Clinical trial results:
Treatment of Pustular Psoriasis with the IL-1 receptor antagonist anakinra: a randomised, placebo controlled trial and associated mechanistic studies

Summary

EudraCT number	2015-003600-23
Trial protocol	GB
Global end of trial date	10 August 2020

Results information

Result version number	v1 (current)
This version publication date	01 October 2023
First version publication date	01 October 2023
Summary attachment (see zip file)	Report (APRICOT Report - V1.0 (20SEP2021).pdf)

Trial information

Trial identification

Sponsor protocol code	APRICOT

Additional study identifiers

ISRCTN number	ISRCTN13127147
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Guy's and St Thomas NHS Foundation Trust
Sponsor organisation address	Great Maze Pond, London, United Kingdom, SE1 9RT
Public contact	Prof. Catherine Smith, Guy's and St Thomas Foundation Trust, 40 207185 5375, catherine.smith@kcl.ac.uk
Scientific contact	Prof. Catherine Smith, Guy's and St Thomas Foundation Trust, 40 207185 5375, catherine.smith@kcl.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	23 September 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 August 2020
Global end of trial reached?	Yes
Global end of trial date	10 August 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy of anakinra in treatment of adults with PPP compared to placebo. The primary endpoint is change in disease activity over 8 weeks, adjusted for baseline (visit 1), measured using fresh pustule count, the default primary outcome, unless PPPASI is more discriminating (to be reviewed at the end of stage one).

The Stage 1 review occurred on 22nd January 2018. As a result of this review the DMC recommended the primary outcome to be PPPASI and this was passed by the TSC. Fresh pustule count will be a secondary outcome.

Protection of trial subjects:

Participants have the right to withdraw from the study at any time for any reason. The investigator also has the right to withdraw patients from the study drug in the event of inter-current illness, AEs, SAEs, SUSARs, protocol violations, administrative reasons or other reasons.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 August 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 64
Worldwide total number of subjects	64
EEA total number of subjects	64

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)	60
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	64
Number of subjects completed	64

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Vehicle solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo will be provided in identical, matched syringes, containing 0.67 ml vehicle solution only. Placebo formulation contains 140 mM Sodium Chloride, 10 mM Sodium Citrate, 0.5 mM EDTA, 0.1% (w/w) non-animal derived Polysorbate 80, pH 6.5.

Arm title	Anakinra

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Anakinra
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Anakinra: A pre-filled syringe (27G x 1/2in. Needle) will be supplied by SOBI i.e.: Kineret 100 mg/0.67 ml solution for injection in pre-filled syringe. Each pre-filled syringe contains 100 mg of anakinra* per 0.67 ml (150 mg/ml). It is a clear, colourless-to-white solution for injection that may contain some product-related translucent-to-white amorphous particles.

Number of subjects in period 1	Placebo	Anakinra
Started	33	31
Completed	27	26
Not completed	6	5
Consent withdrawn by subject	2	1
Physician decision	1	-
Adverse event, non-fatal	1	4
Lost to follow-up	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Anakinra
Reporting group description: -	

Reporting group values	Placebo	Anakinra	Total
Number of subjects	33	31	64
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	51.7	49.9	
standard deviation	± 13.6	± 11.9	-
Gender categorical Units: Subjects			
Female	27	27	54
Male	6	4	10

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Anakinra
Reporting group description: -	

Primary: PalmoPlantarPustulosis Area and Severity Index (PPPASI) score

End point title	PalmoPlantarPustulosis Area and Severity Index (PPPASI)

End point description:

End point type	Primary

End point timeframe:

Baseline to Week 8

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: Please see uploaded report

End point values	Placebo	Anakinra		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	31		
Units: score				
arithmetic mean (standard deviation)				
baseline	18.0 (± 10.4)	17.5 (± 10.8)		
Week 8	15.4 (± 10.1)	13.9 (± 7.4)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Baseline to week 20	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	23
Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Anakinra
Reporting group description: -	

Serious adverse events	Placebo	Anakinra	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 33 (0.00%)	0 / 31 (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	Placebo	Anakinra	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 33 (78.79%)	29 / 31 (93.55%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Synovial cyst			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Haematuria			
subjects affected / exposed	1 / 33 (3.03%)	2 / 31 (6.45%)	
occurrences (all)	1	2	
Hypertension			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	

Pregnancy, puerperium and perinatal conditions			
Gestational diabetes			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Pregnancy			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
constusion			
subjects affected / exposed	2 / 33 (6.06%)	1 / 31 (3.23%)	
occurrences (all)	2	1	
Decreased appetite			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	2	0	
Flushing			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Injection site discomfort			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Injection site erythema			
subjects affected / exposed	1 / 33 (3.03%)	2 / 31 (6.45%)	
occurrences (all)	1	2	
Injection site pain			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Injection site pruritus			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Injection site rash			

subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Injection site reaction			
subjects affected / exposed	1 / 33 (3.03%)	19 / 31 (61.29%)	
occurrences (all)	1	20	
Injection site swelling			
subjects affected / exposed	1 / 33 (3.03%)	2 / 31 (6.45%)	
occurrences (all)	1	2	
Lethargy			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	2	0	
Oedema peripheral			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Immune system disorders			
Rhinitis allergic			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
metrorrhagia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Catarrh			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
cough			
subjects affected / exposed	2 / 33 (6.06%)	4 / 31 (12.90%)	
occurrences (all)	2	5	
Oropharyngeal pain			

subjects affected / exposed	1 / 33 (3.03%)	3 / 31 (9.68%)	
occurrences (all)	1	3	
Pharyngeal oedema			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	0 / 33 (0.00%)	3 / 31 (9.68%)	
occurrences (all)	0	3	
Investigations			
Blood creatine increased			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Blood pressure increased			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
C-reactive protein increased			
subjects affected / exposed	1 / 33 (3.03%)	1 / 31 (3.23%)	
occurrences (all)	1	1	
DNA antibody positive			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Glucose urine present			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Hepatitis B antibody positive			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Mean cell volume increased			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Monocyte count increased			

subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Neutrophil count increased			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Transaminases increased			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Urine analysis abnormal			
subjects affected / exposed	1 / 33 (3.03%)	2 / 31 (6.45%)	
occurrences (all)	1	2	
White blood cell count increased			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
White blood cells urine positive			
subjects affected / exposed	2 / 33 (6.06%)	0 / 31 (0.00%)	
occurrences (all)	2	0	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Post procedural infection			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 33 (6.06%)	6 / 31 (19.35%)	
occurrences (all)	4	6	
Migraine			
subjects affected / exposed	2 / 33 (6.06%)	0 / 31 (0.00%)	
occurrences (all)	2	0	
Neuralgia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			

Eosinophilia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Lymphadenopathy			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Visual acuity reduced			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	0 / 33 (0.00%)	5 / 31 (16.13%)	
occurrences (all)	0	5	
Nausea			
subjects affected / exposed	2 / 33 (6.06%)	2 / 31 (6.45%)	
occurrences (all)	2	2	
Toothache			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	0 / 33 (0.00%)	2 / 31 (6.45%)	
occurrences (all)	0	2	
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	1 / 33 (3.03%)	4 / 31 (12.90%)	
occurrences (all)	1	4	
Skin and subcutaneous tissue disorders			
Biopsy skin			

subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	1	0	
Dermatitis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Folliculitis			
subjects affected / exposed	1 / 33 (3.03%)	1 / 31 (3.23%)	
occurrences (all)	1	2	
Pain of skin			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Psoriasis			
subjects affected / exposed	2 / 33 (6.06%)	3 / 31 (9.68%)	
occurrences (all)	2	3	
Psoriatic arthropathy			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Pustular psoriasis			
subjects affected / exposed	2 / 33 (6.06%)	2 / 31 (6.45%)	
occurrences (all)	2	2	
Rash macular			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Rash papular			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Skin irritation			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Skin lesion			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			

Glomerular filtration rate decreased			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Proteinuria			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Pyuria			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Endocrine disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Back injury			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Osteoporosis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	1 / 33 (3.03%)	1 / 31 (3.23%)	
occurrences (all)	1	1	
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	

Influenza like illness			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Lower respiratory tract infection			
subjects affected / exposed	3 / 33 (9.09%)	3 / 31 (9.68%)	
occurrences (all)	3	3	
Nasopharyngitis			
subjects affected / exposed	3 / 33 (9.09%)	4 / 31 (12.90%)	
occurrences (all)	3	5	
Rhinitis			
subjects affected / exposed	1 / 33 (3.03%)	1 / 31 (3.23%)	
occurrences (all)	1	1	
Sinusitis			
subjects affected / exposed	1 / 33 (3.03%)	2 / 31 (6.45%)	
occurrences (all)	1	2	
Skin infection			
subjects affected / exposed	2 / 33 (6.06%)	1 / 31 (3.23%)	
occurrences (all)	2	1	
Synovitis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Tonsillitis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	3 / 33 (9.09%)	4 / 31 (12.90%)	
occurrences (all)	3	4	
Viral infection			
subjects affected / exposed	2 / 33 (6.06%)	0 / 31 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 31 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 September 2016	Protocol v2
27 September 2016	Protocol v3
15 June 2017	Protocol v4
16 May 2018	Protocol v5
23 May 2019	Protocol v6
14 October 2019	protocol v6.1

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported