Clinical trial results:
An Open Label, Randomized, Crossover, Single Dose Bioavailability Study in Healthy Adult Subjects to Evaluate the Pharmacokinetic Profile of an Exploratory Avacopan Pediatric Liquid Formulation Compared to Avacopan 10 mg Capsule Formulation

Summary

EudraCT number	2023-000381-34
Trial protocol	Outside EU/EEA
Global end of trial date	15 August 2022

Results information

Result version number	v1 (current)
This version publication date	25 August 2023
First version publication date	25 August 2023

Trial information

Trial identification

Sponsor protocol code	CL019_168

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 120784

Notes:

Sponsors

Sponsor organisation name	ChemoCentryx
Sponsor organisation address	850 Maude Avenue, Mountain View, California, United States, 94043
Public contact	Study Director, Amgen Inc, +1 8665726436, medinfo@amgen.com
Scientific contact	Study Director, Amgen Inc, +1 8665726436, medinfo@amgen.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002023-PIP01-16
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 February 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Assess the pharmacokinetics (PK) of an exploratory pediatric liquid formulation of avacopan given under fasted and fed conditions compared to an avacopan capsule formulation given under fasted or fed conditions

Protection of trial subjects:

Celerion attests that the clinical portion of this study was performed in compliance with Celerion Standard Operating Procedures (SOPs). The SOPs are written based on the principles and requirements of GCP as defined by the regulatory agencies standards and guidance listed in the Celerion Global Quality Manual. These SOPs are also in accordance with the ethical requirements referred to in the European Union (EU) directive 2001/20/EC and the ethical principles set forth in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 March 2022
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 States: 31
Worldwide total number of subjects	31
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)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	31
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects reported to the clinical research unit (CRU) for eligibility screening within approximately 3 weeks prior to the first drug administration.

Period 1

Period 1 title	Stage 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

This was an open-label study. Subjects were randomized to treatment sequences to minimize assignment bias. Because the primary endpoints of this study were objective PK measurements, blinding was not necessary. A crossover design was used to control for the variability between subjects. A 10-day washout between doses was considered sufficient to eliminate carry-over effects of the treatments.

Arms

Are arms mutually exclusive?	No
Arm title	Treatment A

Arm description:

30 mg Avacopan liquid formulation fasted

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

Dosage and administration details:

A single oral dose of 30 mg avacopan liquid formulation (5 mL of 6 mg/mL). The study drugs were administered orally with 240 mL of water under fasted conditions

Arm title	Treatment B

Arm description:

30 mg Avacopan liquid formulation fed

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

Dosage and administration details:

A single oral dose of 30 mg avacopan liquid formulation (5 mL of 6 mg/mL). The study drugs were administered orally with 240 mL of water under fed conditions

Arm title	Treatment C

Arm description:

30 mg Avacopan capsules fasted

Arm type	Experimental

Investigational medicinal product name	Avacopan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The avacopan capsules contained 10 mg avacopan. A single oral dose of 30 mg avacopan (3 x 10 mg capsules) under fasted conditions.

Number of subjects in period 1	Treatment A	Treatment B	Treatment C
Started	15	15	15
Completed	15	15	15

Period 2

Period 2 title	Stage 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

This was a open label study. Subjects were randomized to treatment sequences to minimize assignment bias. Because the primary endpoints of this study were objective PK measurements, blinding was not necessary. A crossover design was used to control for the variability between subjects. A 10-day washout between doses was considered sufficient to eliminate carry-over effects of the treatments.

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment D

Arm description:

30 mg avacopan liquid formulation fed, high fat, high calorie food. The total number of subjects reflects 8 subjects who started on treatment D and crossed over to treatment E, and 8 subjects who started on treatment E and crossed over to treatment D, and .

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

Dosage and administration details:

A single oral dose of 30 mg avacopan liquid formulation (5 mL of 6 mg/mL). The study drugs were administered orally with 240 mL of water

Arm title	Treatment E

Arm description:

30 mg avacopan liquid formulation fed, low fat, low calorie food. The total number of subjects reflects 8 subjects who started on treatment E and crossed over to treatment D, and 8 subjects who started on

treatment D and crossed over to treatment E.

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

Dosage and administration details:

A single oral dose of 30 mg avacopan liquid formulation (5 mL of 6 mg/mL). The study drugs were administered orally with 240 mL of water

Number of subjects in period 2	Treatment D	Treatment E
Started	16	16
Completed	16	16

Baseline characteristics

Reporting groups[1]	
Reporting group title	Stage 1
Reporting group description:	
Baseline characteristics for the safety population involved in stage 1. The safety population included all randomized subjects who received at least 1 dose of the study drug.	

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.
Justification: Stage 1 and stage 2 baseline characteristics are captured separately

Reporting group values	Stage 1	Total	
Number of subjects	15	15	
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)	15	15	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	38.5		
standard deviation	± 10.41	-	
Gender categorical Units: Subjects			
Female	9	9	
Male	6	6	
Race Units: Subjects			
White	15	15	
Ethnicity Units: Subjects			
Hispanic or Latino	10	10	
Not Hispanic or Latino	5	5	
Weight Units: kilogram(s)			
arithmetic mean	72.753		
standard deviation	± 13.2988	-	
Height Units: centimetre			
arithmetic mean	166.1		
standard deviation	± 10.41	-	
Body Mass Index Units: kilogram(s)/square metre			

arithmetic mean	26.24		
standard deviation	± 3.171	-	

Subject analysis sets	
Subject analysis set title	Stage 2
Subject analysis set type	Safety analysis

Subject analysis set description:

Baseline characteristics for the safety population involved in stage 2. The safety population included all randomized subjects who received at east 1 dose of the study drug.

Reporting group values	Stage 2		
Number of subjects	16		
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)	16		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean	38.8		
standard deviation	± 11.29		
Gender categorical Units: Subjects			
Female	10		
Male	6		
Race Units: Subjects			
White	15		
Ethnicity Units: Subjects			
Hispanic or Latino	16		
Not Hispanic or Latino			
Weight Units: kilogram(s)			
arithmetic mean	76.806		
standard deviation	± 15.2264		
Height Units: centimetre			
arithmetic mean	166.8		
standard deviation	± 8.90		
Body Mass Index Units: kilogram(s)/square metre			

arithmetic mean standard deviation	27.48 ± 3.949		

End points

End points reporting groups

Reporting group title	Treatment A
Reporting group description:	
30 mg Avacopan liquid formulation fasted	
Reporting group title	Treatment B
Reporting group description:	
30 mg Avacopan liquid formulation fed	
Reporting group title	Treatment C
Reporting group description:	
30 mg Avacopan capsules fasted	
Reporting group title	Treatment D
Reporting group description:	
30 mg avacopan liquid formulation fed, high fat, high calorie food. The total number of subjects reflects 8 subjects who started on treatment D and crossed over to treatment E, and 8 subjects who started on treatment E and crossed over to treatment D, and .	
Reporting group title	Treatment E
Reporting group description:	
30 mg avacopan liquid formulation fed, low fat, low calorie food. The total number of subjects reflects 8 subjects who started on treatment E and crossed over to treatment D, and 8 subjects who started on treatment D and crossed over to treatment E.	
Subject analysis set title	Stage 2
Subject analysis set type	Safety analysis
Subject analysis set description:	
Baseline characteristics for the safety population involved in stage 2. The safety population included all randomized subjects who received at east 1 dose of the study drug.	

Primary: Area under the plasma concentration-time curve from Time 0 to 24h of Avacopan in Plasma for the Overall Trial

End point title	Area under the plasma concentration-time curve from Time 0 to 24h of Avacopan in Plasma for the Overall Trial[1]
End point description:	
Area under the plasma concentration-time curve from Time 0 to 24h of Avacopan in Plasma for the overall trial	
End point type	Primary
End point timeframe:	
Baseline to end of study	

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: No statistical analysis has been performed on pharmacokinetic endpoints.

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	15	15	16
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	85.84 (± 87.8)	840.1 (± 37.4)	607.3 (± 45.5)	958.5 (± 31.2)

End point values	Treatment E			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	919.9 (± 31.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Area under the plasma concentration-time curve from Time 0 to 72h of Avacopan in Plasma for the Overall trial

End point title	Area under the plasma concentration-time curve from Time 0 to 72h of Avacopan in Plasma for the Overall trial[2]

End point description:

Area under the plasma concentration-time curve from Time 0 to 72h of Avacopan in Plasma for overall trial

End point type	Primary

End point timeframe:

Baseline to end of study

Notes:

[2] - 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: No statistical analysis has been performed on pharmacokinetic endpoints.

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	15	15	16
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	129.9 (± 78.9)	1008 (± 37.4)	707.9 (± 49.5)	1146 (± 30.4)

End point values	Treatment E			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	1097 (± 32.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Area under the plasma concentration-time curve from Time 0 to last of

Avacopan in Plasma for the Overall trial

End point title	Area under the plasma concentration-time curve from Time 0 to last of Avacopan in Plasma for the Overall trial[3]

End point description:

Area under the plasma concentration-time curve from Time 0 to last of Avacopan in Plasma for the Overall trial

End point type	Primary

End point timeframe:

Baseline to end of study

Notes:

[3] - 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: No statistical analysis has been performed on pharmacokinetic endpoints.

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	15	15	16
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	75.52 (± 137.0)	1142 (± 41.2)	763.4 (± 61.0)	1329 (± 31.4)

End point values	Treatment E			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	1241 (± 37.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Area under the plasma concentration-time curve from Time 0 to Infinity of Avacopan in Plasma for the Overall trial

End point title	Area under the plasma concentration-time curve from Time 0 to Infinity of Avacopan in Plasma for the Overall trial[4]

End point description:

Area under the plasma concentration-time curve from Time 0 to Infinity of Avacopan in Plasma for Overall trial

End point type	Primary

End point timeframe:

Baseline to end of study

Notes:

[4] - 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: No statistical analysis has been performed on pharmacokinetic endpoints.

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	15	15	16
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	140.4 (± 106.8)	1391 (± 44.7)	898.1 (± 71.1)	1589 (± 32.5)

End point values	Treatment E			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	1477 (± 39.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Plasma Concentration (Cmax) of Avacopan in the Overall trial

End point title	Maximum Plasma Concentration (Cmax) of Avacopan in the Overall trial[5]

End point description:

Maximum Plasma Concentration (Cmax) of Avacopan for the overall trial

End point type	Primary

End point timeframe:

Baseline to end of study

Notes:

[5] - 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: No statistical analysis has been performed on pharmacokinetic endpoints.

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	15	15	16
Units: ng/mL				
geometric mean (geometric coefficient of variation)	6.661 (± 138.0)	110.3 (± 43.0)	128.1 (± 33.4)	127.6 (± 24.2)

End point values	Treatment E			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	130.6 (± 24.1)			

Statistical analyses

No statistical analyses for this end point

Primary: Time to maximum Concentration (Tmax) of Avacopan for the Overall trial

End point title	Time to maximum Concentration (Tmax) of Avacopan for the Overall trial[6]

End point description:

Time to maximum Concentration (Tmax) of Avacopan for the Overall trial

End point type	Primary

End point timeframe:

Baseline to end of study

Notes:

[6] - 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: No statistical analysis has been performed on pharmacokinetic endpoints.

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	15	15	16
Units: hour				
median (full range (min-max))	5.999 (3.00 to 12.03)	6.000 (2.01 to 8.06)	1.527 (1.50 to 2.50)	4.000 (1.50 to 8.06)

End point values	Treatment E			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: hour				
median (full range (min-max))	4.001 (2.00 to 8.05)			

Statistical analyses

No statistical analyses for this end point

Primary: Area under the plasma concentration-time curve from Time 0 to 24h of Avacopan M1 metabolite in Plasma for the Overall trial

End point title	Area under the plasma concentration-time curve from Time 0 to 24h of Avacopan M1 metabolite in Plasma for the Overall trial[7]

End point description:

Area under the plasma concentration-time curve from Time 0 to 24h of Avacopan M1 metabolite in Plasma for the overall trial

End point type	Primary

End point timeframe:

Baseline to end of study

Notes:

[7] - 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: No statistical analysis has been performed on pharmacokinetic endpoints.

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	15	15	15
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	54.50 (± 55.6)	296.8 (± 18.8)	381.4 (± 24.8)	311.9 (± 15.9)

End point values	Treatment E			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	320.2 (± 19.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Area under the plasma concentration-time curve from Time 0 to 72h of Avacopan M1 Metabolite in Plasma for the Overall trial

End point title	Area under the plasma concentration-time curve from Time 0 to 72h of Avacopan M1 Metabolite in Plasma for the Overall trial[8]

End point description:

Area under the plasma concentration-time curve from Time 0 to 72h of Avacopan M1 Metabolite in Plasma for the Overall trial

End point type	Primary

End point timeframe:

Baseline to end of study

Notes:

[8] - 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: No statistical analysis has been performed on pharmacokinetic endpoints.

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	15	15	15
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	93.23 (± 75.2)	493.4 (± 20.9)	563.5 (± 27.4)	501.5 (± 17.3)

End point values	Treatment E			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	519.5 (± 23.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Area under the plasma concentration-time curve from Time 0 to last of Avacopan M1 Metabolite in Plasma for the Overall Trial

End point title	Area under the plasma concentration-time curve from Time 0 to last of Avacopan M1 Metabolite in Plasma for the Overall Trial[9]

End point description:

Area under the plasma concentration-time curve from Time 0 to last of Avacopan M1 Metabolite in Plasma for the Overall trial

End point type	Primary

End point timeframe:

Baseline to End of Study

Notes:

[9] - 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: No statistical analysis has been performed on pharmacokinetic endpoints.

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	15	15	15
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	25.20 (± 250.7)	585.7 (± 35.5)	647.6 (± 40.7)	623.8 (± 23.6)

End point values	Treatment E			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: ng*hr/mL				

geometric mean (geometric coefficient of variation)	645.2 (± 32.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Area under the plasma concentration-time curve from Time 0 to Infinity of Avacopan M1 Metabolite in Plasma for the Overall trial

End point title	Area under the plasma concentration-time curve from Time 0 to Infinity of Avacopan M1 Metabolite in Plasma for the Overall trial[10]

End point description:

Area under the plasma concentration-time curve from Time 0 to Infinity of Avacopan M1 Metabolite in Plasma for the Overall trial

End point type	Primary

End point timeframe:

Baseline to end of study

Notes:

[10] - 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: No statistical analysis has been performed on pharmacokinetic endpoints.

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	15	15	15
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	104.6 (± 120.1)	706.7 (± 28.0)	758.0 (± 38.3)	738.5 (± 21.8)

End point values	Treatment E			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	763.3 (± 31.1)			

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Plasma Concentration (Cmax) of Avacopan M1 Metabolite in the Overall trial

End point title	Maximum Plasma Concentration (Cmax) of Avacopan M1 Metabolite in the Overall trial[11]

End point description:

Maximum Plasma Concentration (Cmax) of Avacopan M1 Metabolite in the Overall trial

End point type	Primary

End point timeframe:

Baseline to end of study

Notes:

[11] - 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: No statistical analysis has been performed on pharmacokinetic endpoints.

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	15	15	15
Units: ng/mL				
geometric mean (geometric coefficient of variation)	3.090 (± 84.3)	24.36 (± 23.0)	51.48 (± 23.6)	25.60 (± 12.3)

End point values	Treatment E			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	28.82 (± 19.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Time to maximum Concentration (Tmax) of Avacopan M1 Metabolite in the Overall trial

End point title	Time to maximum Concentration (Tmax) of Avacopan M1 Metabolite in the Overall trial[12]

End point description:

Time to maximum Concentration (Tmax) of Avacopan M1 Metabolite in the Overall trial

End point type	Primary

End point timeframe:

Baseline to end of study

Notes:

[12] - 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: No statistical analysis has been performed on pharmacokinetic endpoints.

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	15	15	15
Units: hour				
median (full range (min-max))	5.998 (4.00 to 8.01)	7.998 (2.99 to 8.06)	2.500 (1.52 to 3.02)	5.997 (3.00 to 8.06)

End point values	Treatment E			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: hour				
median (full range (min-max))	5.999 (3.00 to 8.05)			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs) during the trial

End point title	Incidence of treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs) during the trial

End point description:

Incidence of treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs) during the trial

End point type	Secondary

End point timeframe:

Baseline to end of study

End point values	Treatment A	Treatment B	Treatment C	Treatment D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	15	15	8
Units: Number				
TEAEs	2	2	1	1
SAEs	0	0	0	0

End point values	Treatment E			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Number				
TEAEs	4			

SAEs	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Baseline to end of study	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1
Reporting groups	
Reporting group title	Treatment A
Reporting group description: 30 mg Avacopan liquid formulation fasted	
Reporting group title	Treatment B
Reporting group description: 30 mg Avacopan liquid formulation fed	
Reporting group title	Treatment C
Reporting group description: 30 mg Avacopan capsules fasted	
Reporting group title	Treatment D
Reporting group description: 30 mg avacopan liquid formulation fed, high fat, high calorie food	
Reporting group title	Treatment E
Reporting group description: 30 mg avacopan liquid formulation fed, low fat, low calorie food	

Serious adverse events	Treatment A	Treatment B	Treatment C
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 15 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Treatment D	Treatment E	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (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: 5 %

Non-serious adverse events	Treatment A	Treatment B	Treatment C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 15 (13.33%)	2 / 15 (13.33%)	1 / 15 (6.67%)
Investigations			
Heart rate increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Sunburn			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Vessel puncture site bruise			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Vessel puncture site pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Lip scab			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Abdominal distension			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Flatulence			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Treatment D	Treatment E	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 16 (6.25%)	4 / 16 (25.00%)	
Investigations			
Heart rate increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Sunburn			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	1 / 16 (6.25%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Vessel puncture site bruise			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Vessel puncture site pain			

subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Lip scab			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Abdominal distension			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Flatulence			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	1 / 16 (6.25%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 April 2022	Clarity to staging timings, footnote corrections, inclusion criteria for men and women updated from 90 to 120 days, removal of the need to have a seated or supine blood test for PK samples, clarity for healthy subjects. Consistency made throughout, clarity added and corrections made throughout.
14 June 2022	Consistency made throughout, clarity added and corrections made throughout.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported