	85.6 (76.6 to 92.1)	83.9 (74.8 to 90.7)	84.4 (78.3 to 89.4)
week 66	80.5 (73.8 to 86.1)	88.1 (79.2 to 94.1)	82.0 (72.5 to 89.4)	85.7 (79.6 to 90.5)
week 76	80.0 (73.3 to 85.7)	87.7 (78.5 to 93.9)	85.6 (76.6 to 92.1)	85.5 (79.3 to 90.4)
week 80	76.9 (69.9 to 82.9)	76.5 (65.8 to 85.2)	81.8 (72.2 to 89.2)	82.4 (75.8 to 87.8)

Notes:

[9] - subjects analysed at w 42 - 184; w 54 - 180; w 66 - 174 - w 76 - 175; w 80 - 173

[10] - subjects analysed at w 42 - 90; w 54 - 90; w 66 - 84; w 76 - 81; w 80 - 81

[11] - subjects analysed at w 42 - 96; w 54 - 93; w 66 - 89; w 76 - 90; w 80 - 88

[12] - subjects analysed at w 42 - 187; w 54 - 180; w 66 - 175; w 76 - 172; w 80 - 170

End point values	Full Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	564[13]			
Units: percentage of participants				
number (confidence interval 100%)				
week 30	83.9 (80.6 to 86.8)			
week 42	86.2 (83.0 to 88.9)			
week 54	84.0 (80.6 to 87.0)			
week 66	83.7 (80.3 to 86.8)			
week 76	84.0 (80.5 to 87.0)			
week 80	79.5 (75.7 to 82.9)			

Notes:

[13] - subjects analysed at w 42- 557; w 54 - 543; w 66 - 522; w 76 - 518; w 80 - 512

Statistical analyses

No statistical analyses for this end point

Secondary: ACR50 Summary of response rate over time: Period I

End point title	ACR50 Summary of response rate over time: Period I

End point description:

The ACR50 response criteria over time is defined as a 50% improvement in tender joint count, swollen joint count (68/66 joint count) and improvement in at least 3 of the following 5 other specified ACR Core Data Set elements from Baseline (Week 0 of study FKB327-002):

- Acute phase reactant (CRP).
- Patient global assessment of disease activity.
- Physician global assessment of disease activity.
- Patient pain scale.
- Disability/functional questionnaire (patient completed HAQ-DI)

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8, 12 and 24 (Period I)

End point values	FKB327-FKB327	Humira-FKB327	FKB327-Humira	Humira-Humira
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	215[14]	108[15]	108[16]	212[17]
Units: percentage of patients				
number (confidence interval 100%)				
week 0	48.4 (41.5 to 55.3)	46.3 (36.7 to 56.2)	48.1 (38.4 to 58.0)	51.4 (44.5 to 58.3)
week 4	52.1 (45.2 to 59.0)	48.6 (38.8 to 58.5)	47.6 (37.8 to 57.6)	55.3 (48.3 to 62.2)
week 8	51.7 (44.6 to 58.7)	49.0 (39.1 to 59.0)	51.5 (41.4 to 61.4)	60.8 (53.7 to 67.5)
week 12	52.5 (45.3 to 59.5)	53.4 (43.3 to 63.3)	52.0 (41.8 to 62.0)	64.5 (57.5 to 71.1)
week 24	57.9 (50.6 to 64.9)	51.6 (41.1 to 62.0)	56.0 (45.7 to 65.9)	63.8 (56.7 to 70.5)

Notes:

[14] - subjects analysed at week 4 - 211; w 8 - 205; w 12 - 202; w 24 - 197

[15] - subjects analysed at week 4 - 107; w 8 - 104; w 12 - 103; w 24 - 95

[16] - subjects analysed at week 4 - 105; w 8 - 103; w 12 - 102; w 24 - 100

[17] - subjects analysed at week 4 - 208; w 8 - 204; w 12 - 203; w 24 - 199

End point values	Full Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	643[18]			
Units: percentage of patients				
number (confidence interval 100%)				
week 0	49.0 (45.1 to 52.9)			
week 4	51.8 (47.8 to 55.8)			
week 8	54.2 (50.2 to 58.2)			
week 12	56.6 (52.5 to 60.5)			

week 24	58.5 (54.5 to 62.5)			

Notes:

[18] - Subjects analysed at week 4 - 631; w 8 - 616; w 12 - 610; w 24 - 591

Statistical analyses

No statistical analyses for this end point

Secondary: ACR50 Summary of response rate over time: Period II

End point title	ACR50 Summary of response rate over time: Period II

End point description:

The ACR50 response criteria over time is defined as a 50% improvement in tender joint count, swollen joint count (68/66 joint count) and improvement in at least 3 of the following 5 other specified ACR Core Data Set elements from Baseline (Week 0 of study FKB327-002):

- Acute phase reactant (CRP).
- Patient global assessment of disease activity.
- Physician global assessment of disease activity.
- Patient pain scale.
- Disability/functional questionnaire (patient completed HAQ-DI)

End point type	Secondary

End point timeframe:

Weeks 30, 42, 54, 66, 76 and 80 (Period II)

End point values	FKB327-FKB327-FKB327	Humira-FKB327-FKB327	FKB327-Humira-FKB327	Humira-Humira-FKB327
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	185[19]	92[20]	98[21]	189[22]
Units: percentage of patients				
number (confidence interval 100%)				
Week 30	60.5 (53.1 to 67.6)	54.3 (43.6 to 64.8)	58.2 (47.8 to 68.1)	59.8 (52.4 to 66.8)
Week 42	61.4 (54.0 to 68.5)	60.0 (49.1 to 70.2)	49.0 (38.6 to 59.4)	61.5 (54.1 to 68.5)
Week 54	58.9 (51.3 to 66.2)	48.9 (38.2 to 59.7)	51.1 (40.4 to 61.7)	61.1 (53.6 to 68.3)
Week 66	63.2 (55.6 to 70.4)	54.8 (43.5 to 65.7)	53.9 (43.0 to 64.6)	65.1 (57.6 to 72.2)
Week76	61.7 (54.1 to 68.9)	53.1 (41.7 to 64.3)	65.6 (54.8 to 75.3)	62.4 (54.8 to 69.7)
Week 80	59.0 (51.2 to 66.4)	53.1 (41.7 to 64.3)	53.4 (42.5 to 64.1)	65.9 (58.2 to 73.0)

Notes:

[19] - subjects analysed at week 42 - 184; w 54 - 180; w 66 - 174; w 76 - 175; w 80 - 173

[20] - subjects analysed at week 42 - 90; w 54 - 90; w 66 - 84; w 76 - 81 - w 80 - 81

[21] - subjects analysed at week 42 - 96; w 54 - 92; w 66 - 89; w 76 - 90; w 80 - 88

[22] - subjects analysed at week 42 - 187; w 54 - 180; w 66 - 175; w 76 -173; w 80 - 170

End point values	Full Analysis Set			

Subject group type	Subject analysis set			
Number of subjects analysed	564[23]			
Units: percentage of patients				
number (confidence interval 100%)				
Week 30	58.9 (54.7 to 63.0)			
Week 42	59.1 (54.9 to 63.2)			
Week 54	56.6 (52.4 to 60.9)			
Week 66	60.9 (56.6 to 65.1)			
Week76	61.3 (56.9 to 65.5)			
Week 80	59.4 (55.0 to 63.7)			

Notes:

[23] - subjects analysed at week 42 - 557; w 54 - 542; w 66 - 522; w 76 - 519; w 80 - 512

Statistical analyses

No statistical analyses for this end point

Secondary: ACR70 Summary of response rate over time: Period I

End point title	ACR70 Summary of response rate over time: Period I

End point description:

The ACR70 response criteria over time is defined as a 70% improvement in tender joint count, swollen joint count (68/66 joint count) and improvement in at least 3 of the following 5 other specified ACR Core Data Set elements from Baseline (Week 0 of study FKB327-002):

- Acute phase reactant (CRP).
- Patient global assessment of disease activity.
- Physician global assessment of disease activity.
- Patient pain scale.
- Disability/functional questionnaire (patient completed HAQ-DI)

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8, 12, and 24 (Period I)

End point values	FKB327-FKB327	Humira-FKB327	FKB327-Humira	Humira-Humira
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	216[24]	108[25]	108[26]	212[27]
Units: percentage of patients				
number (confidence interval 100%)				
Week 0	20.8 (15.6 to 26.9)	21.3 (14.0 to 30.2)	21.3 (14.0 to 30.2)	26.4 (20.6 to 32.9)
Week 4	25.6 (19.8 to 32.0)	27.1 (19.0 to 36.6)	28.8 (20.4 to 38.6)	26.1 (20.2 to 32.6)
Week 8	29.9 (23.7 to 36.7)	25.0 (17.0 to 34.4)	28.2 (19.7 to 37.9)	35.3 (28.7 to 42.3)
Week 12	29.1 (22.9 to 35.8)	28.2 (19.7 to 37.9)	27.5 (19.1 to 37.2)	34.0 (27.5 to 41.0)
Week 24	33.0 (26.5 to 40.0)	26.3 (17.8 to 36.4)	30.3 (21.5 to 40.4)	40.2 (33.3 to 47.4)

Notes:

[24] - subjects analysed at week 4 - 211; w 8 - 204; w 12 - 203; w 24 - 197

[25] - subjects analysed at week 4 - 107; w 8 - 104; w 12 - 103; w 24 - 95

[26] - subjects analysed at week 4 - 104; w 8 - 103; w 12 - 102; w 24 - 99

[27] - subjects analysed at week 4 - 207; w 8 - 204; w 12 - 203; w 24 - 199

End point values	Full Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	644[28]			
Units: percentage of patients				
number (confidence interval 100%)				
Week 0	22.8 (19.6 to 26.3)			
Week 4	26.6 (23.1 to 30.2)			
Week 8	30.6 (26.9 to 34.4)			
Week 12	30.3 (26.7 to 34.1)			
Week 24	33.9 (30.1 to 37.9)			

Notes:

[28] - subjects analysed at week 4 - 629; w 8 - 615; w 12 - 611; w 24 - 590

Statistical analyses

No statistical analyses for this end point

Secondary: ACR70 Summary of response rate over time: Period II

End point title	ACR70 Summary of response rate over time: Period II

End point description:

The ACR70 response criteria over time is defined as a 70% improvement in tender joint count, swollen joint count (68/66 joint count) and improvement in at least 3 of the following 5 other specified ACR Core Data Set elements from Baseline (Week 0 of study FKB327-002):

- Acute phase reactant (CRP).
- Patient global assessment of disease activity.
- Physician global assessment of disease activity.
- Patient pain scale.
- Disability/functional questionnaire (patient completed HAQ-DI)

End point type	Secondary

End point timeframe:

Weeks 30, 42, 54, 66, 76 and 80 (Period II)

End point values	FKB327-FKB327-FKB327	Humira-FKB327-FKB327	FKB327-Humira-FKB327	Humira-Humira-FKB327
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	185[29]	92[30]	99[31]	189[32]
Units: percentage of patients				
number (confidence interval 100%)				
Week 30	36.2 (29.3 to 43.6)	30.4 (21.3 to 40.9)	33.3 (24.2 to 43.5)	39.2 (32.2 to 46.5)

Week 42	39.1 (32.0 to 46.6)	28.9 (19.8 to 39.4)	28.1 (19.4 to 38.2)	39.6 (32.5 to 47.0)
Week 54	38.3 (31.2 to 45.9)	21.1 (13.2 to 31.0)	31.2 (22.0 to 41.6)	38.3 (31.2 to 45.9)
Week 66	39.7 (32.3 to 47.3)	29.8 (20.3 to 40.7)	32.6 (23.0 to 43.3)	41.7 (34.3 to 49.4)
Week 76	41.1 (33.8 to 48.8)	24.7 (15.8 to 35.5)	34.4 (24.7 to 45.2)	41.0 (33.6 to 48.8)
Week 80	37.2 (30.0 to 44.9)	30.9 (21.1 to 42.1)	30.7 (21.3 to 41.4)	40.6 (33.1 to 48.4)

Notes:

[29] - subjects analysed at week 42 - 184; w 54 - 180; w 66 - 174; w 76 - 175; w 80 - 172

[30] - subjects analysed at week 42 - 90; w 54 - 90; w 66 - 84; w 76 - 81; w 80 -81

[31] - Subjects analysed at week 42 - 96; w 54 - 93; w 66 - 89; w 76 - 90; w 80 - 88

[32] - subjects analysed at week 42 - 187; w 54 - 180; w 66 - 175; w 76 - 173; w 80 - 170

End point values	Full Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	565[33]			
Units: percentage of patients				
number (confidence interval 100%)				
Week 30	35.8 (31.8 to 39.9)			
Week 42	35.7 (31.7 to 39.9)			
Week 54	34.3 (30.3 to 38.4)			
Week 66	37.5 (33.4 to 41.9)			
Week 76	37.4 (33.2 to 41.7)			
Week 80	36.2 (32.0 to 40.5)			

Notes:

[33] - subjects analysed at week 42 - 557; w 54 - 543; w 66 - 522; w 76 - 519; w 80 - 511

Statistical analyses

No statistical analyses for this end point

Secondary: DAS28-CRP Summary and changes over time: Period I

End point title	DAS28-CRP Summary and changes over time: Period I

End point description:

Changes over time in Disease Activity Score 28- C-reactive Protein (DAS28-CRP) compared to Baseline week 0 in Study FKB327-002:
DAS28-CRP assessment involved evaluating 28 predefined tender and 28 predefined swollen joints, serum CRP, and global assessment of disease activity (VAS from 0 [very well] to 100 [extremely bad]). The DAS28-CRP is a number on a scale from 0 to 10 indicating the current activity of the patient's RA.

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8, 12 and 24 (Period I) and changes from Baseline in Study FKB327-002 at week 0, 4, 8, 12 and 24 (Period I).

End point values	FKB327-FKB327	Humira-FKB327	FKB327-Humira	Humira-Humira
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	216[34]	108[35]	108[36]	213[37]
Units: units on a scale				
arithmetic mean (full range (min-max))				
Baseline_002	6.02 (3.3 to 8.1)	5.99 (3.7 to 7.9)	6.12 (2.9 to 8.5)	6.11 (4.0 to 8.0)
Week 0	3.46 (1.2 to 7.3)	3.65 (1.2 to 7.2)	3.49 (1.2 to 7.4)	3.36 (1.2 to 7.0)
Week 0 change from Baseline	-2.56 (-5.7 to 1.0)	-2.33 (-5.4 to 0.9)	-2.63 (-6.4 to 1.2)	-2.75 (-5.7 to 1.3)
Week 4	3.33 (1.2 to 7.0)	3.53 (1.3 to 6.7)	3.37 (1.2 to 7)	3.29 (1.2 to 7.6)
Week 4 change from Baseline	-2.64 (-6.1 to 1.8)	-2.48 (-4.9 to 1.6)	-2.76 (-6.9 to 0.9)	-2.81 (-6.1 to 1.8)
Week 8	3.28 (1.2 to 7.2)	3.51 (1.2 to 6.6)	3.37 (1.2 to 6.9)	3.25 (1.2 to 7.1)
Week 8 change from Baseline	-2.72 (-5.9 to 2.7)	-2.47 (-4.8 to 0.9)	-2.74 (-6.9 to 0.8)	-2.84 (-5.8 to 0.2)
Week 12	3.31 (1.2 to 6.9)	3.40 (1.3 to 6.2)	3.30 (1.2 to 7.1)	3.21 (1.2 to 6.5)
Week 12 change from Baseline	-2.70 (-5.9 to 0.8)	-2.57 (-4.9 to 0.5)	-2.80 (-6.9 to 0.3)	-2.88 (-5.8 to 0.9)
Week 24	3.13 (1.2 to 7.8)	3.40 (1.2 to 7.7)	3.27 (1.2 to 7.1)	3.07 (1.2 to 7.5)
Week 24 change from Baseline	-2.89 (-6.1 to 1.3)	-2.57 (-5.4 to 1.7)	-2.86 (-6.7 to 0.9)	-3.04 (-6.0 to -0.0)

Notes:

[34] - Baseline_002 number of patients n=215

[35] - Baseline_002 number of patients n=108

[36] - Baseline_002 number of patients n=107

[37] - Baseline_002 number of patients n=213

Statistical analyses

No statistical analyses for this end point

Secondary: DAS28-CRP Summary over time: Period II

End point title	DAS28-CRP Summary over time: Period II

End point description:

Changes over time in Disease Activity Score 28- C-reactive Protein (DAS28-CRP) compared to Baseline week 0 in Study FKB327-002 presented per treatment sequence and summarized for FKB327. During Period II, mean DAS28-CRP decreased from week 30 to week 76. A slight increase in DAS28-CRP was seen at week 80, possibly due to stopping treatment at week 76, but values remained below Baseline values.
DAS28-CRP assessment involved evaluating 28 predefined tender and 28 predefined swollen joints, serum CRP, and global assessment of disease activity (VAS from 0 [very well] to 100 [extremely bad]). The DAS28-CRP is a number on a scale from 0 to 10 indicating the current activity of the patient's RA.

End point type	Secondary

End point timeframe:

Weeks 30, 42, 54, 66, 76 and 80 and changes from Baseline in Study FKB327-002 at weeks 30, 42, 54, 66, 76 and 80 (Period II)

End point values	FKB327-FKB327-FKB327	Humira-FKB327-FKB327	FKB327-Humira-FKB327	Humira-Humira-FKB327
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	183	92	99	189
Units: units on a scale				
arithmetic mean (full range (min-max))				
Week 30	3.04 (1.2 to 7.1)	3.20 (1.3 to 6.3)	3.28 (1.2 to 7.1)	3.13 (1.2 to 7.4)
Week 30 Change from Baseline_002	-2.99 (-6.1 to 0.3)	-2.78 (-5.3 to 0.4)	-2.84 (-6.6 to 0.5)	-2.95 (-6.2 to 1.9)
Week 42	3.05 (1.2 to 6.8)	3.08 (1.3 to 6.0)	3.28 (1.2 to 6.1)	3.07 (1.2 to 7.3)
Week 42 Change from Baseline_002	-2.97 (-5.6 to 0.9)	-2.88 (-5.5 to -0.0)	-2.83 (-6.2 to -0.2)	-3.01 (-5.8 to 0.6)
Week 54	3.04 (1.2 to 7.5)	3.26 (1.2 to 6.2)	3.22 (1.2 to 6.2)	2.96 (1.2 to 6.8)
Week 54 Change from Baselin_002	-2.99 (-5.9 to 0.4)	-2.70 (-5.4 to 0.4)	-2.90 (-6.2 to 0.9)	-3.12 (-5.6 to 1.6)
Week 66	2.96 (1.2 to 7.0)	3.09 (1.3 to 5.6)	3.17 (1.2 to 5.7)	2.91 (1.2 to 6.9)
Week 66 Change from Baseline_002	-3.09 (-5.9 to 0.3)	-2.83 (-5.5 to 0.8)	-2.96 (-6.9 to -0.0)	-3.15 (-5.6 to 0.2)
Week 76	2.97 (1.2 to 7.8)	3.12 (1.3 to 7.0)	3.02 (1.2 to 6.2)	2.94 (1.2 to 6.4)
Week 76 Change from Baseline_002	-3.04 (-5.9 to 0.2)	-2.79 (-5.5 to 1.0)	-3.11 (-6.1 to 0.4)	-3.14 (-5.7 to -0.2)
Week 80	2.98 (1.2 to 7.1)	3.25 (1.2 to 6.7)	3.09 (1.2 to 6.9)	3.06 (1.2 to 6.7)
Week 80 Change from Baseline_002	-3.05 (-6.2 to 2.2)	-2.66 (-5.4 to 0.2)	-3.05 (-6.9 to -0.3)	-3.02 (-5.8 to 0.2)

End point values	Full Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	563			
Units: units on a scale				
arithmetic mean (full range (min-max))				
Week 30	3.14 (1.2 to 7.4)			
Week 30 Change from Baseline_002	-2.92 (-6.6 to 1.9)			
Week 42	3.10 (1.2 to 7.3)			
Week 42 Change from Baseline_002	-2.95 (-6.2 to 0.9)			
Week 54	3.08 (1.2 to 7.5)			
Week 54 Change from Baselin_002	-2.97 (-6.2 to 1.6)			
Week 66	3.00 (1.2 to 7.0)			
Week 66 Change from Baseline_002	-3.05 (-6.9 to 0.8)			
Week 76	2.99 (1.2 to 7.8)			

Week 76 Change from Baseline_002	-3.04 (-6.1 to 1.0)			
Week 80	3.07 (1.2 to 7.1)			
Week 80 Change from Baseline_002	-2.98 (-6.9 to 2.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration to Compare Treatment Across: Period I

End point title	Serum Concentration to Compare Treatment Across: Period I

End point description:

Repeated Measures model fitted to log-transformed PK trough concentrations at Weeks 12, 24 and 30 with fixed effect terms for week, treatment group and week × treatment group.
Covariance structure: unstructured. Since the treatment * week interaction effect was found to be not significant at the 10% level
(p-value = 0.4640) only the estimates across all time-points are displayed. - could not figure out how to present this Table 11.14

Mean serum drug concentrations at Week 0 were higher in the sequence groups that had been administered FKB327 in the previous study (ie, F-F and F-H). The inter-individual variability in systemic exposure was high throughout Period I, with CV ranging from 60.7% to 89.6%, across the treatment sequences. Mean serum drug concentration appeared generally stable between Week 0 to Week 30 for patients in the F-F, H-F and H-H treatment sequences, whilst a slight downward trend was observed for patients in the F-H treatment sequence.

End point type	Secondary

End point timeframe:

PK-serum concentrations at weeks 0, 12, 24 and 30 (Period I)

End point values	FKB327-FKB327	Humira-FKB327	FKB327-Humira	Humira-Humira
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	208	107	105	210
Units: ng/mL				
least squares mean (confidence interval 95%)				
Average over all time points	4235.0 (3656.7 to 4904.7)	4735.2 (3849.1 to 5825.3)	3399.4 (2767.2 to 4176.0)	4521.5 (3904.9 to 5235.4)

Statistical analyses

No statistical analyses for this end point

Secondary: ADA comparison and summary of status: Period I

End point title	ADA comparison and summary of status: Period I

End point description:

Blood samples for assessment of ADA activity were collected from Baseline week 0 to last sampling day.

The proportion of patients with positive ADA status was highest prior to dosing at Week 0 (Baseline). The proportion of patients with positive ADA status decreased over time to Week 30 and was similar for both FKB327 and Humira at all timepoints.

End point type	Secondary

End point timeframe:

Weeks 0, 12, 24 and 30 (Period I)

End point values	FKB327-FKB327	Humira-FKB327	FKB327-Humira	Humira-Humira
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	216	108	108	213
Units: percentage of positive number (not applicable)				
Week 0	61.6	62.0	63.9	58.0
Week 12	53.0	52.4	58.3	50.0
Week 24	50.3	49.0	58.0	50.3
Week 30	51.9	45.2	61.0	51.6

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Patients were carefully monitored for AEs from signing of informed consent until week 80 for patients who completed the study. For patients who discontinued the study early, a follow-up period of 4 weeks was added from the Early Termination Visit.

Adverse event reporting additional description:

SAEs were followed until resolution, the investigator confirmed the event was unlikely to resolve or the patient was recorded as lost to follow-up.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	FKB327-FKB327

Reporting group description:

This arm included patients who were treated with FKB327 in the preceding Study FKB327-002 and were randomised to continue on FKB327 treatment during Period I of Study FKB327-003.

Reporting group title	FKB327-Humira

Reporting group description:

This arm included patients who were treated with FKB327 in the preceding Study FKB327-002 and were randomised to the reference product Humira during Period I of Study FKB327-003.

Reporting group title	Humira-FKB327

Reporting group description:

This arm included patients who were treated with the reference product Humira in the preceding Study FKB327-002 and were randomised to FKB327 treatment during Period I of Study FKB327-003.

Reporting group title	Humira-Humira

Reporting group description:

This arm included patients who were treated with the reference product Humira in the preceding Study FKB327-002 and were randomised to contiune on Humira during Period I of Study FKB327-003.

Reporting group title	FKB327-FKB327-FKB327

Reporting group description:

This treatment arm included patients that had been treated with FKB327 in the preceding study, FKB327-002 and were re-randomised to continue on FKB327 in Period I of FKB327-003 study. At week 30 all patients were transferred to treatment with FKB327. (Period II)

Reporting group title	FKB327-Humira-FKB327

Reporting group description:

This treatment arm included patients that had been treated with FKB327 in the preceding study, FKB327-002 and were randomised to the reference product Humira in Period I of FKB327-003 study. At week 30 all patients were transferred to treatment with FKB327. (Period II)

Reporting group title	Humira-FKB327-FKB327

Reporting group description:

This treatment arm included patients that had been treated with the reference product Humira in the preceding study, FKB327-002 and were randomised to FKB327 in Period I of FKB327-003 study. At week 30 all patients were transferred to treatment with FKB327. (Period II)

Reporting group title	Humira-Humira-FKB327

Reporting group description:

This treatment arm included patients that had been treated with the reference product Humira in the preceding study, FKB327-002 and were re-randomised to continue on Humira in Period I of FKB327-003 study. At week 30 all patients were transferred to treatment with FKB327. (Period II)

Serious adverse events	FKB327-FKB327	FKB327-Humira	Humira-FKB327
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 216 (2.31%)	7 / 108 (6.48%)	5 / 108 (4.63%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix carcinoma			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Lymphostasis			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Hip arthroplasty			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint surgery			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Knee arthroplasty			

subjects affected / exposed	0 / 216 (0.00%)	1 / 108 (0.93%)	0 / 108 (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
Synovectomy			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death	Additional description: no cause of death terminology recorded		
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 216 (0.00%)	1 / 108 (0.93%)	0 / 108 (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
Sudden death			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Reproductive system and breast disorders			
Cervical dysplasia			

subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial hyperplasia			
subjects affected / exposed	0 / 216 (0.00%)	1 / 108 (0.93%)	0 / 108 (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
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary mass			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Maternal exposure during pregnancy			

subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle rupture			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 216 (0.00%)	1 / 108 (0.93%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Anterior spinal artery syndrome			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			

subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Oesophageal rupture			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis chronic			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 216 (0.46%)	0 / 108 (0.00%)	0 / 108 (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
Hepatocellular injury			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hydronephrosis			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 216 (0.46%)	0 / 108 (0.00%)	0 / 108 (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 failure chronic			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 216 (0.46%)	1 / 108 (0.93%)	0 / 108 (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
Back disorder			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Rheumatoid arthritis			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	1 / 216 (0.46%)	0 / 108 (0.00%)	0 / 108 (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
Spinal column stenosis			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylolisthesis			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	1 / 216 (0.46%)	0 / 108 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 216 (0.00%)	1 / 108 (0.93%)	0 / 108 (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
Pyelonephritis			

subjects affected / exposed	1 / 216 (0.46%)	0 / 108 (0.00%)	0 / 108 (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
Sepsis			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 216 (0.00%)	1 / 108 (0.93%)	0 / 108 (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
Erysipelas			
subjects affected / exposed	1 / 216 (0.46%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary mycosis			
subjects affected / exposed	0 / 216 (0.00%)	1 / 108 (0.93%)	0 / 108 (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
Urinary tract infection			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 216 (0.00%)	0 / 108 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Humira-Humira	FKB327-FKB327-	FKB327-Humira-

		FKB327	FKB327
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 213 (3.29%)	8 / 189 (4.23%)	8 / 100 (8.00%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 213 (0.00%)	1 / 189 (0.53%)	0 / 100 (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
Cervix carcinoma			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Lymphostasis			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Hip arthroplasty			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint surgery			
subjects affected / exposed	1 / 213 (0.47%)	0 / 189 (0.00%)	0 / 100 (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
Knee arthroplasty			

subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovectomy			
subjects affected / exposed	0 / 213 (0.00%)	1 / 189 (0.53%)	0 / 100 (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
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death	Additional description: no cause of death terminology recorded		
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Cervical dysplasia			

subjects affected / exposed	0 / 213 (0.00%)	1 / 189 (0.53%)	0 / 100 (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
Endometrial hyperplasia			
subjects affected / exposed	0 / 213 (0.00%)	1 / 189 (0.53%)	0 / 100 (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
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 213 (0.00%)	1 / 189 (0.53%)	0 / 100 (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
Pulmonary mass			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Maternal exposure during pregnancy			

subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle rupture			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Anterior spinal artery syndrome			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			

subjects affected / exposed	1 / 213 (0.47%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Oesophageal rupture			
subjects affected / exposed	0 / 213 (0.00%)	1 / 189 (0.53%)	0 / 100 (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
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	1 / 213 (0.47%)	0 / 189 (0.00%)	0 / 100 (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
Cholelithiasis chronic			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatocellular injury			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	1 / 100 (1.00%)
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			
Calculus urinary			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hydronephrosis			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure chronic			
subjects affected / exposed	1 / 213 (0.47%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back disorder			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Rheumatoid arthritis			
subjects affected / exposed	0 / 213 (0.00%)	1 / 189 (0.53%)	0 / 100 (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
Rotator cuff syndrome			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal column stenosis			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylolisthesis			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis			
subjects affected / exposed	1 / 213 (0.47%)	0 / 189 (0.00%)	0 / 100 (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			
Pneumonia			
subjects affected / exposed	1 / 213 (0.47%)	0 / 189 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	1 / 213 (0.47%)	0 / 189 (0.00%)	0 / 100 (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
Bronchitis			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			

subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary mycosis			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 213 (0.00%)	1 / 189 (0.53%)	0 / 100 (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
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 213 (0.00%)	0 / 189 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Humira-FKB327-	Humira-Humira-	

	FKB327	FKB327	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 93 (6.45%)	11 / 190 (5.79%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	1	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 93 (0.00%)	1 / 190 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix carcinoma			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Lymphostasis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Hip arthroplasty			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint surgery			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Knee arthroplasty			

subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovectomy			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	1 / 93 (1.08%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death	Additional description: no cause of death terminology recorded		
subjects affected / exposed	0 / 93 (0.00%)	1 / 190 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Non-cardiac chest pain			
subjects affected / exposed	1 / 93 (1.08%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Cervical dysplasia			

subjects affected / exposed	0 / 93 (0.00%)	1 / 190 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial hyperplasia			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mass			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 93 (0.00%)	1 / 190 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Maternal exposure during pregnancy			

subjects affected / exposed	1 / 93 (1.08%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle rupture			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 93 (0.00%)	1 / 190 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Anterior spinal artery syndrome			
subjects affected / exposed	0 / 93 (0.00%)	1 / 190 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			

subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	0 / 93 (0.00%)	1 / 190 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Oesophageal rupture			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis chronic			
subjects affected / exposed	1 / 93 (1.08%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular injury			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	1 / 93 (1.08%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hydronephrosis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure chronic			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 93 (0.00%)	1 / 190 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back disorder			
subjects affected / exposed	0 / 93 (0.00%)	1 / 190 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc degeneration			
subjects affected / exposed	1 / 93 (1.08%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Rheumatoid arthritis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylolisthesis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovitis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 93 (2.15%)	1 / 190 (0.53%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 93 (1.08%)	1 / 190 (0.53%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 93 (1.08%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			

subjects affected / exposed	0 / 93 (0.00%)	1 / 190 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 93 (1.08%)	1 / 190 (0.53%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	0 / 93 (0.00%)	1 / 190 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mycosis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 93 (0.00%)	0 / 190 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 93 (0.00%)	1 / 190 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	FKB327-FKB327	FKB327-Humira	Humira-FKB327
Total subjects affected by non-serious adverse events			
subjects affected / exposed	103 / 216 (47.69%)	59 / 108 (54.63%)	59 / 108 (54.63%)
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	12 / 216 (5.56%)	7 / 108 (6.48%)	5 / 108 (4.63%)
occurrences (all)	15	8	7
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	7 / 216 (3.24%)	9 / 108 (8.33%)	6 / 108 (5.56%)
occurrences (all)	7	9	6
Bronchitis			
subjects affected / exposed	10 / 216 (4.63%)	3 / 108 (2.78%)	2 / 108 (1.85%)
occurrences (all)	10	3	2
Upper respiratory tract infection			
subjects affected / exposed	3 / 216 (1.39%)	2 / 108 (1.85%)	3 / 108 (2.78%)
occurrences (all)	3	2	3
Urinary tract infection			
subjects affected / exposed	6 / 216 (2.78%)	3 / 108 (2.78%)	3 / 108 (2.78%)
occurrences (all)	7	4	5
Pharyngitis			
subjects affected / exposed	6 / 216 (2.78%)	3 / 108 (2.78%)	3 / 108 (2.78%)
occurrences (all)	11	3	3

Non-serious adverse events	Humira-Humira	FKB327-FKB327-FKB327	FKB327-Humira-FKB327
Total subjects affected by non-serious adverse events			
subjects affected / exposed	117 / 213 (54.93%)	114 / 189 (60.32%)	61 / 100 (61.00%)
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	8 / 213 (3.76%)	7 / 189 (3.70%)	6 / 100 (6.00%)
occurrences (all)	10	9	9
Infections and infestations			
Nasopharyngitis			

subjects affected / exposed	13 / 213 (6.10%)	23 / 189 (12.17%)	8 / 100 (8.00%)
occurrences (all)	16	25	8
Bronchitis			
subjects affected / exposed	11 / 213 (5.16%)	5 / 189 (2.65%)	3 / 100 (3.00%)
occurrences (all)	11	6	3
Upper respiratory tract infection			
subjects affected / exposed	7 / 213 (3.29%)	14 / 189 (7.41%)	1 / 100 (1.00%)
occurrences (all)	7	14	2
Urinary tract infection			
subjects affected / exposed	4 / 213 (1.88%)	9 / 189 (4.76%)	3 / 100 (3.00%)
occurrences (all)	4	11	3
Pharyngitis			
subjects affected / exposed	4 / 213 (1.88%)	5 / 189 (2.65%)	2 / 100 (2.00%)
occurrences (all)	4	5	3

Non-serious adverse events	Humira-FKB327-FKB327	Humira-Humira-FKB327	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 93 (54.84%)	114 / 190 (60.00%)	
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	4 / 93 (4.30%)	8 / 190 (4.21%)	
occurrences (all)	4	9	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	11 / 93 (11.83%)	18 / 190 (9.47%)	
occurrences (all)	11	20	
Bronchitis			
subjects affected / exposed	5 / 93 (5.38%)	8 / 190 (4.21%)	
occurrences (all)	5	8	
Upper respiratory tract infection			
subjects affected / exposed	3 / 93 (3.23%)	6 / 190 (3.16%)	
occurrences (all)	3	6	
Urinary tract infection			
subjects affected / exposed	5 / 93 (5.38%)	7 / 190 (3.68%)	
occurrences (all)	8	8	
Pharyngitis			

subjects affected / exposed occurrences (all)	6 / 93 (6.45%) 6	4 / 190 (2.11%) 4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2014	Global Amendment 1 (substantial): changes were implemented following Regulatory Authority feed-back on the protocol for Study FKB327-002. These changes were made before the protocol was submitted in any country.
23 March 2015	Global Amendment 2 (substantial): following Regulatory Authority feed-back, changes were made to selected exclusion criteria that were part of the preceding study FKB327-002 protocol that should also be applied to the FKB327-003 protocol. In addition, the FKB327-002 completion status required for entry into FKB327-003 was clarified. Other administrative changes were completed to the protocol.
18 August 2015	Global Amendment 3 (substantial): changes were completed to the study protocol following realisation of a potential safety issue (latex allergy) which may have affected handling of the study drug for site staff and patients enrolled on the FKB327-003 study protocol. The issue concerned the comparator treatment arm only. In addition, a number of non substantial changes were introduced in this global amendment, i.e. an increase in the planned number of patients. Other minor administrative changes were completed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported