



Clinical trial results:

A Randomized, Double-Blind, Drug Repositioning Clinical Trial comparative with placebo, to Evaluate the Efficacy and Safety of FDA-277 in Combination with Standard of Care in the Treatment of Infection Caused by SARS-CoV-2, in Patients With early Stage COVID-19 Disease, Receiving Primary Care Treatment.

Summary

EudraCT number	2021-001228-17
Trial protocol	ES
Global end of trial date	03 November 2022

Results information

Result version number	v1 (current)
This version publication date	06 January 2023
First version publication date	06 January 2023
Summary attachment (see zip file)	Summary (Summary Clinical Study Report_FINAL_CSIC-FDA277-2021-01 version 1 15-11-2022.pdf)

Trial information

Trial identification

Sponsor protocol code	CSIC-FDA277-2021-01
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Agencia Estatal Consejo Superior de Investigaciones Científicas, M.P.
Sponsor organisation address	Calle Serrano, 117, Madrid, Spain, 28006
Public contact	Sponsor, Agencia Estatal Consejo Superior de Investigaciones Científicas, M.P., 34 918373112, ana.martinez@csic.es
Scientific contact	Sponsor, Agencia Estatal Consejo Superior de Investigaciones Científicas, M.P., 34 918373112, ana.martinez@csic.es

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	08 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 November 2022
Global end of trial reached?	Yes
Global end of trial date	03 November 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the efficacy of FDA-277 combined with standard of care on reducing the SARS-CoV-2 viral load.

Protection of trial subjects:

All patients could be treated for symptoms due to SARS-CoV-2 infection as per standard of care recommendation:

- In mild clinical conditions:
 - o Acetaminophen 500 mg 1-4 times daily for control of fever and as an analgesic.
 - o Non-steroidal anti-inflammatory drugs in the doses indicated as per their fact sheet.
 - o Symptomatic treatment.
 - o Adequate hydration.
- In moderate clinical conditions:
 - o Only in the case of suspected bacterial co-infection/superinfection antibiotic treatment will be introduced with:
 - o Amoxicillin/Clavulanic Acid 875 mg/125 mg every 8 hours for 7 days.
 - o Alternatively, levofloxacin 500 mg every 12 hours on the first day and 500 mg every 24 hours for 4 days [thereafter].
 - o Symptomatic treatment.
 - o Adequate hydration.
 - o BRONCHODILATORS: If required, they were preferably administered in pressurized cartridge with individual holding chamber (spacer), to avoid aerosol generation: salbutamol, 100 mcg/inhalation plus Ipratropium Bromide 20 mcg/inhalation: 2 inhalations every 4-6 hours; inhaled corticosteroids: only used in patients with bronchial asthma or COPD.
 - o SYSTEMIC CORTICOSTEROIDS: Use in outpatients without the need for oxygen therapy is not recommended. Its use could be counterproductive in patients who do not require oxygen therapy. They were exclusively recommended at low doses in patients requiring oxygen therapy.
 - o ANTITHROMBOTIC PROPHYLAXIS: Low molecular weight heparin at prophylactic doses for patients immobilized or with risk factors: Enoxaparin 4,000 IU (40 mg) subcutaneously once daily. If creatinine clearance is observed at 15-30 mL/min, enoxaparin 2000 IU (20 mg) could be administered subcutaneously once daily. Enoxaparin was not recommended if creatinine clearance was less than 15 mL/min. Bemiparin could be used as an alternative.

In all cases, home isolation was required, according to the rules applicable at the time of study

Background therapy:

Standard of care

Evidence for comparator:

Standard of care

Actual start date of recruitment	23 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	Spain: 173
Worldwide total number of subjects	173
EEA total number of subjects	173

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)	146
From 65 to 84 years	27
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first patient was included in the study on March 23, 2022. The last patient was included on October 6, 2022. The last patient last visit was completed on November 3, 2022.

Pre-assignment

Screening details:

The patients must be diagnosed of active SARS-CoV-2 infection confirmed by compatible symptoms and a positive result in the detection tests for active infection (DTAI), rapid antigen detection test or in the PCR for viral RNA detection test.

Period 1

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

Blinding implementation details:

Allocation ratio 1:1 of study groups Domperidone plus SOC versus placebo plus SOC group.

The random allocation sequence was generated by an independent technician, in random blocks of 4 and 6 treatments to distribute 10 randomization number envelopes by centre.

Arms

Are arms mutually exclusive?	Yes
Arm title	Domperidone

Arm description:

Domperidone 3 daily doses of 10 mg (30 mg/day) for 7 days

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

Dosage and administration details:

Domperidone 3 daily doses of 10 mg (30 mg/day) for 7 days

Arm title	Placebo
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Arm description:

Matching Placebo 3 daily doses for 7 days

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

Dosage and administration details:

3 daily doses of matching placebo for 7 days

Number of subjects in period 1	Domperidone	Placebo
Started	87	86
Completed	83	82
Not completed	4	4
Consent withdrawn by subject	-	2
Adverse event, non-fatal	2	-
Lost to follow-up	2	2

Baseline characteristics

Reporting groups

Reporting group title	Treatment and Follow-up period
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Reporting group description:

This analysis population consist of all patients included in the "all randomized patient population" who have not violated the protocol so that it may affect the assessment of the effect of the study drug on the primary endpoint, ie, without major protocol deviations. The criteria for identifying major protocol deviations were reviewed prior to the start of the analysis and unblinding of treatment and was described in the analysis plan.

180 patients were randomized. Seven patients were excluded from the data set due to protocol deviation (placebo group 4; domperidone group 3). The set population was 173 patients.

Reporting group values	Treatment and Follow-up period	Total	
Number of subjects	173	173	
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)	146	146	
From 65-84 years	27	27	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	47.8		
standard deviation	± 15.2	-	
Gender categorical			
Units: Subjects			
Female	109	109	
Male	64	64	
SARS-CoV-2 infection severity			
Severity of SARS-CoV-2 infection at baseline			
Units: Subjects			
Asymptomatic	3	3	
Mild disease	166	166	
Moderate disease	4	4	
SARS-CoV-2 complete vaccination			
Units: Subjects			
No	14	14	
Yes	159	159	
SARS-CoV-2 infection before the study			
Presence or absence of previous SARS-CoV-2 infection before the one for the selection for the study			
Units: Subjects			
No	146	146	
Yes	27	27	

Systolic Blood Pressure Units: mmHg arithmetic mean standard deviation	124.6 ± 13.2	-	
Diastolic Blood Pressure Units: mmHg arithmetic mean standard deviation	76.7 ± 9.9	-	
Respiratory rate Units: Inspirations/minute arithmetic mean standard deviation	15.9 ± 5.5	-	
Oxygen saturation Units: Saturation % arithmetic mean standard deviation	97.2 ± 0.1	-	
Heart rate Units: Pulses/minute arithmetic mean standard deviation	81.8 ± 1	-	
Temperature			
Axillary temperature			
Units: °C arithmetic mean standard deviation	36.4 ± 0.1	-	
Time from previous SARS-CoV-2 infection Units: Months arithmetic mean standard deviation	14.2 ± 1.7	-	
Time from last SRS-CoV-2 vaccination dose Units: Month arithmetic mean standard deviation	6.3 ± 0.3	-	

End points

End points reporting groups

Reporting group title	Domperidone
Reporting group description:	Domperidone 3 daily doses of 10 mg (30 mg/day) for 7 days
Reporting group title	Placebo
Reporting group description:	Matching Placebo 3 daily doses for 7 days

Primary: Change in ORF1ab viral load (Ct) Day4-Baseline

End point title	Change in ORF1ab viral load (Ct) Day4-Baseline
End point description:	Baseline – 4 days difference ORF1ab RT-PCR number of cycles. The viral load was estimated by the number of cycles (Cts) until detection of three specific genes of the SARS-Cov-2 pathogenic viral strain, using the TaqPath COVID-19 CE-IVD RT-PCR Kit (Thermofisher, USA), which detects three highly conserved regions of the RNA SARS-CoV-2 virus along with an internal positive control (MS2-IPC) in a single PCR reaction: genes encoding ORF1ab, N Protein, S Protein, with a sensitivity of >99% and Specificity of 99.5%. For the correct interpretation of data: an increase in the number of amplified cycles means a better result as a reduction in the viral load. So, the difference D4-D0 positive means an improvement, better as the figure is higher. If the difference D4-D0 is negative, it means a worsening.
End point type	Primary
End point timeframe:	Baseline - Day 4 of treatment

End point values	Domperidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	86		
Units: Number of RT-PCR cycles				
arithmetic mean (standard error)	5.7 (± 0.5)	6.1 (± 0.5)		

Attachments (see zip file)	ORF1ab_Baseline_Day4.pdf
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Statistical analyses

Statistical analysis title	Student t test for independent groups
Statistical analysis description:	Student t test for independent groups
Comparison groups	Domperidone v Placebo

Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.551
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.01
upper limit	1.9
Variability estimate	Standard error of the mean
Dispersion value	0.7

Primary: Change in N Protein viral load (Ct) Day4-Baseline

End point title	Change in N Protein viral load (Ct) Day4-Baseline
End point description:	
Baseline – 4 days difference ORF1ab RT-PCR number of cycles. The viral load was estimated by the number of cycles (Cts) until detection of three specific genes of the SARS-Cov-2 pathogenic viral strain, using the TaqPath COVID-19 CE-IVD RT-PCR Kit (Thermofisher, USA), which detects three highly conserved regions of the RNA SARS-CoV-2 virus along with an internal positive control (MS2-IPC) in a single PCR reaction: genes encoding ORF1ab, N Protein, S Protein, with a sensitivity of >99% and Specificity of 99.5%. For the correct interpretation of data: an increase in the number of amplified cycles means a better result as a reduction in the viral load. So, the difference D4-D0 positive means an improvement, better as the figure is higher. If the difference D4-D0 is negative, it means a worsening.	
End point type	Primary
End point timeframe:	
Baseline - Day 4 of treatment	

End point values	Domperidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	86		
Units: Number of RT-PCR cycles				
arithmetic mean (standard error)	5.6 (± 0.5)	6 (± 0.5)		

Attachments (see zip file)	NProtein_Baseline_Day4.pdf
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Statistical analyses

Statistical analysis title	Student t test for independent groups
Comparison groups	Domperidone v Placebo

Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.505
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	1.8
Variability estimate	Standard error of the mean
Dispersion value	0.7

Primary: Change in S Protein viral load (Ct) Day4-Baseline

End point title	Change in S Protein viral load (Ct) Day4-Baseline
End point description:	
<p>Baseline – 4 days difference ORF1ab RT-PCR number of cycles.</p> <p>The viral load was estimated by the number of cycles (Cts) until detection of three specific genes of the SARS-Cov-2 pathogenic viral strain, using the TaqPath COVID-19 CE-IVD RT-PCR Kit (Thermofisher, USA), which detects three highly conserved regions of the RNA SARS-CoV-2 virus along with an internal positive control (MS2-IPC) in a single PCR reaction: genes encoding ORF1ab, N Protein, S Protein, with a sensitivity of >99% and Specificity of 99.5%.</p> <p>For the correct interpretation of data: an increase in the number of amplified cycles means a better result as a reduction in the viral load. So, the difference D4-D0 positive means an improvement, better as the figure is higher. If the difference D4-D0 is negative, it means a worsening.</p>	
End point type	Primary
End point timeframe:	
Baseline - Day 4 of treatment	

End point values	Domperidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	86		
Units: Number of RT-PCR cycles				
arithmetic mean (standard error)	3.6 (± 0.5)	3.7 (± 0.6)		

Attachments (see zip file)	SProtein_Baseline_Day4.pdf
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Statistical analyses

Statistical analysis title	Student t test for independent groups
Comparison groups	Domperidone v Placebo

Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.981
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	1.5
Variability estimate	Standard error of the mean
Dispersion value	0.8

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Timeframe from Day 1 to Day 28

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.0
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Placebo

Reporting group title	Domperidone
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Reporting group description:

Domperidone 3 daily doses of 10 mg (30 mg/day) for 7 days

Serious adverse events	Placebo	Domperidone	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 86 (0.00%)	0 / 87 (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	Placebo	Domperidone	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 86 (10.47%)	14 / 87 (16.09%)	
Investigations			
Oxygen saturation decreased			
subjects affected / exposed	0 / 86 (0.00%)	1 / 87 (1.15%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Traumatic fracture			
subjects affected / exposed	0 / 86 (0.00%)	1 / 87 (1.15%)	
occurrences (all)	0	1	
Vascular disorders			

Hypertension subjects affected / exposed occurrences (all)	1 / 86 (1.16%) 1	0 / 87 (0.00%) 0	
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	0 / 86 (0.00%) 0	2 / 87 (2.30%) 2	
Presyncope subjects affected / exposed occurrences (all)	1 / 86 (1.16%) 1	0 / 87 (0.00%) 0	
Tachycardia subjects affected / exposed occurrences (all)	1 / 86 (1.16%) 1	0 / 87 (0.00%) 0	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	1 / 86 (1.16%) 1	0 / 87 (0.00%) 0	
Paresthesia subjects affected / exposed occurrences (all)	1 / 86 (1.16%) 1	0 / 87 (0.00%) 0	
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	1 / 86 (1.16%) 1	0 / 87 (0.00%) 0	
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	1 / 86 (1.16%) 1	0 / 87 (0.00%) 0	
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 86 (0.00%) 0	1 / 87 (1.15%) 1	
Abdominal pain subjects affected / exposed occurrences (all)	0 / 86 (0.00%) 0	1 / 87 (1.15%) 1	
Abdominal pain upper			

subjects affected / exposed	1 / 86 (1.16%)	1 / 87 (1.15%)	
occurrences (all)	1	1	
Dyspepsia			
subjects affected / exposed	0 / 86 (0.00%)	1 / 87 (1.15%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	2 / 86 (2.33%)	0 / 87 (0.00%)	
occurrences (all)	2	0	
Tongue pruritus			
subjects affected / exposed	1 / 86 (1.16%)	0 / 87 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	0 / 86 (0.00%)	1 / 87 (1.15%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Menometrorrhagia			
subjects affected / exposed	0 / 86 (0.00%)	1 / 87 (1.15%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 86 (0.00%)	1 / 87 (1.15%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 86 (0.00%)	1 / 87 (1.15%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	1 / 86 (1.16%)	0 / 87 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Bacterial infection			
subjects affected / exposed	0 / 86 (0.00%)	1 / 87 (1.15%)	
occurrences (all)	0	1	
Herpes simplex			
subjects affected / exposed	1 / 86 (1.16%)	0 / 87 (0.00%)	
occurrences (all)	1	0	

Vulvovaginitis			
subjects affected / exposed	0 / 86 (0.00%)	2 / 87 (2.30%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported