Clinical trial results:
Prospective, open-label, single arm, multicenter, pharmacokinetic, and safety study of a single dose intravenous human plasma-derived C1 Esterase Inhibitor (C1-INH) concentrate in patients with congenital C1-INH deficiency and hereditary angioedema

Summary

EudraCT number	2019-001693-28
Trial protocol	DE
Global end of trial date	17 February 2021

Results information

Result version number	v1 (current)
This version publication date	17 February 2022
First version publication date	17 February 2022

Trial information

Trial identification

Sponsor protocol code	CONE-01

Additional study identifiers

ISRCTN number	ISRCTN36746902
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Octapharma Pharmazeutika Produktionsges.m.b.H.
Sponsor organisation address	Oberlaaer Strasse 235, Vienna, Austria, 1100
Public contact	Global Clinical Project Manager, Octapharma Pharmazeutika Produktionsges.m.b.H., +43 (0)1 610 320, christiane.thomasser@octapharma.com
Scientific contact	Global Clinical Project Manager, Octapharma Pharmazeutika Produktionsges.m.b.H., +43 (0)1 610 320, christiane.thomasser@octapharma.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	09 September 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 February 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to assess the pharmacokinetic (PK) characteristics of OCTA-C1-INH after a single intravenous (IV) administration in HAE patients who are not experiencing an HAE attack.

Protection of trial subjects:

This trial was conducted in accordance to the principles of ICH- GCP, ensuring that the rights, safety and well-being of patients are protected and in consistency with the Declaration of Helsinki and national regulatory requirements. Inclusion and exclusion criteria were carefully defined in order to protect subjects from contraindications, interactions with other medication and risk factors associated with the investigational medicinal product. Throughout the study safety was assessed, such as monitoring of adverse events and concomitant medication.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 September 2020
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	Belarus: 2
Country: Number of subjects enrolled	Russian Federation: 11
Country: Number of subjects enrolled	Ukraine: 7
Worldwide total number of subjects	20
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)	19
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients with documented congenital C1-INH deficiency and hereditary angioedema type I and type II were screened according to predefined in- and exclusion criteria.

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	OCTA-C1-INH

Arm description:

The IP was given as a single dose of 20 IU/kg BW administered by slow IV injection during mandatory hospitalization.

Arm type	Experimental
Investigational medicinal product name	OCTA-C1-INH
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

The IP was to be reconstituted with a 2.5 mL WFI syringe by using a vial adapter and transferring the WFI into the vial containing the concentrate and was given as a single dose of 20 IU/kg BW administered by slow IV injection during mandatory hospitalization.

Number of subjects in period 1	OCTA-C1-INH
Started	20
Completed	20

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	20	20	
Age categorical Units: Subjects			
Age continuous Units: years median full range (min-max)	 38.5 18 to 66	 -	
Gender categorical Units: Subjects			
Female	11	11	
Male	9	9	

End points

End points reporting groups

Reporting group title	OCTA-C1-INH
Reporting group description:	
The IP was given as a single dose of 20 IU/kg BW administered by slow IV injection during mandatory hospitalization.	
Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description:	
Full analysis set (FAS) is defined according to the intention-to-treat (ITT) principle and consists of all patients of the safety analysis set who satisfy all eligibility criteria and for whom any postbaseline data is available; it is the set of eligible patients with treatment effects measured.	
Subject analysis set title	Preinjection
Subject analysis set type	Full analysis
Subject analysis set description:	
Preinjection	
Subject analysis set title	0 minutes
Subject analysis set type	Full analysis
Subject analysis set description:	
0 minutes	
Subject analysis set title	15 minutes
Subject analysis set type	Full analysis
Subject analysis set description:	
15 minutes	
Subject analysis set title	1 hour
Subject analysis set type	Full analysis
Subject analysis set description:	
1 hour	
Subject analysis set title	2 hours
Subject analysis set type	Full analysis
Subject analysis set description:	
2 hours	
Subject analysis set title	6 hours
Subject analysis set type	Full analysis
Subject analysis set description:	
6 hours	
Subject analysis set title	12 hours
Subject analysis set type	Full analysis
Subject analysis set description:	
12 hours	
Subject analysis set title	24 hours
Subject analysis set type	Full analysis
Subject analysis set description:	
24 hours	
Subject analysis set title	48 hours
Subject analysis set type	Full analysis
Subject analysis set description:	
48 hours	
Subject analysis set title	72 hours
Subject analysis set type	Full analysis

Subject analysis set description: 72 hours	
Subject analysis set title	120 hours
Subject analysis set type	Full analysis
Subject analysis set description: 120 hours	
Subject analysis set title	144 hours
Subject analysis set type	Full analysis
Subject analysis set description: 144 hours	
Subject analysis set title	168 hours
Subject analysis set type	Full analysis
Subject analysis set description: 168 hours	

Primary: C1-INH Activity concentrations

End point title	C1-INH Activity concentrations[1]

End point description:

Blood concentrations of C1-INH at each sampling time (Preinjection, 0 minutes, 15 minutes, 1 hour, 2 hours, 6 hours, 12 hours,24 hours, 48 hours, 72 hours, 120 hours, 144 hours, 168 hours)

End point type	Primary

End point timeframe:

Preinjection, 0 minutes, 15 minutes, 1 hour, 2 hours, 6 hours, 12 hours,24 hours, 48 hours, 72 hours, 120 hours, 144 hours, 168 hours

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: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	Preinjection	0 minutes	15 minutes	1 hour
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	17	17	20	20
Units: IU/mL				
number (not applicable)				
Mean	0.0841	1.09	0.826	0.8
SD	0.168	1.1	0.215	0.184
Median	0	0.73	0.76	0.765
Min	0	0.35	0.58	0.57
Max	0.51	5.2	1.53	1.29
(n)	17	17	20	20

End point values	2 hours	6 hours	12 hours	24 hours
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	20	20
Units: IU/mL				
number (not applicable)				
Mean	0.765	0.682	0.637	0.603
SD	0.156	0.116	0.13	0.118
Median	0.745	0.67	0.59	0.605

Min	0.55	0.47	0.45	0.38
Max	1.21	0.88	0.88	0.85
(n)	20	20	20	20

End point values	48 hours	72 hours	120 hours	144 hours
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	20	20
Units: IU/mL				
number (not applicable)				
Mean	0.453	0.35	0.142	0.127
SD	0.106	0.0772	0.137	0.136
Median	0.44	0.335	0.2	0.1
Min	0.22	0.24	0	0
Max	0.73	0.52	0.33	0.36
(n)	20	20	20	20

End point values	168 hours			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: IU/mL				
number (not applicable)				
Mean	0.053			
SD	0.109			
Median	0			
Min	0			
Max	0.3			
(n)	20			

Statistical analyses

No statistical analyses for this end point

Primary: C1-INH Activity AUC inf

End point title	C1-INH Activity AUC inf[2]

End point description:

Area under the concentration-time curve from time zero extrapolated to infinite time

End point type	Primary

End point timeframe:

Day 0 to Day 7 after IMP injection

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: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: h*IU/mL				
number (not applicable)				
Mean	102			
Median	102			
Min	102			
Max	102			
Geometric mean	102			
(n)	1			

Statistical analyses

No statistical analyses for this end point

Primary: C1-INH Activity AUCnorm

End point title	C1-INH Activity AUCnorm[3]

End point description:

Area under the concentration-time curve normalized by the dose

End point type	Primary

End point timeframe:

Day 0 to Day 7 after IMP injection

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: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: h*IU/mL/IU				
number (not applicable)				
Mean	0.055			
Median	0.055			
Min	0.055			
Max	0.055			
Geometric mean	0.055			
(n)	1			

Statistical analyses

No statistical analyses for this end point

Primary: C1-INH Activity AUC last

End point title	C1-INH Activity AUC last[4]

End point description:

Area under the concentration-time curve from time 0 to the time of the last measurable concentration

End point type	Primary

End point timeframe:

Day 0 to Day 7 after IMP injection

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: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: h*IU/mL				
number (not applicable)				
Mean	51.6			
SD	17.9			
Median	49.7			
Min	25.6			
Max	83.9			
Geometric mean	48.6			
Geometric mean CV (%)	36.7			
(n)	20			

Statistical analyses

No statistical analyses for this end point

Primary: C1-INH Activity CL

End point title	C1-INH Activity CL[5]

End point description:

Clearance

End point type	Primary

End point timeframe:

Day 0 to Day 7 after IMP injection

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: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: L/h				
number (not applicable)				
Mean	0.0182			

Median	0.0182			
Min	0.0182			
Max	0.0182			
Geometric mean	0.0182			
(n)	1			

Statistical analyses

No statistical analyses for this end point

Primary: C1-INH Activity Cmax

End point title	C1-INH Activity Cmax[6]

End point description:

Maximum observed blood concentration

End point type	Primary

End point timeframe:

Day 0 to Day 7 after IMP injection

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: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: IU/mL				
number (not applicable)				
Mean	1.14			
SD	0.989			
Median	0.85			
Min	0.85			
Max	5.2			
Geometric mean	0.973			
Geometric mean CV (%)	49.8			
(n)	20			

Statistical analyses

No statistical analyses for this end point

Primary: C1-INH Activity Cmax/D

End point title	C1-INH Activity Cmax/D[7]

End point description:

Maximum observed blood concentration normalized by the dose

End point type	Primary

End point timeframe:

Day 0 to Day 7 after IMP injection

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: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: IU/mL/IU				
number (not applicable)				
Mean	0.00083			
SD	0.000841			
Median	0.000664			
Min	0.000353			
Max	0.00433			
Geometric mean	0.000687			
Geometric mean CV (%)	54.7			
(n)	20			

Statistical analyses

No statistical analyses for this end point

Primary: C1-INH Activity T 1/2

End point title	C1-INH Activity T 1/2[8]

End point description:

Elimination half-life

End point type	Primary

End point timeframe:

Day 0 to Day 7 after IMP injection

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: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: (h)				
number (not applicable)				
Mean	74.1			
SD	19			
Median	77.2			
Min	39.5			
Max	109			

Geometric mean	71.6			
Geometric mean CV (%)	28.1			
(n)	20			

Statistical analyses

No statistical analyses for this end point

Primary: C1-INH Activity MRT

End point title	C1-INH Activity MRT[9]

End point description:

Mean residence time

End point type	Primary

End point timeframe:

Day 0 to Day 7 after IMP injection

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: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: (h)				
number (not applicable)				
Mean	85.5			
Median	85.5			
Min	85.5			
Max	85.5			
Geometric mean	85.5			
(n)	1			

Statistical analyses

No statistical analyses for this end point

Primary: C1-INH Activity Tmax

End point title	C1-INH Activity Tmax[10]

End point description:

Time to maximum blood concentration

End point type	Primary

End point timeframe:

Day 0 to Day 7 after IMP injection

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: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: (h)				
number (not applicable)				
Mean	0.598			
SD	0.716			
Median	0.308			
Min	0.0667			
Max	2.08			
Geometric mean	0.295			
Geometric mean CV (%)	189			
(n)	20			

Statistical analyses

No statistical analyses for this end point

Primary: C1-INH Activity Vd	
End point title	C1-INH Activity Vd[11]
End point description: Volume of distribution	
End point type	Primary
End point timeframe: Day 0 to Day 7 after IMP injection	

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: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: (L)				
number (not applicable)				
Mean	1.52			
Median	1.52			
Min	1.52			
Max	1.52			
Geometric mean	1.52			
(n)	1			

Statistical analyses

No statistical analyses for this end point

Primary: C1-INH Activity IR

End point title	C1-INH Activity IR[12]

End point description:

Incremental recovery

End point type	Primary

End point timeframe:

Day 0 to Day 7 after IMP injection

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: The system does not permit reporting of statistical analyses for studies with only 1 arm/reporting group. Therefore, only results for this endpoint are provided.

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: ([IU*kg]/[IU*mL])				
number (not applicable)				
Mean	0.0466			
SD	0.051			
Median	0.0388			
Min	-0.0065			
Max	0.246			
Geometric mean	0.0367			
Geometric mean CV (%)	91.4			
(n)	20			

Statistical analyses

No statistical analyses for this end point

Secondary: C1-INH Antigen Concentrations

End point title	C1-INH Antigen Concentrations

End point description:

Blood concentrations of C1-INH antigen at each sampling time (Preinjection, 0 minutes, 15 minutes, 1 hour, 2 hours, 6 hours, 12 hours,24 hours, 48 hours, 72 hours, 120 hours, 144 hours, 168 hours)

End point type	Secondary

End point timeframe:

Preinjection, 0 minutes, 15 minutes, 1 hour, 2 hours, 6 hours, 12 hours,24 hours, 48 hours, 72 hours,

End point values	Preinjection	0 minutes	15 minutes	1 hour
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	17	16	20	20
Units: g/L				
number (not applicable)				
Mean	0.1	0.216	0.211	0.201
SD	0.107	0.105	0.0961	0.102
Median	0.05	0.18	0.19	0.17
Min	0	0.12	0.12	0.09
Max	0.37	0.51	0.54	0.51
(n)	17	16	20	20

End point values	2 hours	6 hours	12 hours	24 hours
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	20	20
Units: g/L				
number (not applicable)				
Mean	0.192	0.195	0.179	0.167
SD	0.0822	0.0816	0.0797	0.085
Median	0.165	0.18	0.155	0.14
Min	0.1	0.1	0.1	0.11
Max	0.47	0.48	0.47	0.46
(n)	20	20	20	20

End point values	48 hours	72 hours	120 hours	144 hours
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	20	20
Units: g/L				
number (not applicable)				
Mean	0.142	0.126	0.093	0.0865
SD	0.0766	0.0815	0.088	0.0921
Median	0.12	0.1	0.07	0.06
Min	0.09	0.08	0.02	0
Max	0.41	0.4	0.41	0.42
(n)	20	20	20	20

End point values	168 hours			

Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: g/L				
number (not applicable)				
Mean	0.085			
SD	0.0919			
Median	0.06			
Min	0.03			
Max	0.43			
(n)	20			

Statistical analyses

No statistical analyses for this end point

Secondary: C1-INH Antigen AUCinf

End point title	C1-INH Antigen AUCinf

End point description:

Area under the concentration-time curve from time zero extrapolated to infinite time

End point type	Secondary

End point timeframe:

Day 0 to Day 7 after IMP injection

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: h*g/L				
number (not applicable)				
Mean	17.8			
SD	0.871			
Median	17.8			
Min	17.1			
Max	18.4			
Geometric mean	17.8			
Geometric mean CV (%)	4.91			
(n)	2			

Statistical analyses

No statistical analyses for this end point

Secondary: C1-INH Antigen AUCnorm

End point title	C1-INH Antigen AUCnorm

End point description:
Area under the concentration-time curve normalized by the dose

End point type	Secondary

End point timeframe:
Day 0 to Day 7 after IMP injection

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: h*g/L/g				
number (not applicable)				
Mean	46.7			
SD	6.82			
Median	46.7			
Min	41.9			
Max	51.5			
Geometric mean	46.4			
Geometric mean CV (%)	14.7			
(n)	2			

Statistical analyses

No statistical analyses for this end point

Secondary: C1-INH Antigen AUClast

End point title	C1-INH Antigen AUClast

End point description:
Area under the concentration-time curve from time 0 to the time of the last measurable concentration

End point type	Secondary

End point timeframe:
Timeframe: Day 0 to Day 7 after IMP injection

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: h*g/L/g				
number (not applicable)				
Mean	20.7			
SD	14			
Median	16.2			
Min	13.8			
Max	71.5			

Geometric mean	18.5			
Geometric mean CV (%)	43.4			
(n)	20			

Statistical analyses

No statistical analyses for this end point

Secondary: C1-INH Antigen CL

End point title	C1-INH Antigen CL
End point description: Clearance	
End point type	Secondary
End point timeframe: Day 0 to Day 7 after IMP injection	

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: L/h				
number (not applicable)				
Mean	0.0216			
SD	0.00316			
Median	0.0216			
Min	0.0194			
Max	0.0239			
Geometric mean	0.0215			
Geometric mean CV (%)	14.7			
(n)	2			

Statistical analyses

No statistical analyses for this end point

Secondary: C1-INH Antigen Cmax

End point title	C1-INH Antigen Cmax
End point description: Maximum observed blood concentration	
End point type	Secondary
End point timeframe: Day 0 to Day 7 after IMP injection	

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: g/L				
number (not applicable)				
Mean	0.239			
SD	0.1			
Median	0.205			
Min	0.15			
Max	0.54			
Geometric mean	0.224			
Geometric mean CV (%)	35.4			
(n)	20			

Statistical analyses

No statistical analyses for this end point

Secondary: C1-INH Antigen Cmax/D

End point title	C1-INH Antigen Cmax/D
End point description:	
Maximum observed blood concentration normalized by the dose	
End point type	Secondary
End point timeframe:	
Day 0 to Day 7 after IMP injection	

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: g/L/g				
number (not applicable)				
Mean	0.718			
SD	0.368			
Median	0.655			
Min	0.341			
Max	1.78			
Geometric mean	0.655			
Geometric mean CV (%)	43			
(n)	20			

Statistical analyses

No statistical analyses for this end point

Secondary: C1-INH Antigen T1/2

End point title	C1-INH Antigen T1/2
End point description: Elimination half-life	
End point type	Secondary
End point timeframe: Day 0 to Day 7 after IMP injection	

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	19			
Units: (h)				
number (not applicable)				
Mean	118			
SD	76.4			
Median	104			
Min	46.9			
Max	416			
Geometric mean	106			
Geometric mean CV (%)	46.1			
(n)	19			

Statistical analyses

No statistical analyses for this end point

Secondary: C1-INH Antigen MRT

End point title	C1-INH Antigen MRT
End point description: Mean residence time	
End point type	Secondary
End point timeframe: Day 0 to Day 7 after IMP injection	

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: (h)				
number (not applicable)				
Mean	78.5			
SD	12.8			
Median	78.5			
Min	69.4			
Max	87.5			
Geometric mean	78			
Geometric mean CV (%)	16.4			
(n)	2			

Statistical analyses

No statistical analyses for this end point

Secondary: C1-INH Antigen Tmax

End point title	C1-INH Antigen Tmax
End point description: Time to maximum blood concentration	
End point type	Secondary
End point timeframe: Day 0 to Day 7 after IMP injection	

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: (h)				
number (not applicable)				
Mean	1.54			
SD	2.38			
Median	0.317			
Min	0			
Max	6.1			
Geometric mean	0.453			
Geometric mean CV (%)	420			
(n)	20			

Statistical analyses

No statistical analyses for this end point

Secondary: C1-INH Antigen Vd

End point title	C1-INH Antigen Vd
End point description: Volume of distribution	
End point type	Secondary
End point timeframe: Day 0 to Day 7 after IMP injection	

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: (L)				
number (not applicable)				
Mean	1.57			
SD	0.0674			
Median	1.57			
Min	1.52			
Max	1.61			
Geometric mean	1.57			
Geometric mean CV (%)	4.31			
(n)	2			

Statistical analyses

No statistical analyses for this end point

Secondary: C4 Antigen Concentrations

End point title	C4 Antigen Concentrations
End point description: Blood concentrations of C4 Antigen at each sampling time (Preinjection, 0 minutes, 15 minutes, 1 hour, 2 hours, 6 hours, 12 hours,24 hours, 48 hours, 72 hours, 120 hours, 144 hours, 168 hours)	
End point type	Secondary
End point timeframe: Preinjection, 0 minutes, 15 minutes, 1 hour, 2 hours, 6 hours, 12 hours,24 hours, 48 hours, 72 hours, 120 hours, 144 hours, 168 hours	

End point values	Preinjection	0 minutes	15 minutes	1 hour
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	17	17	20	20
Units: g/L				
number (not applicable)				
Mean	0.0482	0.04	0.0425	0.0465
SD	0.0238	0.0203	0.0234	0.027
Median	0.05	0.04	0.04	0.04
Min	0.02	0.01	0.01	0.02
Max	0.11	0.1	0.1	0.11
(n)	17	17	20	20

End point values	2 hours	6 hours	12 hours	24 hours
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	20	20
Units: g/L				
number (not applicable)				
Mean	0.049	0.073	0.0765	0.087
SD	0.0288	0.0305	0.0248	0.0292
Median	0.05	0.07	0.08	0.09
Min	0	0.03	0.03	0.04
Max	0.1	0.13	0.13	0.18
(n)	20	20	20	20

End point values	48 hours	72 hours	120 hours	144 hours
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	20	20
Units: g/L				
number (not applicable)				
Mean	0.11	0.115	0.0945	0.082
SD	0.0361	0.0444	0.0389	0.0405
Median	0.105	0.11	0.09	0.08
Min	0.06	0.06	0.01	0.01
Max	0.22	0.27	0.21	0.21
(n)	20	20	20	20

End point values	168 hours			
Subject group type	Subject analysis set			
Number of subjects analysed	20			

Units: g/L				
number (not applicable)				
Mean	0.072			
SD	0.0409			
Median	0.07			
Min	0.02			
Max	0.21			
(n)	20			

Statistical analyses

No statistical analyses for this end point

Secondary: C4 Antigen AUCinf

End point title	C4 Antigen AUCinf

End point description:

Area under the concentration-time curve from time zero extrapolated to infinite time

End point type	Secondary

End point timeframe:

Day 0 to Day 7 after IMP injection

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: h*g/L				
number (not applicable)				
Mean	13.4			
SD	5.9			
Median	13.4			
Min	9.25			
Max	17.6			
Geometric mean	12.8			
Geometric mean CV (%)	47.9			
(n)	2			

Statistical analyses

No statistical analyses for this end point

Secondary: C4 Antigen AUClast

End point title	C4 Antigen AUClast

End point description:

Area under the concentration-time curve from time 0 to the time of the last measurable concentration

End point type	Secondary
End point timeframe:	
Day 0 to Day 7 after IMP injection	

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: h*g/L				
number (not applicable)				
Mean	15.8			
SD	4.68			
Median	15.7			
Min	8.37			
Max	28.4			
Geometric mean	15.1			
Geometric mean CV (%)	30.9			
(n)	20			

Statistical analyses

No statistical analyses for this end point

Secondary: C4 Antigen Cmax

End point title	C4 Antigen Cmax
End point description:	
Maximum observed blood concentration	
End point type	Secondary
End point timeframe:	
Day 0 to Day 7 after IMP injection	

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: g/L				
number (not applicable)				
Mean	0.129			
SD	0.0467			
Median	0.125			
Min	0.07			
Max	0.27			
Geometric mean	0.122			
Geometric mean CV (%)	33.1			

(n)	20			

Statistical analyses

No statistical analyses for this end point

Secondary: C4 Antigen T1/2

End point title	C4 Antigen T1/2
End point description: Elimination half-life	
End point type	Secondary
End point timeframe: Day 0 to Day 7 after IMP injection	

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	13			
Units: (h)				
number (not applicable)				
Mean	85.4			
SD	34.8			
Median	82.6			
Min	27.5			
Max	134			
Geometric mean	77.3			
Geometric mean CV (%)	53.7			
(n)	13			

Statistical analyses

No statistical analyses for this end point

Secondary: C4 Antigen MRT

End point title	C4 Antigen MRT
End point description: Mean residence time	
End point type	Secondary
End point timeframe: Day 0 to Day 7 after IMP injection	

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: (h)				
number (not applicable)				
Mean	89.7			
SD	3.91			
Median	89.7			
Min	86.9			
Max	92.4			
Geometric mean	89.6			
Geometric mean CV (%)	4.37			
(n)	2			

Statistical analyses

No statistical analyses for this end point

Secondary: C4 Antigen Tmax

End point title	C4 Antigen Tmax
End point description: Time to maximum blood concentration	
End point type	Secondary
End point timeframe: Day 0 to Day 7 after IMP injection	

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: (h)				
number (not applicable)				
Mean	53.7			
SD	22.8			
Median	59.4			
Min	6			
Max	72.7			
Geometric mean	44.3			
Geometric mean CV (%)	93.8			
(n)	20			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Throughout the whole study from V1 (screeening) up to final visit (Visit 9 or early discontinuation).	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0
Reporting groups	
Reporting group title	Safety analysis (SA) set
Reporting group description: The safety analysis (SA) set consists of all patients who receive any amount of the IMP injection.	

Serious adverse events	Safety analysis (SA) set		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Safety analysis (SA) set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 20 (35.00%)		
Investigations			
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Congenital, familial and genetic disorders			
Hereditary angioedema			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Nervous system disorders			
Headache			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Psychiatric disorders			
Mixed anxiety and depressive disorder			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Osteoporosis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 November 2019	Protocol V03 + Amendment V01: Implementation of German competent authority (PEI) comments in their letter of deficiency dated 07-Nov-2019 to initial study submission: • one additional PK at timepoint 2 hours after IMP administration • Wells probability score for DVT and PE at 3 timepoints and subsequent D-dimer testing and where required a Doppler screening for DVT • include Adverse Events of Special Interest (AESI) of thromboembolic event (TEE) type as standalone safety endpoint
30 January 2020	Protocol V02.2 (Submitted in UKR only): • Implementation of Ukrainian competent authority comments in their Letter of deficiency dated 22 Nov 2019 to initial study submission. Development phase was re-classified to "phase 1" • Mandatory hospitalization for patient observation during and after IMP administration (24 hours from Day 0 to Day 1).
29 April 2020	Protocol V04 + Amendment V03: • Implementation of Ukrainian competent authority comments to include mandatory hospitalization for 24 hours. • Serology testing was added for more precise testing.
03 May 2020	Protocol V04.1 (Submitted in UKR only) • Implementation of German competent authority comments (PEI): - one additional PK at timepoint 2 hours after IMP administration - Wells probability score for DVT and PE at 3 timepoints and subsequent D-dimer testing and where required a Doppler screening for DVT - including Adverse Events of Special Interest (AESI) of thromboembolic event (TEE) type as standalone safety endpoint • Serology testing was added for more precise testing.
30 December 2020	Protocol V05.1 (Submitted in UKR only): • Adaption of exclusion criterion #5 to exclude also female patients on specific androgen therapy.
30 December 2020	Protocol V05 + Amendment V04: • Adaption of exclusion criterion #5 to exclude also female patients on specific androgen therapy

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported