Clinical trial results:
Multicentre Study of Nomacopan in Paediatric Haematopoietic Stem-Cell Transplant associated Thrombotic Microangiopathy

Summary

EudraCT number	2020-000086-17
Trial protocol	GB PL
Global end of trial date	15 May 2024

Results information

Result version number	v1 (current)
This version publication date	16 May 2025
First version publication date	16 May 2025

Trial information

Trial identification

Sponsor protocol code	AK901

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04784455
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Akari Therapeutic Plc.
Sponsor organisation address	75-76 Wimpole Street, London, United Kingdom, W1G 9RT
Public contact	Information Desk, Akari Therapeutics Plc, +44 2080040261, info@akaritx.com
Scientific contact	Information Desk, Akari Therapeutics Plc, +44 2080040261, info@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 November 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 May 2024
Global end of trial reached?	Yes
Global end of trial date	15 May 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Part A (7 patients aged ≥ 0.5 to < 18 years, in three age range cohorts)
Dose algorithm confirmation:

▪ To confirm the effective dose of nomacopan for the ablation of terminal complement activity. The data derived from Part A of the trial will be used together with existing data for PK/PD simulation modelling to define an age-based dosing regimen to completely control terminal complement activity in paediatric patients treated with nomacopan in Part B safety and efficacy trial.

The trial was closed after completion of Part A and did not proceed to Part B.

Protection of trial subjects:

Where possible study specific blood samples were taken at the same time as routine sampling for clinical care.

The volume of blood taken from patients was monitored very carefully. Sites monitored and recorded the blood volume taken for each patient to ensure daily blood samples was not greater than 3% of the patient's total blood volume. Further, the "Day 3" and "Day 7 - 6 hour" blood samples were not taken in the youngest cohort (≥ 0.5 to < 2 years).

Background therapy:

No background therapy was specified for the study. Any background treatment was as prescribed by the treating clinician (except eculizumab or any other complement blocker therapy - which were trial exclusion criteria)

Evidence for comparator:

Not applicable

Actual start date of recruitment	24 July 2020
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	United Kingdom: 9
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	10
EEA total number of subjects	0

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)	1
Children (2-11 years)	5
Adolescents (12-17 years)	4
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

AK901 was open to recruitment from 24 July 2020 to 15 May 2024. The study was open in 4 UK sites, 4 US sites and 1 Polish site.

Pre-assignment

Screening details:

Paediatric patients who underwent allogeneic or autologous haematopoietic stem cell transplantation (HSCT) and within a year developed thrombotic microangiopathy (HSCT-TMA) with elevated complement activity and proteinuria. The maximum period between screening and starting nomacopan was 21 days, but treatment was started as soon as possible.

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:

Patients were administered nomacopan subcutaneously, twice daily for a maximum of 24 weeks

Arm type	Experimental
Investigational medicinal product name	Nomacopan
Investigational medicinal product code	PRD4020816
Other name	Coversin
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Patients were given an ablating dose on Day 1, 12 hours apart which was determined by the child's weight on Day1:

Ablating Dose:
- 0.5 to < 2 years =1.7 mg/kg
- 2 to < 9 years =1.3 mg/kg
- 9 to < 18 years =1.0 mg/kg

For children in the youngest two cohorts (≥ 0.5 to < 2 years, and ≥ 2 to <9 years), the dose was re-calculated at the week 8 and week 16 visits using the child's new weight measured at that visit.

The starting maintenance dose, administered 12 hours apart, from Day2 until the end of treatment was 0.30 mg/kg for all 3 age groups.

If required, from pre-dose Day 7onwards, a dose escalation was permitted if the CH50 results were > 10U Eq/mL and/or the unbound nomacopan in serum was < 55 ng/mL.

Two dose escalations were permitted -an increase from the maintenance dose of 0.30 mg/kg to 0.45 mg/kg with a further increase to 0.60 mg/kg if required. Dose increases were preceded by an ablating dose as determined by age as per Day 1.

Number of subjects in period 1	Nomacopan
Started	10
Treated patients	10
Completed	6
Not completed	4
Adverse event, serious fatal	4

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial
Reporting group description:	
Patients treated with nomacopan	

Reporting group values	Overall Trial	Total	
Number of subjects	10	10	
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)	1	1	
Children (2-11 years)	5	5	
Adolescents (12-17 years)	4	4	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	6	6	
Male	4	4	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	1	
White	9	9	
More than one race	0	0	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Nomacopan

Reporting group description:

Patients were administered nomacopan subcutaneously, twice daily for a maximum of 24 weeks

Primary: RBC transfusion independence for ≥ 28 Days immediately prior to any scheduled clinical visit up to Week 24 or Urine Protein Creatinine Ratio (UPCR) ≤ 2 mg/mg maintained over ≥ 28 Days immediately prior to any scheduled clinical visit up to Week 24

End point title	RBC transfusion independence for ≥ 28 Days immediately prior to any scheduled clinical visit up to Week 24 or Urine Protein Creatinine Ratio (UPCR) ≤ 2 mg/mg maintained over ≥ 28 Days immediately prior to any scheduled clinical visit up to Week 24[1]

End point description:

RBC Transfusion Independence for ≥ 28 Days Immediately Prior to any Scheduled Clinical Visit up to Week 24 or Urine Protein Creatinine Ratio ≤ 2 mg/mg Maintained Over ≥ 28 Days Immediately Prior to any Scheduled Clinical Visit up to Week 24

Transfusion independence is defined as no RBC transfusion attributable to, or required to manage, thrombotic microangiopathy (TMA). Transfusions required for causes other than TMA will not be considered within the evaluation of the endpoints.

End point type	Primary

End point timeframe:

24 Weeks

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: Due to the early termination of the study only descriptive primary and secondary efficacy data are presented.

End point values	Nomacopan			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Patients				
RBC transfusion independent for ≥ 28 days	2			
UPCR ≤ 2 mg/mg for ≥ 28 days	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Normalisation of Lab Parameters

End point title	Normalisation of Lab Parameters

End point description:

End point type	Secondary

End point timeframe:

24 Weeks

End point values	Nomacopan			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Patients				
Plasma sC5b-9 ≤ ULN	10			
Lactate dehydrogenase (LDH) ≤ULN	2			
Normalization of haptoglobin	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Platelet transfusion independence for ≥ 28 Days immediately prior to any scheduled clinical visit up to Week 24

End point title	Platelet transfusion independence for ≥ 28 Days immediately prior to any scheduled clinical visit up to Week 24

End point description:

Platelet Transfusion Independence for ≥ 28 Days Immediately Prior to any Scheduled Clinical Visit up to Week 24.

Transfusion independence is defined as no platelet transfusion attributable to, or required to manage, thrombotic microangiopathy(TMA). Transfusions required for causes other than TMA will not be considered within the evaluation of the endpoints.

End point type	Secondary

End point timeframe:

24 Weeks

End point values	Nomacopan			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Patients				
Platelet Transfusion Independence for ≥ 28 days	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the time of consent until end of study (maximum 2 year follow-up)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27

Reporting groups

Reporting group title	Treated patients

Reporting group description: -

Serious adverse events	Treated patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 10 (80.00%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events	4		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Generalised tonic-clonic seizure †			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Blood and lymphatic system disorders			
Cytopenia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombotic microangiopathy			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Generalised oedema			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 2		
Infections and infestations			
Pneumonia parainfluenzae viral			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypoglycaemia			

subjects affected / exposed	1 / 10 (10.00%)		
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	Treated patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)		
Investigations			
Blood Creatinine Increased			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	6		
Blood bicarbonate decreased			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	4		
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	5		
Vascular disorders			
Hypotension			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	4		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 10 (40.00%)		
occurrences (all)	18		
Leukopenia			
subjects affected / exposed	4 / 10 (40.00%)		
occurrences (all)	13		
Neutropenia			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	8		
Thrombocytopenia			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	25		

General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	5 / 10 (50.00%)		
occurrences (all)	18		
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	5 / 10 (50.00%)		
occurrences (all)	20		
Hypermagnesaemia			
subjects affected / exposed	4 / 10 (40.00%)		
occurrences (all)	12		
Hypernatraemia			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	5		
Hypoalbuminaemia			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	7		
Hypocalcaemia			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	7		
Hypoglycaemia			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	4		
Hypokalaemia			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	9		
Hypomagnesaemia			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	4		
Hyponatraemia			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	6		
Hypophosphataemia			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 June 2021	- sC5b-9 samples were listed as serum instead of plasma, and samples to be analysed centrally rather than locally or centrally - PK samples were listed as plasma instead of serum - Inclusion of urine pregnancy testing at sites that are unable to perform serum pregnancy testing - The 12h samples can be taken at 9 hours if logistical reasons prevent sampling and processing at 12 hours - CH50 and PK samples not required for patients in the youngest cohort on Day 3, Day 7 - 6h, and Week 4 - 6 hours to minimise the blood draw volume - Haematology parameters updated to include lymphocytes, monocytes, basophils, and eosinophils - Clarification that LTB4 will be measured in a 24-hour urine sample
10 November 2021	- Inclusion - time from HSCT to TMA diagnosis increased from 100 days to a year - Exclusion - time to initiate nomacopan increased from 14 days to 21 days - Section regarding previous clinical exposure and experience to nomacopan updated

Notes:

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.

Part A of the trial was exploratory with a small number of subjects. Due to early closure only 2 of 6 patients alive at Week 24 were followed up at 1 and 2 years. The trial was closed for business reasons unrelated to safety in this or other trials.

Notes: