Clinical trial results:
A multicenter, randomized, active controlled, open label, platform trial on the efficacy and safety of experimental therapeutics for patients with COVID-19 (caused by infection with severe acute respiratory syndrome coronavirus-2)

ACOVACT (Austrian CoronaVirus Adaptive Clinical Trial)

Summary

EudraCT number	2020-001302-30
Trial protocol	AT
Global end of trial date	03 November 2022

Results information

Result version number	v1 (current)
This version publication date	19 November 2023
First version publication date	19 November 2023
Summary attachment (see zip file)	Adverse Events (ACOVACT_Adverse_Events.pdf)

Trial information

Trial identification

Sponsor protocol code	ACOVACT

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University of Vienna
Sponsor organisation address	Währinger Gürtel 18-20, Vienn, Austria, 1090
Public contact	Sponsor, Medical University of Vienna, Department of Clinical Pharmacology, klin-pharmakologie@meduniwien.ac.at
Scientific contact	Sponsor, Medical University of Vienna, Department of Clinical Pharmacology, klin-pharmakologie@meduniwien.ac.at

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 February 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 February 2022
Global end of trial reached?	Yes
Global end of trial date	03 November 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To investigate the efficacy of various experimental therapeutics for patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); for efficacy assessment an ordinal scale for clinical severity assessment as proposed by the World Health Organization was used:
Time to sustained improvement of one category from admission.

Protection of trial subjects:

For "antiviral" treatment arms and sub-studies only hospitalized patients were included and intake of medication was intensly controlled.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 April 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	Austria: 345
Worldwide total number of subjects	345
EEA total number of subjects	345

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)	225
From 65 to 84 years	112
85 years and over	8

Subject disposition

Recruitment

Recruitment details:

Subjects were selected per study site from the pool of admitted patients. No extra recruitment strategies were necessary.

Pre-assignment

Screening details:

During the screening procedure the patients' eligibility for each trial arm was checked. The main prerequisite was a laboratory or radiologically proven infection with SARS-CoV-2.

Period 1

Period 1 title	Treatment period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Main Study

Arm description:

Main "antiviral therapy" study:
Reporting group 1: Resochin/Quensyl
Reporting group 2: Kaletra
Reporting group 3: Veklury
Reporting group 4: Standard of care (SOC) ("control arm" of the study)

Arm type	Active comparator
Investigational medicinal product name	Quensyl
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200mg 2-0-2 Maintenance dose: 200 mg 1-0-1

Investigational medicinal product name	Kaletra
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Kaletra low-dose: Initial and maintenance dose: 200 mg/50 mg 2-0-2
Kaletra high-dose: Initial dose: 200 mg/50 mg 4-0-4, maintenance dose: 200mg/50mg 3-0-3

Investigational medicinal product name	Veklury
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Initial dose: 200mg/day
Maintenance dose: 100mg/day

Arm title	Substudy A

Arm description:

Subjects received Xarelto versus standard of care

Arm type	Active comparator
Investigational medicinal product name	Xarelto
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Initial dose: 10 mg 1/2-0-1/2
Maintenance dose: down-titration allowed in case of high anti-FXa activity before the next dose

Arm title	Substudy B- Cohort 1

Arm description:

- Stay on any RAS blockade: patients with previously known and treated hypertension (treatment according to standard of care).
- Switch to non-RAS blocking agent: switch of patients with previously known and treated hypertension to non-RAS blocking agents (treatment according to standard of care, e.g. nitrendipine, amlodipine or doxazosin)

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Substudy B- Cohort 2

Arm description:

- Treatment with RAS blocking agent: treatment of patients with blood pressure >130/85mmHg in two consecutive measurements with RAS blocking agent candesartan (Blopress)
- Non-RAS blocking agents: treatment according to standard of care, e.g. with nitrendipine, amlodipine or doxazosin, or no treatment, if blood pressure <140/90mmHg.

Arm type	Active comparator
Investigational medicinal product name	Blopress
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Initial dose: candesartan 8 mg 1-0-0;
Maintenance dose: Up-titration to normotension

Arm title	Substudy C - Asunercept

Arm description:

- Asunercept randomized against standard of care (25 mg, 100 mg or 400 mg according to the respective randomized sub-arm)

Arm type	Active comparator
Investigational medicinal product name	Asunercept
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Initial dose: 25 mg, 100 mg or 400 mg once a week according to the respective randomized sub-arm.
Maintenance dose: same as first dosage.

Arm title	Substudy C - Pentaglobin

Arm description:

- Pentaglobin randomized against standard of care

Arm type	Active comparator
Investigational medicinal product name	Pentaglobin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Continuous i.v. application of a total dose of 7ml/kg/day
Infusion over 12h

Number of subjects in period 1	Main Study	Substudy A	Substudy B- Cohort 1
Started	224	145	60
Completed	214	140	59
Not completed	10	5	1
Own Request	3	2	-
screening failure	3	1	-
dropout	4	2	1

Number of subjects in period 1	Substudy B- Cohort 2	Substudy C - Asunercept	Substudy C - Pentaglobin
Started	8	102	34
Completed	7	99	32
Not completed	1	3	2
Own Request	-	3	-
screening failure	1	-	1
dropout	-	-	1

Baseline characteristics

Reporting groups[1]	
Reporting group title	Main Study
Reporting group description:	
Main "antiviral therapy" study: Reporting group 1: Resochin/Quensyl Reporting group 2: Kaletra Reporting group 3: Veklury Reporting group 4: Standard of care (SOC) ("control arm" of the study)	
Reporting group title	Substudy A
Reporting group description:	
Subjects received Xarelto versus standard of care	
Reporting group title	Substudy B- Cohort 1
Reporting group description:	
• Stay on any RAS blockade: patients with previously known and treated hypertension (treatment according to standard of care). • Switch to non-RAS blocking agent: switch of patients with previously known and treated hypertension to non-RAS blocking agents (treatment according to standard of care, e.g. nitrendipine, amlodipine or doxazosin)	
Reporting group title	Substudy B- Cohort 2
Reporting group description:	
• Treatment with RAS blocking agent: treatment of patients with blood pressure >130/85mmHg in two consecutive measurements with RAS blocking agent candesartan (Blopress) • Non-RAS blocking agents: treatment according to standard of care, e.g. with nitrendipine, amlodipine or doxazosin, or no treatment, if blood pressure <140/90mmHg.	
Reporting group title	Substudy C - Asunercept
Reporting group description:	
• Asunercept randomized against standard of care (25 mg, 100 mg or 400 mg according to the respective randomized sub-arm)	
Reporting group title	Substudy C - Pentaglobin
Reporting group description:	
• Pentaglobin randomized against standard of care	

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: Arms were not mutually exclusive. Total number of enrolled subjects was 345.

Reporting group values	Main Study	Substudy A	Substudy B- Cohort 1
Number of subjects	224	145	60
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	144	102	28
From 65-84 years	75	38	32
85 years and over	5	5	0

Gender categorical Units: Subjects			
Female	72	45	23
Male	152	100	37

Reporting group values	Substudy B- Cohort 2	Substudy C - Asunercept	Substudy C - Pentaglobin
Number of subjects	8	102	34
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	7	63	30
From 65-84 years	1	36	4
85 years and over	0	3	0
Gender categorical Units: Subjects			
Female	0	29	8
Male	8	73	26

Reporting group values	Total		
Number of subjects	345		
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)	225		
From 65-84 years	112		
85 years and over	8		
Gender categorical Units: Subjects			
Female	104		
Male	241		

Subject analysis sets

Subject analysis set title	Main study: Quensyl
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subject receiving Quensyl.

Subject analysis set title	Main study: Kaletra
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subjects receiving Kaletra

Subject analysis set title	Main study: Veklury
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subjects receiving Veklury.

Subject analysis set title	Main study: Standard of care
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subjects receiving standard of care.

Subject analysis set title	Substudy A: Xarelto
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subjects receiving Xarelto in substudy A.

Subject analysis set title	Substudy A: standard of care
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subjects receiving standard of care in substudy A.

Subject analysis set title	Substudy B-Cohort 1 Stay on any RAS
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for patients with previously known and treated hypertension (treatment according to standard of care).

Subject analysis set title	Substudy B-Cohort 1 Switch to non RAS
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for patients with previously known and treated hypertension who switch to non-RAS blocking agents (treatment according to standard of care, e.g. nitrendipine, amlodipine or doxazosin)

Subject analysis set title	Substudy B-Cohort 2 Blopress
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for patients with blood pressure >130/85mmHg in two consecutive measurements with treatment of RAS blocking agent candesartan (Blopress)

Subject analysis set title	Substudy B-Cohort 2 non RAS
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subjects with treatment according to standard of care, e.g. with nitrendipine, amlodipine or doxazosin, or no treatment, if blood pressure <140/90mmHg.

Subject analysis set title	Substudy C- Asunercept high dose
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical

performance scale, which were measured daily till day 29 for subject receiving Asunercept high dose (400mg).

Subject analysis set title	Substudy C- Asunercept intermediate dose
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subject receiving for Asunercept intermedian dose (100mg).

Subject analysis set title	Substudy C- Asunercept low dose
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subject receiving Asunercept low dose (25mg).

Subject analysis set title	Substudy C Asunercept standard of care
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subject receiving standard of care in substudy C Asunercept

Subject analysis set title	Substudy C Pentaglobin
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subject receiving Pentaglobin

Subject analysis set title	Substudy C Pentaglobin standard of care
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subject receiving standard of care in substudy C Pentaglobin

Reporting group values	Main study: Quensyl	Main study: Kaletra	Main study: Veklury
Number of subjects	11	101	2
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	8	60	1
From 65-84 years	3	40	1
85 years and over	0	1	0
Gender categorical Units: Subjects			
Female	2	33	1
Male	9	68	1

Reporting group values	Main study: Standard of care	Substudy A: Xarelto	Substudy A: standard of care
Number of subjects	105	70	73

Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	72	49	52
From 65-84 years	30	17	21
85 years and over	3	4	0
Gender categorical Units: Subjects			
Female	34	25	19
Male	71	45	54

Reporting group values	Substudy B-Cohort 1 Stay on any RAS	Substudy B-Cohort 1 Switch to non RAS	Substudy B-Cohort 2 Blopress
Number of subjects	32	28	3
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	13	15	3
From 65-84 years	19	13	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	9	14	0
Male	23	14	3

Reporting group values	Substudy B-Cohort 2 non RAS	Substudy C-Asunercept high dose	Substudy C-Asunercept intermediate dose
Number of subjects	4	25	23
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	14	14
From 65-84 years	1	8	9

85 years and over	0	3	0

Gender categorical Units: Subjects			
Female	0	5	6
Male	4	20	17

Reporting group values	Substudy C-Asunercept low dose	Substudy C Asunercept standard of care	Substudy C Pentaglobin
Number of subjects	26	25	17
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	17	16	15
From 65-84 years	9	9	2
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	5	13	4
Male	21	12	13

Reporting group values	Substudy C Pentaglobin standard of care		
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)	14		
From 65-84 years	2		
85 years and over	0		
Gender categorical Units: Subjects			
Female	4		
Male	12		

End points

End points reporting groups

Reporting group title	Main Study

Reporting group description:

Main "antiviral therapy" study:
Reporting group 1: Resochin/Quensyl
Reporting group 2: Kaletra
Reporting group 3: Veklury
Reporting group 4: Standard of care (SOC) ("control arm" of the study)

Reporting group title	Substudy A

Reporting group description:

Subjects received Xarelto versus standard of care

Reporting group title	Substudy B- Cohort 1

Reporting group description:

- Stay on any RAS blockade: patients with previously known and treated hypertension (treatment according to standard of care).
- Switch to non-RAS blocking agent: switch of patients with previously known and treated hypertension to non-RAS blocking agents (treatment according to standard of care, e.g. nitrendipine, amlodipine or doxazosin)

Reporting group title	Substudy B- Cohort 2

Reporting group description:

- Treatment with RAS blocking agent: treatment of patients with blood pressure >130/85mmHg in two consecutive measurements with RAS blocking agent candesartan (Blopress)
- Non-RAS blocking agents: treatment according to standard of care, e.g. with nitrendipine, amlodipine or doxazosin, or no treatment, if blood pressure <140/90mmHg.

Reporting group title	Substudy C - Asunercept

Reporting group description:

- Asunercept randomized against standard of care (25 mg, 100 mg or 400 mg according to the respective randomized sub-arm)

Reporting group title	Substudy C - Pentaglobin

Reporting group description:

- Pentaglobin randomized against standard of care

Subject analysis set title	Main study: Quensyl
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subject receiving Quensyl.

Subject analysis set title	Main study: Kaletra
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subjects receiving Kaletra

Subject analysis set title	Main study: Veklury
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subjects receiving Veklury.

Subject analysis set title	Main study: Standard of care
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subjects receiving standard of care.

Subject analysis set title	Substudy A: Xarelto

Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subjects receiving Xarelto in substudy A.

Subject analysis set title	Substudy A: standard of care
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subjects receiving standard of care in substudy A.

Subject analysis set title	Substudy B-Cohort 1 Stay on any RAS
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for patients with previously known and treated hypertension (treatment according to standard of care).

Subject analysis set title	Substudy B-Cohort 1 Switch to non RAS
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for patients with previously known and treated hypertension who switch to non-RAS blocking agents (treatment according to standard of care, e.g. nitrendipine, amlodipine or doxazosin)

Subject analysis set title	Substudy B-Cohort 2 Blopress
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for patients with blood pressure >130/85mmHg in two consecutive measurements with treatment of RAS blocking agent candesartan (Blopress)

Subject analysis set title	Substudy B-Cohort 2 non RAS
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subjects with treatment according to standard of care, e.g. with nitrendipine, amlodipine or doxazosin, or no treatment, if blood pressure <140/90mmHg.

Subject analysis set title	Substudy C- Asunercept high dose
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subject receiving Asunercept high dose (400mg).

Subject analysis set title	Substudy C- Asunercept intermediate dose
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subject receiving for Asunercept intermedian dose (100mg).

Subject analysis set title	Substudy C- Asunercept low dose
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subject receiving Asunercept low dose (25mg).

Subject analysis set title	Substudy C Asunercept standard of care
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subject receiving standard of care in substudy C Asunercept

Subject analysis set title	Substudy C Pentaglobin
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subject receiving Pentaglobin

Subject analysis set title	Substudy C Pentaglobin standard of care
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Time to sustained improvement (i.e. >48h) of one category from baseline in the 7-point clinical performance scale, which were measured daily till day 29 for subject receiving standard of care in substudy C Pentaglobin

Primary: Primary Endpoint Kaletra versus standard of care

End point title	Primary Endpoint Kaletra versus standard of care

End point description:

End point type	Primary

End point timeframe:

from day 1 to day 29

End point values	Main study: Kaletra	Main study: Standard of care		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	101	105		
Units: days				
median (inter-quartile range (Q1-Q3))	11 (7 to 21)	9 (6 to 12)		

Statistical analyses

Statistical analysis title	Analysis primary endpoint Kaletra versus SOC
Comparison groups	Main study: Kaletra v Main study: Standard of care
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Logrank

Primary: Primary endpoint substudy A

End point title	Primary endpoint substudy A

End point description:

End point type	Primary
End point timeframe:	
Day 1 to day 29	

End point values	Substudy A: Xarelto	Substudy A: standard of care		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	70	73		
Units: days				
median (inter-quartile range (Q1-Q3))	9 (6 to 12)	8 (5 to 13)		

Statistical analyses

Statistical analysis title	Analysis primary endpoint substudy A
Comparison groups	Substudy A: Xarelto v Substudy A: standard of care
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	> 0.05
Method	Logrank

Notes:

[1] - Analysis is only exploratory due to premature termination of the study.

Primary: Primary endpoint substudy C Asunercept

End point title	Primary endpoint substudy C Asunercept
End point description:	

End point type	Primary
End point timeframe:	
Day 1 to day 29	

End point values	Substudy C-Asunercept high dose	Substudy C-Asunercept intermediate dose	Substudy C-Asunercept low dose	Substudy C Asunercept standard of care
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	25	23	26	25
Units: days				
median (inter-quartile range (Q1-Q3))	10 (7 to 21)	12 (7 to 13)	8 (6 to 11)	7 (5 to 12)

Statistical analyses

Statistical analysis title	Analysis primary endpoint substudy C Asunercept
Comparison groups	Substudy C Asunercept standard of care v Substudy C- Asunercept high dose v Substudy C- Asunercept intermediate dose v Substudy C- Asunercept low dose
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	> 0.05
Method	Logrank

Notes:

[2] - Analysis is only exploratory due to premature termination of the study.

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: Day 1 to day 29	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.1

Frequency threshold for reporting non-serious adverse events: 0 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: All adverse events have been uploaded in PDF

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 April 2020	• Deletion of IMP Chloroquin in main study due to urgent safety measure • Dose increase of IMP Lopinavir/Ritonavir in main study due to new information of required dose in Sars-CoV-2 infection • Additional IMPs for Sub-C: Tocilizumab, Asunercept • Sub-B: Adaptation of blood pressure level • Additional centers: Graz, Neunkirchen, Linz
03 November 2020	• Inactivation of IMP in main study: Hydroxychloroquine • Additional IMP in main study: Remdesivir (if not part of SOC) • Exchange of IMP in main study: Pooled plasma/IVIg against convalescent plasma • Additional IMP for Sub-C: Pentaglobin • Removal of IMPs for Sub-C: Tocilizumab, Clazakizumab
23 November 2020	• Remote SDV
15 December 2020	• Removal of IMP in main study: convalescent plasma
12 February 2021	• Day 90 Follow-up • Addition of interview study

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported