

**Clinical trial results:**  
**EFFICACY OF CYCLOSPORINE A IN THE TREATMENT OF COVID-19**  
**PNEUMONIA: A RANDOMIZED CONTROLLED TRIAL.****Summary**

EudraCT number	2020-002123-11
Trial protocol	ES
Global end of trial date	21 September 2021

**Results information**

Result version number	v1 (current)
This version publication date	16 August 2025
First version publication date	16 August 2025
Summary attachment (see zip file)	Cyclosporine A in hospitalized COVID19 pneumonia patients to prevent the development of interstitial lung disease: a pilot randomized clinical trial (CYCLO TRIAL.pdf)

**Trial information****Trial identification**

Sponsor protocol code	HUIS-04-2020
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**Additional study identifiers**

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

Notes:

**Sponsors**

Sponsor organisation name	Hospital Universitario Infanta Sofía
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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 June 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 September 2021
Global end of trial reached?	Yes
Global end of trial date	21 September 2021
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the efficacy of cyclosporine A (treatment group) versus non treatment (control group) in patients with acute COVID-19 pneumonia .

Protection of trial subjects:

Yes. At each scheduled study visit on day 1, day 4, day 8, at discharge, day 30 and day 90, the detection of possible adverse events will be carried out through an interview with the patient, physical assessment and review of medical records including complementary tests. In addition, a telephone consultation will be carried out between the day of hospital discharge and day 30 (halfway between discharge and day 30), evaluating the patient's condition and possible adverse events.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 May 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	Spain: 33
Worldwide total number of subjects	33
EEA total number of subjects	33

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	23
From 65 to 84 years	10
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

From May 12, 2020 to May 15, 2021

### Pre-assignment

Screening details:

Inclusion criteria:

- Adult  $\geq$  18 years and  $<$ 80 years
- Very characteristic initial symptoms of SARS-CoV2 infection  $\leq$  7 days in duration
- Presence of alveolar-interstitial lung infiltrates
- Basal oxygen saturation  $<$ 95%
- Hospitalization
- Patient status  $\geq$  3 according to the WHO clinical improvement ordinal scale
- Positivity SAR-CoV2 PCR

### Pre-assignment period milestones

Number of subjects started	33
Number of subjects completed	33

### Period 1

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

Blinding implementation details:

Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Control group

Arm description:

NON TREATMENT ASSOCIATED TO STANDARD OF CARE OF THE COVID-19 PNEUMONIA.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

<b>Arm title</b>	Treatment group
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Arm description:

CYCLOSPORINE A ASSOCIATED TO STANDARD OF CARE OF THE COVID-19 PNEUMONIA.

Arm type	Active comparator
Investigational medicinal product name	CYCLOSPORINE A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

- Starting dose:  $<$ 60 kg: 100 mg/day (50-0-50); 60-80 Kg: 150 mg/day (100-0-50),  $>$ 80 kg: 200 mg/day (100-0-100)
  - After 48 hours, if well tolerated:  $<$ 60 kg: 150 mg/day (100-0-50); 60-80 Kg: 200 mg/day (100-0-100);  $>$ 80 kg: 300 mg/day (150-0-150)
  - Monitor every 48 hours with trough levels in a blood or plasma sample (12 hours after the night dose and prior to administration of the morning dose) until the therapeutic range of 100-250 ng/mL is reached.
- Depending on the levels, the dose may be increased or decreased by 50 mg/day up to a maximum of 5

mg/kg/day.

<b>Number of subjects in period 1</b>	Control group	Treatment group
Started	16	17
Completed	11	14
Not completed	5	3
Death	5	1
Lost to follow-up	-	1
Protocol deviation	-	1

## Baseline characteristics

### Reporting groups

Reporting group title	Control group
Reporting group description: NON TREATMENT ASSOCIATED TO STANDARD OF CARE OF THE COVID-19 PNEUMONIA.	
Reporting group title	Treatment group
Reporting group description: CYCLOSPORINE A ASSOCIATED TO STANDARD OF CARE OF THE COVID-19 PNEUMONIA.	

Reporting group values	Control group	Treatment group	Total
Number of subjects	16	17	33
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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
56.7 ± 11.8			
Units: years			
arithmetic mean	60.1	53.6	
standard deviation	± 11.0	± 12.1	-
Gender categorical			
Female sex			
Units: Subjects			
Female	6	5	11
Male	10	12	22

### Subject analysis sets

Subject analysis set title	The full analysis set
Subject analysis set type	Intention-to-treat
Subject analysis set description: The full analysis set included all randomized patients who received at least one dose of treatment.	

Reporting group values	The full analysis set		
Number of subjects	33		
Age categorical			
Units: Subjects			
In utero			

Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
56.7 ± 11.8			
Units: years			
arithmetic mean	56.7		
standard deviation	± 11.8		
Gender categorical			
Female sex			
Units: Subjects			
Female	11		
Male	22		

## End points

### End points reporting groups

Reporting group title	Control group
Reporting group description: NON TREATMENT ASSOCIATED TO STANDARD OF CARE OF THE COVID-19 PNEUMONIA.	
Reporting group title	Treatment group
Reporting group description: CYCLOSPORINE A ASSOCIATED TO STANDARD OF CARE OF THE COVID-19 PNEUMONIA.	
Subject analysis set title	The full analysis set
Subject analysis set type	Intention-to-treat
Subject analysis set description: The full analysis set included all randomized patients who received at least one dose of treatment.	

### Primary: Complete response:

End point title	Complete response:
End point description: The percentage of living patients who had not developed interstitial lung disease and did not require invasive mechanical ventilation (IMV) with orotracheal intubation (IOT) 3 months after the diagnosis of COVID-19 pneumonia.	
End point type	Primary
End point timeframe: 3 months	

End point values	Control group	Treatment group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	17		
Units: Percentage				
number (confidence interval 95%)	50 (25.5 to 74.5)	76.5 (56.3 to 96.7)		

### Statistical analyses

Statistical analysis title	Rate comparison
Comparison groups	Treatment group v Control group
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	Chi-squared

### Secondary: Partial response

End point title	Partial response
End point description: The percentage of living patients who did not develop interstitial lung disease and required invasive mechanical ventilation (IMV) with orotracheal intubation (IOT) 3 months after the diagnosis of COVID-19 pneumonia	
End point type	Secondary
End point timeframe: 3 months	

End point values	Control group	Treatment group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	17		
Units: Percentage				
number (confidence interval 95%)	0 (0 to 0)	5.9 (0 to 17.1)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Complete plus partial response

End point title	Complete plus partial response
End point description: The percentage of living patients who did not develop interstitial lung disease and required or did not require invasive mechanical ventilation (IMV) with orotracheal intubation (IOT) 3 months after the diagnosis of COVID-19 pneumonia.	
End point type	Secondary
End point timeframe: 3 months	

End point values	Control group	Treatment group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	17		
Units: Percentage				
number (confidence interval 95%)	50 (25.5 to 74.5)	82.4 (64.3 to 100)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Not response due to diffuse interstitial lung disease

End point title	Not response due to diffuse interstitial lung disease
End point description: Rate of patients who developing of diffuse interstitial lung disease 3 months after the diagnosis of COVID-19 pneumonia.	
End point type	Secondary
End point timeframe: 3 months	

End point values	Control group	Treatment group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	16		
Units: percentage				
number (confidence interval 95%)	27.3 (5.5 to 49.1)	12.5 (0 to 28.2)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Not response due to death

End point title	Not response due to death
End point description: Rate of patients who died 3 months after the diagnosis of COVID-19 pneumonia	
End point type	Secondary
End point timeframe: 3 months	

End point values	Control group	Treatment group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	17		
Units: Percentage				
number (confidence interval 95%)	31.3 (8.4 to 53.8)	5.9 (0 to 17.1)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Invasive mechanical ventilation (IMV)

End point title	Invasive mechanical ventilation (IMV)
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End point description:

Rate of patients receiving invasive mechanical ventilation (IMV) with orotracheal intubation (OTI) 3 months after the diagnosis of COVID-19 pneumonia.

End point type	Secondary
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End point timeframe:

3 months

End point values	Control group	Treatment group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	17		
Units: Percentage				
number (confidence interval 95%)	37.5 (13.8 to 61.2)	11.8 (0 to 27.1)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Rescue treatment with methylprednisolone

End point title	Rescue treatment with methylprednisolone
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End point description:

Rate of patients requiring rescue treatment with methylprednisolone 3 months after the diagnosis of COVID-19 pneumonia.

End point type	Secondary
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End point timeframe:

3 months

End point values	Control group	Treatment group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	17		
Units: Percentage				
number (confidence interval 95%)	56.3 (32.0 to 80.6)	52.9 (29.2 to 76.6)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Rescue treatment with biological

End point title	Rescue treatment with biological
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End point description:

Rate of patients requiring rescue treatment with biological therapy 3 months after the diagnosis of COVID-19 pneumonia.

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End point type	Secondary
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End point timeframe:

3 months

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End point values	Control group	Treatment group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	17		
Units: Percentage				
number (confidence interval 95%)	12.5 (0 to 28.7)	17.6 (0 to 35.7)		

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### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

3 months

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	23
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### Reporting groups

Reporting group title	Control group
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Reporting group description:

NON TREATMENT ASSOCIATED TO STANDARD OF CARE OF THE COVID-19 PNEUMONIA.

Reporting group title	Treatment group
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Reporting group description:

CYCLOSPORINE A ASSOCIATED TO STANDARD OF CARE OF THE COVID-19 PNEUMONIA.

Serious adverse events	Control group	Treatment group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	
number of deaths (all causes)	5	1	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Control group	Treatment group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 16 (6.25%)	2 / 17 (11.76%)	
Endocrine disorders			
hypoglycemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Infections and infestations			
Pneumonia	Additional description: nosocomial bacterial pneumonia		
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Genital herpes	Additional description: genital (type 2) herpes simplex infection		

subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/38360855>