Clinical trial results:
Efficacy of E-52862 in the early treatment of confirmed mild symptomatic COVID-19 patients

Summary

EudraCT number	2020-003603-33
Trial protocol	ES
Global end of trial date	20 July 2022

Results information

Result version number	v1 (current)
This version publication date	08 November 2023
First version publication date	08 November 2023

Trial information

Trial identification

Sponsor protocol code	SIGMA4COVID

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Consorci Mar Parc de Salut de Barcelona
Sponsor organisation address	Passeig Marítim de la Barceloneta, 25-29, Barcelona, Spain, 08003
Public contact	Jordi Monfort Faure, Hospital del Mar, 34 93248 33 32, JMonfort@parcdesalutmar.cat
Scientific contact	Jordi Monfort Faure, Hospital del Mar, 34 93248 33 32, JMonfort@parcdesalutmar.cat

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	20 July 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 July 2022
Global end of trial reached?	Yes
Global end of trial date	20 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To study the evolution of viral load in mild symptomatic patients with confirmed COVID-19.

Protection of trial subjects:

The trial was conducted in compliance with the approved protocol, the Declaration of Helsinki (amended Fortaleza, Brazil, October 2013),the principles of Good Clinical Practice (GCP) published by ICH (E6 R2).This study was conducted according to Spanish regulations regarding clinical trials (Royal Decree 1090/2015) and biomedical investigations (Organic Law 14/2007 of biomedical investigation and the Royal Decree 1716/2011), which develop the European Directive on clinical trials (Regulation EU No 536/2014). Participants were provided trial treatment for a 14-day period , and remained on the trial for a total of 21 days. Averse Events were collected throughout the trial and treated accordingly. As participation was voluntary, participants were free to discontinue at any given time without giving reason and without it affecting their normal standard of care.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 November 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	Spain: 118
Worldwide total number of subjects	118
EEA total number of subjects	118

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)	109

From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients over 18 years who were visited at one of the participating health care centres, with confirmed COVID-19. Once they expressed their consent and the COVID-19 infection was confirmed by a positive RT-qPCR test, they were randomized to one of the two groups.

Pre-assignment

Screening details:

The participant signed the informed consent document prior to any procedures being done specifically for the study. The first study procedure was the obtention of a nasopharyngeal sample for the RT-qPCR test. Also clinical laboratory parameters, vital signs and ECG were obtained.

Period 1

Period 1 title	Baseline (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The Hospital del Mar’s Pharmacy Department prepared the study medication, according to the randomisation schedule (1:1), and were the only one who knew the actual content of each medication box. The Hospital del Mar’s Pharmacy Department provided study capsules (blinded E-52862 or Placebo, according to the assigned patient ID code).

Arms

Are arms mutually exclusive?	Yes
Arm title	E-52862

Arm description:

Daily dose of 400 mg of E-52862

Arm type	Experimental
Investigational medicinal product name	E-52862
Investigational medicinal product code	MR309
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Patients in the treatment group received a daily dose of 400 mg of E-52862 during 14 days.

Arm title	Placebo

Arm description:

Placebo (corn starch)

Arm type	Placebo
Investigational medicinal product name	Placebo (corn starch)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Daily dose of 400mg of Placebo (corn starch) for 14 days

Number of subjects in period 1	E-52862	Placebo
Started	59	59
Completed	59	59

Baseline characteristics

Reporting groups	
Reporting group title	E-52862
Reporting group description:	
Daily dose of 400 mg of E-52862	
Reporting group title	Placebo
Reporting group description:	
Placebo (corn starch)	

Reporting group values	E-52862	Placebo	Total
Number of subjects	59	59	118
Age categorical Units: Subjects			
Adults (18-64 years)	53	56	109
From 65-84 years	6	3	9
Gender categorical Units: Subjects			
Female	33	34	67
Male	26	25	51

Subject analysis sets	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
Full analysis set (FAS): all the patients, with positive baseline viral load, who undergo randomization and receive at least one dose of the assigned treatment, but regardless that they received or not the complete treatment.	
Subject analysis set title	Virology per protocol analysis set
Subject analysis set type	Per protocol
Subject analysis set description:	
Virology PPAS: will exclude from the corresponding analyses those data points in which protocol deviations may affect the viral load assessment (i.e., assesments made out of the predermined time window)	
Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
Saety Analysis Set (SAS),: all the patients who undergo randomization and receive at least one dose of study medication	

Reporting group values	Full analysis set	Virology per protocol analysis set	Safety analysis set
Number of subjects	118	108	118
Age categorical Units: Subjects			
Adults (18-64 years)	109	99	109
From 65-84 years	9	9	9

Gender categorical Units: Subjects			
Female	67	60	67
Male	51	48	51

End points

End points reporting groups

Reporting group title	E-52862
Reporting group description: Daily dose of 400 mg of E-52862	
Reporting group title	Placebo
Reporting group description: Placebo (corn starch)	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description: Full analysis set (FAS): all the patients, with positive baseline viral load, who undergo randomization and receive at least one dose of the assigned treatment, but regardless that they received or not the complete treatment.	
Subject analysis set title	Virology per protocol analysis set
Subject analysis set type	Per protocol
Subject analysis set description: Virology PPAS: will exclude from the corresponding analyses those data points in which protocol deviations may affect the viral load assessment (i.e., assesments made out of the predermined time window)	
Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description: Saety Analysis Set (SAS),: all the patients who undergo randomization and receive at least one dose of study medication	

Primary: Viral load

End point title	Viral load
End point description: Change in SARS-COV-2 viral load (log10 copies per milliliter) from baseline to day 7 (±1)	
End point type	Primary
End point timeframe: Measured at baseline and Day 7 (±1).	

End point values	E-52862	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	59		
Units: log 10				
arithmetic mean (standard deviation)	-3.21 (± 1.54)	-3.28 (± 1.55)		

Statistical analyses

Statistical analysis title	E-52862 vs Placebo
Statistical analysis description: Full analysis set	

Comparison groups	E-52862 v Placebo
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANOVA

Secondary: Viral load

End point title	Viral load
End point description:	
Change in SARS-COV-2 viral load (log10 copies per milliliter) from baseline to day 4 (±1)	
End point type	Secondary
End point timeframe:	
Measured at baseline and Day 4 (±1)	

End point values	E-52862	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	59		
Units: log10				
arithmetic mean (standard deviation)	-1.80 (± 1.36)	-2.04 (± 1.49)		

Statistical analyses

No statistical analyses for this end point

Secondary: Viral load

End point title	Viral load
End point description:	
Change in SARS-COV-2 viral load (log10 copies per milliliter) from baseline to day 14 (±1)	
End point type	Secondary
End point timeframe:	
Measured at baseline and Day 14 (±1)	

End point values	E-52862	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	59		
Units: log10				
arithmetic mean (standard deviation)	-4.06 (± 1.60)	-4.09 (± 1.72)		

Statistical analyses

No statistical analyses for this end point

Secondary: Viral load

End point title	Viral load

End point description:

End point type	Secondary

End point timeframe:

Viral load to Day 7 (+-1) Per Protocol Analysis Set (PPAS).

End point values	E-52862	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	51		
Units: log10				
arithmetic mean (standard deviation)	-3.21 (± 1.57)	-3.31 (± 1.54)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From baseline to Day 21	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1
Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	E-52862
Reporting group description: -	

Serious adverse events	Placebo	E-52862	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 59 (1.69%)	1 / 59 (1.69%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Investigations			
International normalised ratio increased	Additional description: Patient had a medically important increased anticoagulation titer (INR >8) on study day 11. Relevant medical history includes atrial fibrillation (since December 2019).		
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 59 (1.69%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	E-52862	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 59 (28.81%)	35 / 59 (59.32%)	
General disorders and administration site conditions			

Chest pain			
subjects affected / exposed	0 / 59 (0.00%)	2 / 59 (3.39%)	
occurrences (all)	0	2	
Reproductive system and breast disorders			
Menstrual disorder			
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Nasal dryness			
subjects affected / exposed	1 / 59 (1.69%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 59 (3.39%)	2 / 59 (3.39%)	
occurrences (all)	2	2	
Insomnia			
subjects affected / exposed	1 / 59 (1.69%)	2 / 59 (3.39%)	
occurrences (all)	1	2	
Nervousness			
subjects affected / exposed	1 / 59 (1.69%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Somnolence			
subjects affected / exposed	2 / 59 (3.39%)	2 / 59 (3.39%)	
occurrences (all)	2	2	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 59 (3.39%)	19 / 59 (32.20%)	
occurrences (all)	2	19	
Vertigo			
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			

Deafness			
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Eye disorders			
Eye pain			
subjects affected / exposed	1 / 59 (1.69%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Foreign body in eye			
subjects affected / exposed	1 / 59 (1.69%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Photophobia			
subjects affected / exposed	1 / 59 (1.69%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 59 (0.00%)	2 / 59 (3.39%)	
occurrences (all)	0	2	
Abdominal distention			
subjects affected / exposed	1 / 59 (1.69%)	1 / 59 (1.69%)	
occurrences (all)	1	1	
Abdominal pain upper			
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	0 / 59 (0.00%)	2 / 59 (3.39%)	
occurrences (all)	0	2	
Dry mouth			
subjects affected / exposed	3 / 59 (5.08%)	2 / 59 (3.39%)	
occurrences (all)	3	2	
Dyspepsia			
subjects affected / exposed	0 / 59 (0.00%)	11 / 59 (18.64%)	
occurrences (all)	0	11	
Gastrooesophageal reflux			
subjects affected / exposed	0 / 59 (0.00%)	2 / 59 (3.39%)	
occurrences (all)	0	2	
Glossitis			

subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	1 / 59 (1.69%)	5 / 59 (8.47%)	
occurrences (all)	1	5	
Vomiting			
subjects affected / exposed	0 / 59 (0.00%)	2 / 59 (3.39%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 59 (1.69%)	1 / 59 (1.69%)	
occurrences (all)	1	1	
Papule			
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	1 / 59 (1.69%)	2 / 59 (3.39%)	
occurrences (all)	1	2	
Rash			
subjects affected / exposed	0 / 59 (0.00%)	2 / 59 (3.39%)	
occurrences (all)	0	2	
Skin exfoliation			
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 59 (1.69%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Limb discomfort			
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Infections and infestations			
Atypical pneumonia			
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Viral infection			

subjects affected / exposed occurrences (all)	2 / 59 (3.39%) 2	0 / 59 (0.00%) 0	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 2 / 59 (3.39%) 2	 5 / 59 (8.47%) 5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 December 2021	-Update of participating centers (Barcelona and Galicia) -A PCR for SARS-COV-2 with a positive result in the previous 48 hours carried out as part of the care routine would be accepted as inclusion criteria, so that the baseline quantitative PCR collected at the screening visit (study-specific) could be analyzed a posteriori along with the rest of subsequent samples from each patient. -Telephone follow-up visits are eliminated (since the clinical information for these patients is already collected in the rest of the scheduled visits and access to the clinical history) -The registry of the vaccination status of patients has been added

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported