Clinical trial results:
TapERA:
Maintaining remission in RA while tapering Etanercept.

Summary

EudraCT number	2012-004631-22
Trial protocol	BE
Global end of trial date	31 December 2015

Results information

Result version number	v1 (current)
This version publication date	16 April 2021
First version publication date	16 April 2021

Trial information

Trial identification

Sponsor protocol code	TapERA2012

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University Hospitals Leuven
Sponsor organisation address	herestraat 49, Leuven, Belgium, 3000
Public contact	Patrick Verschueren, University Hospitals Leuven, 32 16342541, patrick.verschueren@uzleuven.be
Scientific contact	Patrick Verschueren, University Hospitals Leuven, 32 16342541, patrick.verschueren@uzleuven.be

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	09 March 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2015
Global end of trial reached?	Yes
Global end of trial date	31 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of the current study is to explore the potential of a dose reduction of Etanercept on safety and persisting remission in RA patients.

Protection of trial subjects:

Patients were pseudonymised.
Informed consent was obtained.
Patient were re-escalated to weekly Etanercept use in case of loss of remission.
Medication (Etanercept) used in this trial was within the marketing authorisation.
Protocol obtained ethics committee approval.
.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 February 2013
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	Belgium: 66
Worldwide total number of subjects	66
EEA total number of subjects	66

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)	54
From 65 to 84 years	12

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

66 eligible patients were recruited between October 2012 and December 2014. There were patients included in 6 Belgian rheumatology centers (2 university hospitals, 3 general hospitals and 1 private practice)

Pre-assignment

Screening details:

There were 73 patients screened .
Of these screened patients 66 were included in the trial. 7 patients did not fulfill the eligibility criteria (e.g. no sustained remission for 6 months based on DAS28CRP/ESR) .

Pre-assignment period milestones

Number of subjects started	73[1]
Number of subjects completed	66

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Protocol deviation: 7

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 7 patients not included due to protocol violation (not meeting inclusion criteria)

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Weekly Etanercept

Arm description:

patients continue their weekly 50 mg etanercept treatment

Arm type	Active comparator
Investigational medicinal product name	Etanercept
Investigational medicinal product code	IMP-228/2014
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

etanercept 50 mg subcutaneously weekly

Arm title	Every other week Etanercept

Arm description:

Etanercept 50 mg weekly every other week.

Arm type	Experimental
Investigational medicinal product name	Etanercept
Investigational medicinal product code	IMP-228/2014
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:
etanercept 50 mg subcutaneously every other week

Number of subjects in period 1	Weekly Etanercept	Every other week Etanercept
Started	34	32
Completed	33	31
Not completed	1	1
Lost to follow-up	-	1
Lack of efficacy	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Weekly Etanercept
Reporting group description:	
patients continue their weekly 50 mg etanercept treatment	
Reporting group title	Every other week Etanercept
Reporting group description:	
Etanercept 50 mg weekly every other week.	

Reporting group values	Weekly Etanercept	Every other week Etanercept	Total
Number of subjects	34	32	66
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	27	27	54
From 65-84 years	7	5	12
85 years and over	0	0	0
Age continuous Units: years			
median	56.0	52.5	
inter-quartile range (Q1-Q3)	48.0 to 64.0	45.5 to 60.5	-
Gender categorical Units: Subjects			
Female	20	25	45
Male	14	7	21
disease duration Units: years			
median	15.0	13.5	
inter-quartile range (Q1-Q3)	9.0 to 19.0	7.0 to 20.5	-
DAS28CRP Units: score			
median	1.9	1.7	
inter-quartile range (Q1-Q3)	1.4 to 2.4	1.3 to 2.1	-

End points

End points reporting groups

Reporting group title	Weekly Etanercept
Reporting group description:	
patients continue their weekly 50 mg etanercept treatment	
Reporting group title	Every other week Etanercept
Reporting group description:	
Etanercept 50 mg weekly every other week.	
Subject analysis set title	Proportion of patients maintaining remission for 6 months
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Proportions of patients maintaining remission for 6 months based on the DAS28-CRP below 2.6. Proportions were compared using the Chi-squared test.	

Primary: Proportion maintaining remission for 6 months

End point title	Proportion maintaining remission for 6 months
End point description:	
proportion of patients maintaining remission (DAS28CRP<2.6) at every study visit until month 6.	
End point type	Primary
End point timeframe:	
6 months	

End point values	Weekly Etanercept	Every other week Etanercept	Proportion of patients maintaining remission for 6 months	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	34	32	66	
Units: number of patients	26	19	45	

Statistical analyses

Statistical analysis title	Chi-squared
Comparison groups	Weekly Etanercept v Every other week Etanercept
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	Chi-squared

Secondary: proportion of patients maintaining remission for 12 months

End point title	proportion of patients maintaining remission for 12 months

End point description:

Proportion of patients maintaining remission for 12 months based on the DAS28-CRP below 2.6. Proportions were compared using the Chi-squared test.

End point type	Secondary

End point timeframe:

12 months

End point values	Weekly Etanercept	Every other week Etanercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	32		
Units: number of patients	21	14		

Statistical analyses

Statistical analysis title	Chi squared
Comparison groups	Weekly Etanercept v Every other week Etanercept
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	Chi-squared

Adverse events

Adverse events information	
Timeframe for reporting adverse events: the entire duration of the trial: 12 months	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	etanercept weekly
Reporting group description: -	
Reporting group title	etanercept every other week
Reporting group description: -	

Serious adverse events	etanercept weekly	etanercept every other week	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 34 (8.82%)	6 / 32 (18.75%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cholesteatoma			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 34 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Knee arthroplasty			
subjects affected / exposed	1 / 34 (2.94%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac pacemaker insertion			

subjects affected / exposed	0 / 34 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid endarterectomy			
subjects affected / exposed	0 / 34 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angioplasty			
subjects affected / exposed	0 / 34 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Therapy change			
subjects affected / exposed	0 / 34 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 34 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	etanercept weekly	etanercept every other week	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 34 (52.94%)	15 / 32 (46.88%)	
Vascular disorders			
Peripheral artery thrombosis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Peripheral artery stenosis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Intermittent claudication			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Surgical and medical procedures			
Bunion operation			
subjects affected / exposed	1 / 34 (2.94%)	1 / 32 (3.13%)	
occurrences (all)	1	1	
Skin lesion removal			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Chest pain			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Injection site reaction			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Calcinosis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	

Respiratory, thoracic and mediastinal disorders			
Vocal cord disorder			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	0 / 34 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Interstitial lung disease			
subjects affected / exposed	0 / 34 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Investigations			
Weight decreased			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Muscle rupture			
subjects affected / exposed	0 / 34 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Radius fracture			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Ventricular extrasystoles			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Myelofibrosis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Glaucoma			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Barrett's oesophagus			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	

Abdominal pain upper			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Gastric disorder			
subjects affected / exposed	0 / 34 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Abdominal discomfort			
subjects affected / exposed	0 / 34 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 34 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Hepatic cirrhosis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Eczema asteatotic			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Dermatitis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Psoriasis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Rotator cuff syndrome			
subjects affected / exposed	0 / 34 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Tendon disorder			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Rheumatoid arthritis			
subjects affected / exposed	0 / 34 (0.00%)	3 / 32 (9.38%)	
occurrences (all)	0	3	

Osteoporosis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Arthralgia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Foot deformity			
subjects affected / exposed	0 / 34 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 34 (5.88%)	3 / 32 (9.38%)	
occurrences (all)	2	3	
Cellulitis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	1 / 34 (2.94%)	3 / 32 (9.38%)	
occurrences (all)	1	3	
Pneumonia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Wound infection			
subjects affected / exposed	1 / 34 (2.94%)	1 / 32 (3.13%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

lower sample size than expected was included in the trial and therfore the power of the trial was not achieved.

Notes: