Clinical trial results:
A PHASE 3, MULTICENTER, RANDOMIZED, OPEN, PROSPECTIVE, CONTROLLED, PARALLEL-GROUP STUDY OF REDUCTION OF THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS IN ONGOING REMISSION
RETRO – REduction of Therapy in RA patients in Ongoing remission, Reduzierung der Therapie bei RA-Patienten in Remission

Summary

EudraCT number	2009-015740-42
Trial protocol	DE
Global end of trial date	15 July 2021

Results information

Result version number	v1 (current)
This version publication date	21 August 2021
First version publication date	21 August 2021

Trial information

Trial identification

Sponsor protocol code	UKER00109STUM3

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Universitätsklinikum Erlangen
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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	15 July 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 July 2021
Global end of trial reached?	Yes
Global end of trial date	15 July 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The current concept of RA-therapy is remission, which is defined by reaching a disease activity score counted in 28 joints of the body (DAS 28) of less than 2,6 as a main target.
Rheumatoid Arthritis nowadays is being treated increasingly successful, due to better treatment with standard medications (dosage until limit, combination of therapies), due to quicker and more flexible therapy schemes (early start of treatment, close mashed therapy monitoring and due to introduction of new preparations. About 30% of RA patients reach clinical remission of RA.
Yet it is still unclear, if and for how long a patient in long lasting and stable remission is to continue therapy or whether it is possible to reduce medication without risking a relapse of the disease.
This study means on one hand to examine the possibility of a reduction of therapy or even a breaking off therapy in RA patients in long lasting remission.

Protection of trial subjects:

Regular lab controls, clinical visits every 3 months, continous documentation and evaluation of AEs

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 May 2010
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	Germany: 258
Worldwide total number of subjects	258
EEA total number of subjects	258

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)	201
From 65 to 84 years	57
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

286 patients were screened at 13 centers. Due to screening failures, withdrawal of IC etc. 258 data sets were available

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Control

Arm description:

continuation of treatment

Arm type	IMP full dose
Investigational medicinal product name	RA treatment with corticosteroids, cDMARDs, bDMARDs (TNF inhibitors, IL-6 inhibitors, IL-1 inhibitors)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet, Concentrate for solution for infusion, Solution for infusion, Solution for injection, Solution for injection in pre-filled injector, Solution for injection in pre-filled syringe, Tablet
Routes of administration	Concentrate for solution for infusion , Injection , Infusion , Oral use

Dosage and administration details:

full dose according to SmPC

Arm title	Reduction

Arm description:

50% reduction of RA-treatment

Arm type	IMP 50% dose
Investigational medicinal product name	RA treatment with corticosteroids, cDMARDs, bDMARDs (TNF inhibitors, IL-6 inhibitors, IL-1 inhibitors)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet, Concentrate for solution for infusion, Solution for infusion, Solution for injection, Solution for injection in pre-filled injector, Solution for injection in pre-filled syringe, Tablet
Routes of administration	Concentrate for solution for infusion , Infusion , Injection , Oral use

Dosage and administration details:

50% dose according to SmPC

Arm title	Reduction/stop

Arm description:

50% reduction of IMP-treatment for 6 months followed by subsequent stopping of trewament when still in remission

Arm type	50% IMP+stop IMP

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Control	Reduction	Reduction/stop
Started	81	85	92
Completed	81	85	92

Period 2	
Period 2 title	Treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	Continuation
Arm description: Continuation of full dose RA-treatment	
Arm type	Full dose IMP
Investigational medicinal product name	RA treatment with corticosteroids, cDMARDs, bDMARDs (TNF inhibitors, IL-6 inhibitors, IL-1 inhibitors)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet, Concentrate for solution for infusion, Solution for infusion, Solution for injection, Solution for injection in pre-filled injector, Solution for injection in pre-filled syringe, Tablet
Routes of administration	Concentrate for solution for infusion , Infusion , Injection , Oral use
Dosage and administration details: full dose according to SmPC	
Arm title	Reduction
Arm description: 50% reduction of RA-treatment	
Arm type	50% reduction
Investigational medicinal product name	RA treatment with corticosteroids, cDMARDs, bDMARDs (TNF inhibitors, IL-6 inhibitors, IL-1 inhibitors)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion, Solution for infusion, Solution for injection, Solution for injection in pre-filled injector, Coated tablet, Solution for injection in pre-filled syringe, Tablet
Routes of administration	Infusion , Injection , Oral use, Concentrate for solution for infusion
Dosage and administration details: full dose according to SmPC	

Arm title	Reduction/stop

Arm description:

50% reduction of RA-treatment with subsequent stopping after 6 months when still in remission

Arm type	50% IMP+stop IMP
Investigational medicinal product name	RA treatment with corticosteroids, cDMARDs, bDMARDs (TNF inhibitors, IL-6 inhibitors, IL-1 inhibitors)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion, Solution for infusion, Solution for injection, Coated tablet, Solution for injection in pre-filled injector, Solution for injection in pre-filled syringe, Tablet
Routes of administration	Infusion , Injection , Oral use, Concentrate for solution for infusion

Dosage and administration details:

full dose according to SmPC

Number of subjects in period 2	Continuation	Reduction	Reduction/stop
Started	81	85	92
Completed	81	85	92

Baseline characteristics

Reporting groups	
Reporting group title	Control
Reporting group description:	
continuation of treatment	
Reporting group title	Reduction
Reporting group description:	
50% reduction of RA-treatment	
Reporting group title	Reduction/stop
Reporting group description:	
50% reduction of IMP-treatment for 6 months followed by subsequent stopping of trewament when still in remission	

Reporting group values	Control	Reduction	Reduction/stop
Number of subjects	81	85	92
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean	57.3	57.9	57.0
standard deviation	± 12.6	± 12.8	± 13.2
Gender categorical			
Units: Subjects			
Female	44	49	53
Male	37	36	39
bDMARD use			
Units: Subjects			
yes	32	39	37
no	49	46	55
Rheumatoid factor			
Units: Subjects			
yes	42	51	49
no	39	34	43
ACPA positivity			
Units: Subjects			
yes	47	49	52
no	34	36	40
Methotrexate use			

Units: Subjects			
yes	64	62	72
no	17	23	20
other cDMARD Units: Subjects			
yes	12	12	12
no	69	73	80
Glucocorticoids use Units: Subjects			
yes	15	15	14
no	66	70	78
Disease duration Units: years			
arithmetic mean	7.2	7.6	6.8
standard deviation	± 7.1	± 7.1	± 8.2
Remission duration Units: months			
arithmetic mean	17.3	14.5	22.1
standard deviation	± 13.8	± 13.0	± 30.8
HAQ standard Units: points			
arithmetic mean	0.2	0.2	0.2
standard deviation	± 0.4	± 0.3	± 0.4
DAS28 Units: unit(s)			
arithmetic mean	1.6	1.6	1.7
standard deviation	± 0.7	± 0.7	± 0.6

Reporting group values	Total		
Number of subjects	258		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	146		
Male	112		

bDMARD use Units: Subjects			
yes	108		
no	150		
Rheumatoid factor Units: Subjects			
yes	142		
no	116		
ACPA positivity Units: Subjects			
yes	148		
no	110		
Methotrexate use Units: Subjects			
yes	198		
no	60		
other cDMARD Units: Subjects			
yes	36		
no	222		
Glucocorticoids use Units: Subjects			
yes	44		
no	214		
Disease duration Units: years arithmetic mean standard deviation	- -		
Remission duration Units: months arithmetic mean standard deviation	- -		
HAQ standard Units: points arithmetic mean standard deviation	- -		
DAS28 Units: unit(s) arithmetic mean standard deviation	- -		

End points

End points reporting groups

Reporting group title	Control
Reporting group description: continuation of treatment	
Reporting group title	Reduction
Reporting group description: 50% reduction of RA-treatment	
Reporting group title	Reduction/stop
Reporting group description: 50% reduction of IMP-treatment for 6 months followed by subsequent stopping of trewament when still in remission	
Reporting group title	Continuation
Reporting group description: Continuation of full dose RA-treatment	
Reporting group title	Reduction
Reporting group description: 50% reduction of RA-treatment	
Reporting group title	Reduction/stop
Reporting group description: 50% reduction of RA-treatment with subsequent stopping after 6 months when still in remission	

Primary: Remission

End point title	Remission
End point description: proportion of subjects still remission after 12 months	
End point type	Primary
End point timeframe: 12 months	

End point values	Continuation	Reduction	Reduction/stop	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	81	85	92	
Units: subjects	69	50	41	

Statistical analyses

Statistical analysis title	Remission continuation vs reduction
Comparison groups	Continuation v Reduction

Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logrank

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From time of enrollment until visit 4 (month 12)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups	
Reporting group title	Control
Reporting group description: continuation of treatment	
Reporting group title	Reduction
Reporting group description: 50% reduction of RA-treatment	
Reporting group title	Reduction/stop
Reporting group description: 50% reduction of IMP-treatment for 6 months followed by subsequent stopping of trewament when still in remission	

Serious adverse events	Control	Reduction	Reduction/stop
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 81 (12.35%)	7 / 85 (8.24%)	13 / 92 (14.13%)
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)			
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 81 (1.23%)	0 / 85 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Synovial rupture			
subjects affected / exposed	1 / 81 (1.23%)	0 / 85 (0.00%)	0 / 92 (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
Lower limb fracture			

subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	1 / 81 (1.23%)	0 / 85 (0.00%)	0 / 92 (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
Procedural intestinal perforation			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Patella fracture			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Removal of internal fixation			
subjects affected / exposed	1 / 81 (1.23%)	0 / 85 (0.00%)	0 / 92 (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
Large intestinal polypectomy			
subjects affected / exposed	1 / 81 (1.23%)	0 / 85 (0.00%)	0 / 92 (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
Heart valve operation			

subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 92 (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
Radical prostatectomy			
subjects affected / exposed	1 / 81 (1.23%)	0 / 85 (0.00%)	0 / 92 (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
Coronary arterial stent insertion			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 92 (1.09%)
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			
Atrial flutter			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 92 (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
Acute myocardial infarction			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 92 (1.09%)
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 / 81 (0.00%)	1 / 85 (1.18%)	0 / 92 (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
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 92 (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
Headache			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 92 (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
Myasthenia gravis crisis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 92 (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 / 81 (0.00%)	0 / 85 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 81 (1.23%)	0 / 85 (0.00%)	0 / 92 (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
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 85 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary fibrosis			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			

subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Diverticulitis			
subjects affected / exposed	2 / 81 (2.47%)	0 / 85 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2.5 %

Non-serious adverse events	Control	Reduction	Reduction/stop
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 81 (59.26%)	55 / 85 (64.71%)	45 / 92 (48.91%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Syncope			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	2 / 92 (2.17%)
occurrences (all)	0	0	2
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 81 (0.00%)	2 / 85 (2.35%)	0 / 92 (0.00%)
occurrences (all)	0	2	0
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	4 / 81 (4.94%)	2 / 85 (2.35%)	2 / 92 (2.17%)
occurrences (all)	4	2	2
Respiratory, thoracic and mediastinal disorders			

Rhinitis allergic			
subjects affected / exposed	1 / 81 (1.23%)	2 / 85 (2.35%)	1 / 92 (1.09%)
occurrences (all)	1	2	1
Injury, poisoning and procedural complications			
Soft tissue injury			
subjects affected / exposed	1 / 81 (1.23%)	5 / 85 (5.88%)	2 / 92 (2.17%)
occurrences (all)	1	5	2
Multiple injuries			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	2 / 92 (2.17%)
occurrences (all)	0	0	2
Rib fracture			
subjects affected / exposed	0 / 81 (0.00%)	2 / 85 (2.35%)	0 / 92 (0.00%)
occurrences (all)	0	2	0
Radius fracture			
subjects affected / exposed	2 / 81 (2.47%)	0 / 85 (0.00%)	0 / 92 (0.00%)
occurrences (all)	2	0	0
Nervous system disorders			
Sciatica			
subjects affected / exposed	1 / 81 (1.23%)	3 / 85 (3.53%)	3 / 92 (3.26%)
occurrences (all)	3	3	4
Carpal tunnel syndrome			
subjects affected / exposed	2 / 81 (2.47%)	0 / 85 (0.00%)	2 / 92 (2.17%)
occurrences (all)	3	0	2
Migraine			
subjects affected / exposed	1 / 81 (1.23%)	1 / 85 (1.18%)	1 / 92 (1.09%)
occurrences (all)	1	2	1
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 81 (0.00%)	2 / 85 (2.35%)	1 / 92 (1.09%)
occurrences (all)	0	2	1
Eye disorders			
Cataract			
subjects affected / exposed	0 / 81 (0.00%)	3 / 85 (3.53%)	1 / 92 (1.09%)
occurrences (all)	0	3	1
Gastrointestinal disorders			

Gastritis			
subjects affected / exposed	3 / 81 (3.70%)	1 / 85 (1.18%)	0 / 92 (0.00%)
occurrences (all)	3	1	0
Colon adenoma			
subjects affected / exposed	1 / 81 (1.23%)	2 / 85 (2.35%)	1 / 92 (1.09%)
occurrences (all)	1	2	1
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 81 (1.23%)	2 / 85 (2.35%)	2 / 92 (2.17%)
occurrences (all)	1	2	2
Pruritus			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	2 / 92 (2.17%)
occurrences (all)	0	0	2
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	2 / 92 (2.17%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 81 (6.17%)	5 / 85 (5.88%)	1 / 92 (1.09%)
occurrences (all)	5	4	1
Bursitis			
subjects affected / exposed	1 / 81 (1.23%)	1 / 85 (1.18%)	1 / 92 (1.09%)
occurrences (all)	1	2	1
Synovial cyst			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	2 / 92 (2.17%)
occurrences (all)	0	0	2
Trigger finger			
subjects affected / exposed	1 / 81 (1.23%)	2 / 85 (2.35%)	0 / 92 (0.00%)
occurrences (all)	1	2	0
Myalgia			
subjects affected / exposed	0 / 81 (0.00%)	2 / 85 (2.35%)	0 / 92 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Upper respiratory tract infection			

subjects affected / exposed	24 / 81 (29.63%)	25 / 85 (29.41%)	20 / 92 (21.74%)
occurrences (all)	31	43	25
Gastroenteritis			
subjects affected / exposed	2 / 81 (2.47%)	2 / 85 (2.35%)	3 / 92 (3.26%)
occurrences (all)	2	2	3
Oral herpes			
subjects affected / exposed	3 / 81 (3.70%)	3 / 85 (3.53%)	1 / 92 (1.09%)
occurrences (all)	3	3	1
Urinary tract infection			
subjects affected / exposed	2 / 81 (2.47%)	2 / 85 (2.35%)	1 / 92 (1.09%)
occurrences (all)	2	2	1
Sinusitis			
subjects affected / exposed	1 / 81 (1.23%)	2 / 85 (2.35%)	1 / 92 (1.09%)
occurrences (all)	1	2	1
Soft tissue infection			
subjects affected / exposed	1 / 81 (1.23%)	2 / 85 (2.35%)	2 / 92 (2.17%)
occurrences (all)	1	2	2
Conjunctivitis			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	2 / 92 (2.17%)
occurrences (all)	0	0	2
Erysipelas			
subjects affected / exposed	2 / 81 (2.47%)	0 / 85 (0.00%)	1 / 92 (1.09%)
occurrences (all)	2	0	1
Candida infection			
subjects affected / exposed	2 / 81 (2.47%)	0 / 85 (0.00%)	0 / 92 (0.00%)
occurrences (all)	2	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 June 2011	participation of more centres; Restruction of ICF, actualisation of medication information
12 March 2012	wording in some protocol areas; wordings SAE=serious adverse event
12 November 2012	adress of Sponsor; participation of more centres; wording protocol; CCS Erlangen as central safety organization; personel changes
16 February 2015	Abatacept and Tocilizumab s.c. as study medication; wording of questionaaires; wording treament group-> reduction group; wording documents; timeline: May 2010-> app. 6/2022 (due to long-term observation)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported