Clinical trial results:
A Phase IIa open label single arm study of safety and efficacy of rVA576 in adult mild to moderate Bullous Pemphigoid subjects

Summary

EudraCT number	2017-002836-18
Trial protocol	NL DE
Global end of trial date	29 April 2020

Results information

Result version number	v1 (current)
This version publication date	15 May 2021
First version publication date	15 May 2021

Trial information

Trial identification

Sponsor protocol code	AK801

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Akari Therapeutics Plc
Sponsor organisation address	75-76 Wimpole Street, London, United Kingdom, W1G 9RT
Public contact	Chief Scientific Officer, Akari Therapeutics Plc, +44 (0)2080040261, miles.nunn@akaritx.com
Scientific contact	Chief Scientific Officer, Akari Therapeutics Plc, +44 (0)2080040261, miles.nunn@akaritx.com

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	14 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 April 2020
Global end of trial reached?	Yes
Global end of trial date	29 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to assess the safety of rVA576 (also known as nomacopan) in adult subjects with mild to moderate BP.

Protection of trial subjects:

The study was performed in accordance with the current version of the Declaration of Helsinki. The trial was conducted in agreement with the International Conference on Harmonisation (ICH) guidelines on Good Clinical Practice (GCP) E6(R1) which were current at the time of the trial.

Background therapy:

Topical 0.1% mometasone applied only to lesions up to 30gram/week allowed as maximal background therapy for first 21 days.

Evidence for comparator:

No comparator, single arm.

Actual start date of recruitment	25 September 2018
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	Netherlands: 4
Country: Number of subjects enrolled	Germany: 5
Worldwide total number of subjects	9
EEA total number of subjects	9

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)	1

From 65 to 84 years	7
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients were screened up to 14 days prior to study treatment to confirm eligibility for the study. A total of 13 patients were screened with 4 not being eligible, due to 3 not meeting the exclusion criteria, and 1 not providing consent for the study.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Nomacopan

Arm description:

All patients who received at least one dose of nomacopan.

Arm type	Experimental
Investigational medicinal product name	Nomacopan
Investigational medicinal product code	rVA576
Other name	coversin, OmCl, VA576
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Day 1 - 60 mg nomacopan administered subcutaneously followed by 30 mg Nomacopan subcutaneously 12 hours later
Days 2-42 - 30 mg nomacopan administered subcutaneously once daily

Note: nomacopan is a lyophilised powder for reconstitution for injection

Number of subjects in period 1	Nomacopan
Started	9
Completed	9

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial
Reporting group description:	
All patients who received at least one dose of nomacopan.	

Reporting group values	Overall Trial	Total	
Number of subjects	9	9	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	1	1	
From 65-84 years	7	7	
85 years and over	1	1	
Gender categorical Units: Subjects			
Female	5	5	
Male	4	4	
Karnofsky Performance Status Units: Subjects			
90%	1	1	
80%	5	5	
70%	2	2	
60%	1	1	
Height Units: Centimetre (cm)			
median	163.0		
full range (min-max)	156.5 to 179.0	-	
Weight Units: kilogram(s)			
median	89.4		
full range (min-max)	64.4 to 120.8	-	
BMI Units: kilogram(s)/square meter			
median	30.2		
full range (min-max)	25.2 to 43.2	-	

End points

End points reporting groups

Reporting group title	Nomacopan

Reporting group description:

All patients who received at least one dose of nomacopan.

Primary: Proportion of participants reporting CTCAE grade 3,4 and 5 adverse events, related/possibly related to nomacopan during days 1 to day 42

End point title	Proportion of participants reporting CTCAE grade 3,4 and 5 adverse events, related/possibly related to nomacopan during days 1 to day 42[1]

End point description:

End point type	Primary

End point timeframe:

Day 1 (baseline) to Day 42 (end of nomacopan treatment)

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: Only descriptive statistical were planned and undertaken for evaluation of the primary endpoint.

End point values	Nomacopan			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Participants				
Grade 3 Adverse Event	0			
Grade 4 Adverse Event	0			
Grade 5 Adverse Event	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean absolute change in BPDAI activity scores between Baseline (Day 1) and Day 42

End point title	Mean absolute change in BPDAI activity scores between Baseline (Day 1) and Day 42

End point description:

The BPDAI (Bullous Pemphigoid Disease Area Index) quantifies lesion number and size thresholds. Lesions are rated based on the regions affected. The BPDAI gives additional weighting to areas of the skin primarily affected in BP, such as the limbs, and less emphasis to scalp and face, to better differentiate clinical response in BP.
BPDAI activity scores of <20, 20 - 56 and >57, respectively, are considered to define mild, moderate and severe disease.
The minimum clinically important difference (MCID) in disease symptom improvement is considered a 4 point decrease in BPDAI activity score.
The total BPDAI activity score is the arithmetic sum of three subcomponents - cutaneous

blisters/erosions, cutaneous urticaria/erythema, and mucosal blisters/erosions.

End point type	Secondary

End point timeframe:

Day 1 (baseline) to Day 42 (end of nomacopan treatment)

End point values	Nomacopan			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Percentage Change				
arithmetic mean (standard deviation)				
Day 7	-8.39 (± 27.31)			
Day 14	-21.12 (± 23.56)			
Day 21	-27.85 (± 38.84)			
Day 28	-41.03 (± 57.98)			
Day 42	-30.23 (± 63.91)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients whose BPDAI activity score decreased by 4 or more points between Baseline (day 1) and Day 42

End point title	Proportion of patients whose BPDAI activity score decreased by 4 or more points between Baseline (day 1) and Day 42

End point description:

The BPDAI (Bullous Pemphigoid Disease Area Index) quantifies lesion number and size thresholds. Lesions are rated based on the regions affected. The BPDAI gives additional weighting to areas of the skin primarily affected in BP, such as the limbs, and less emphasis to scalp and face, to better differentiate clinical response in BP. The minimum clinically important difference (MCID) in disease symptom improvement is considered a 4 point decrease in BPDAI activity score.
The total BPDAI activity score is the arithmetic sum of three subcomponents - cutaneous blisters/erosions, cutaneous urticaria/erythema, and mucosal blisters/erosions.

End point type	Secondary

End point timeframe:

Day 1 (baseline) to Day 42 (end of nomacopan treatment)

End point values	Nomacopan			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Number patients reduced ≥4 points BPDAI				
Day 7	4			
Day 14	6			
Day 21	7			
Day 28	7			
Day 42	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients whose BPDAI activity score increased by 3 or more points between Baseline (Day 1) and Day 42

End point title	Proportion of patients whose BPDAI activity score increased by 3 or more points between Baseline (Day 1) and Day 42

End point description:

The BPDAI (Bullous Pemphigoid Disease Area Index) quantifies lesion number and size thresholds. Lesions are rated based on the regions affected. The BPDAI gives additional weighting to areas of the skin primarily affected in BP, such as the limbs, and less emphasis to scalp and face, to better differentiate clinical response in BP. The minimum clinically important difference (MCID) in disease symptom worsening is considered a 3 point increase in BPDAI activity score.
The total BPDAI activity score is the arithmetic sum of three subcomponents - cutaneous blisters/erosions, cutaneous urticaria/erythema, and mucosal blisters/erosions.

End point type	Secondary

End point timeframe:

Day 1 (baseline) to Day 42 (end of nomacopan treatment)

End point values	Nomacopan			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Number patients increased ≥3points BPDAI				
Day 7	2			
Day 14	1			
Day 21	1			
Day 28	2			
Day 42	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean absolute change in BPDAI pruritis index between Day 1 (Baseline) and Day 42

End point title	Mean absolute change in BPDAI pruritis index between Day 1 (Baseline) and Day 42

End point description:

The BPDAI-pruritus index component is based on a visual analogue scale (VAS), measuring the severity of itch during the past 24 h (0 - 10), the past week (0 - 10) and the past month (0 - 10) with a total score of 30.

End point type	Secondary

End point timeframe:

Day 1 (baseline) to Day 42 (end of nomacopan treatment)

End point values	Nomacopan			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Absolute decrease in Pruritus score				
arithmetic mean (standard deviation)	6.8 (± 7.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in Dermatology Life Quality Index (DLQI) between Baseline (Day 1) and Day 42

End point title	Mean change in Dermatology Life Quality Index (DLQI) between Baseline (Day 1) and Day 42

End point description:

The DLQI questionnaire was designed to measure how much a persons skin problems have affected their life over the last week. It features 10 items which relate to possible functional, physical, and psychological repercussions on quality of life. The interpretation of the DLQI scores range from 0-30, and are typically that a score of 0-1 has no effect on the patient's life, 2-5 has a small effect, 6-10 a moderate effect, and 11-20 a very large effect.

End point type	Secondary

End point timeframe:

Day 1 (baseline) to Day 42 (end of nomacopan treatment)

End point values	Nomacopan			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: DLQI score				
arithmetic mean (standard deviation)				
Screening	11.33 (± 6.69)			
Day 21	6.22 (± 5.76)			
Day 42	6.44 (± 6.11)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in treatment of Autoimmune Bullous Disease Quality of Life (TABQOL) between Baseline (Day 1) and Day 42

End point title	Mean change in treatment of Autoimmune Bullous Disease Quality of Life (TABQOL) between Baseline (Day 1) and Day 42

End point description:

The TABQOL questionnaire was designed to measure the degree of impact on quality of life attributable to the effects of treatment. It features 17 items which relate to possible functional, physical, psychological, and financial repercussions on quality of life. Each item is scored from 0 to 3 points, with higher scores denoting poorer quality of life. The sum of these scores gives the total TABQOL score ranging from 0 to 51.

End point type	Secondary

End point timeframe:

Day 1 (baseline) to Day 42 (end of nomacopan treatment)

End point values	Nomacopan			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: TABQOL score				
arithmetic mean (standard deviation)				
Screening	14.63 (± 8.07)			
Day 21	12.38 (± 7.52)			
Day 42	10.33 (± 8.02)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 (Baseline) to Day 72 (follow up visit)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Nomacopan

Reporting group description: -

Serious adverse events	Nomacopan		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 9 (33.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Condition aggravated	Additional description: Worsening of existing BP disorder		
subjects affected / exposed	2 / 9 (22.22%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Localised infection (knee)			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Nomacopan		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)		
Vascular disorders			
Haematoma			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Malaise			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Feeling cold			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Influenza like illness			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Investigations			
C-reactive protein increased			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Blood urea increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Blood pressure increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Eosinophil count increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Neutrophil count increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
White blood cell count increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			

Fall subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Limb injury subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Burns first degree subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Cardiac disorders Ventricular extrasystoles subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 3		
Syncope subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Taste disorder subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Eosinophilia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Lymphopenia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		

Faeces soft subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) Erythema subjects affected / exposed occurrences (all) Lichen planus subjects affected / exposed occurrences (all) Skin ulcer subjects affected / exposed occurrences (all) Livedo reticularis subjects affected / exposed occurrences (all)	 2 / 9 (22.22%) 2 1 / 9 (11.11%) 1 1 / 9 (11.11%) 1 1 / 9 (11.11%) 1 1 / 9 (11.11%) 1		
Renal and urinary disorders Renal failure subjects affected / exposed occurrences (all)	 1 / 9 (11.11%) 1		
Musculoskeletal and connective tissue disorders Joint swelling subjects affected / exposed occurrences (all) Musculoskeletal stiffness subjects affected / exposed occurrences (all)	 1 / 9 (11.11%) 1 1 / 9 (11.11%) 1		
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all) Respiratory tract infection	 3 / 9 (33.33%) 5		

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Bacterial test positive			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Hyponatraemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 August 2018	Protocol amendment 4 - To allow patients help with dosing at home, if required.
09 May 2019	Protocol amendment 5 -To allow enrolment of patients receiving systemic treatment for the current episode of BP, provided current treatment was stopped before Day 1. - Change of exclusion criterion from 'oral' steroids to 'systemic' steroids. - To allow patient visits to be conducted at home by suitable staff, to decrease patient burden. - Inclusion Criteria: Clarification added for patients with disability. - Addition of disease control assessment at Baseline, any unscheduled and follow-up visits. - Addition of global BPDAI and Visual Analogue Pruritus assessments at follow-up visit.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported