EU Clinical Trials Register

Clinical trial results:
Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of Apremilast (CC-10004) in the Treatment of Ankylosing Spondylitis (AS)

Summary

EudraCT number	2008-004229-40
Trial protocol	GB
Global end of trial date	18 January 2011

Results information

Result version number	v1 (current)
This version publication date	18 December 2019
First version publication date	18 December 2019

Trial information

Trial identification

Sponsor protocol code	112008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00944658
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Imperial College London
Sponsor organisation address	South Kensingston Campus, London, United Kingdom, SW7 2AZ
Public contact	Sonya Abraham, Imperial College London, +44 (0)20 3313 4114, s.abraham@imperial.ac.uk
Scientific contact	Sonya Abraham, Imperial College London, +44 (0)20 3313 4114, s.abraham@imperial.ac.uk

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	31 January 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 January 2011
Global end of trial reached?	Yes
Global end of trial date	18 January 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the effect of apremilast on magnetic resonance imaging lesions in ankylosing spondylitis.

To explore the effect of apremilast on the signs and symptoms of ankylosing spondylitis.

Protection of trial subjects:	
None	
Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	03 August 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Scientific research
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 38
Worldwide total number of subjects	38
EEA total number of subjects	38

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)	38

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a single-centre, randomised, double-blind, placebo controlled, Phase II, investigator-led, pilot study carried out at the Kennedy Clinical Trials Unit between Aug 2009 to Jan 2011.

Pre-assignment

Screening details:

55 patients were screened (6 failing to demonstrate bone oedema on MRI) and 38 were enrolled into this study. With the exception of 2 patients (both receiving apremilast), all others completed the study. The two withdrawals discontinued treatment within 1 week of commencing due to non-serious adverse events.

Period 1

Period 1 title	Treatment (12 weeks)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

An unblinded pharmacist allocated patients to receive either placebo or active drug according to a randomisation code generated by Celgene. All other study person remained blinded to treatment until the end of the double-blind period.

Arms

Are arms mutually exclusive?	Yes
Arm title	Apremilast

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Apremilast
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10mg twice daily and the dose was titrated by 20mg every 2days until the maximum dose of 30mg twice daily was achieved on day 5. Apremilast was then given daily until day 85 (week 12).

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10mg twice daily and the dose was titrated by 20mg every 2days until the maximum dose of 30mg twice daily was achieved on day 5. Apremilast was then given daily until day 85 (week 12).

Number of subjects in period 1	Apremilast	Placebo
Started	19	19
Completed	17	19
Not completed	2	0
non serious adverse event	2	-

Period 2

Period 2 title	Follow up
Is this the baseline period?	Yes[1]
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Apremilast

Arm description: -

Arm type	Experimental
Investigational medicinal product name	No intervention follow up
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

No intervention, follow up

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	No intervention, follow up
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

No intervention, follow up

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: 2 participants withdraw after 1 week of treatment due to non-serious adverse event, they were excluded from efficacy analysis

Number of subjects in period 2[2]	Apremilast	Placebo
Started	17	19
Completed	17	19

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 2 participants withdraw after 1 week of treatment due to non-serious adverse event

Baseline characteristics

Reporting groups

Reporting group title	Apremilast
Reporting group description: -	
Reporting group title	Placebo

Reporting group description: -

Reporting group values	Apremilast	Placebo	Total
Number of subjects	17	19	36
Age categorical Units: Subjects			
Adults (18-64 years)	17	19	36
Age continuous Units: years			
geometric mean	44.88	39.21	
standard deviation	± 11.1	± 13.3	-
Gender categorical Units: Subjects			
Female	2	2	4
Male	15	17	32

End points

End points reporting groups

Reporting group title	Apremilast
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Apremilast
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Changes in BASDAI Score From Baseline

End point title	Changes in BASDAI Score From Baseline
End point description:	
Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), 0 – 10 score, higher reduction in the scores suggest better suboptimal control of disease.	
End point type	Primary
End point timeframe:	
Baseline and 12 weeks	

End point values	Apremilast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	19		
Units: unit on scale				
geometric mean (standard deviation)	-1.59 (± 1.48)	-0.77 (± 1.47)		

Statistical analyses

Statistical analysis title	Bath Ankylosing Spondylitis Disease Activity Index
Comparison groups	Apremilast v Placebo
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.139
Method	ANCOVA

Primary: Changes of Apremilast on the signs and symptoms of AS, night pain from baseline

End point title	Changes of Apremilast on the signs and symptoms of AS, night pain from baseline

End point description:

Changes of Apremilast on the signs and symptoms of AS, night pain from baseline
This endpoint the night time pain score change was recorded by questionnaire to evaluate the
Apremilast effect on symptom, higher reduction better improvement.
scale is 0-10

End point type	Primary

End point timeframe:
Baseline and 12 weeks

End point values	Apremilast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	19		
Units: score on a scale				
geometric mean (standard deviation)	-0.81 (± 3.01)	-0.23 (± 2.75)		

Statistical analyses

Statistical analysis title	Changes in Night pain baseline to after treatment
Comparison groups	Placebo v Apremilast
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.587
Method	ANCOVA

Primary: Changes in BASFI Score from baseline

End point title	Changes in BASFI Score from baseline

End point description:

End point type	Primary

End point timeframe:
Baseline and 12 weeks

End point values	Apremilast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	19		
Units: score on a scale				
geometric mean (standard deviation)	-1.74 (± 1.91)	-0.28 (± 1.61)		

Statistical analyses

Statistical analysis title	BASFI
Comparison groups	Apremilast v Placebo
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.108
Method	ANCOVA

Secondary: The safety and tolerability of Apremilast in AS, Number of Participants with Adverse Events

End point title	The safety and tolerability of Apremilast in AS, Number of Participants with Adverse Events

End point description:

End point type	Secondary

End point timeframe:

16 weeks

End point values	Apremilast	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	19		
Units: Count of participants	18	17		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

16 weeks

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10

Reporting groups

Reporting group title	Apremilast

Reporting group description: -

Reporting group title	Placebo

Reporting group description: -

Serious adverse events	Apremilast	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Apremilast	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 19 (94.74%)	17 / 19 (89.47%)	
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 19 (42.11%)	5 / 19 (26.32%)	
occurrences (all)	8	5	
Blood and lymphatic system disorders			
Raised serum amylase			
subjects affected / exposed	2 / 19 (10.53%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Loose stools			
subjects affected / exposed	5 / 19 (26.32%)	2 / 19 (10.53%)	
occurrences (all)	5	2	

Nausea			
subjects affected / exposed	3 / 19 (15.79%)	3 / 19 (15.79%)	
occurrences (all)	3	3	
Flatulance			
subjects affected / exposed	2 / 19 (10.53%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Diarrhoea			
subjects affected / exposed	2 / 19 (10.53%)	2 / 19 (10.53%)	
occurrences (all)	2	2	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	6 / 19 (31.58%)	6 / 19 (31.58%)	
occurrences (all)	6	6	

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

 None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/22984171