Clinical trial results:
Randomized open pilot study to evaluate the efficacy of subcutaneous sarilumab in patients with moderate-severe COVID-19 infection.

Summary

EudraCT number	2020-001634-36
Trial protocol	ES
Global end of trial date	04 December 2020

Results information

Result version number	v1 (current)
This version publication date	28 April 2022
First version publication date	28 April 2022
Summary attachment (see zip file)	SARCOVID_Summary Report (Summary Sarcovid report_V1.pdf)

Trial information

Trial identification

Sponsor protocol code	SARCOVID

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04357808
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Rheumatology Service, Hospital Universitario de la Princesa
Sponsor organisation address	Diego de León 62, Madrid, Spain, 28006
Public contact	Rosario García de Vicuña, Rosario García de Vicuña, 0034 915202473, mariadelrosario.garcia@salud.madrid.org
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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	04 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 December 2020
Global end of trial reached?	Yes
Global end of trial date	04 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

-To evaluate the efficacy of the early administration of sarilumab subcutaneously in patients with moderate-severe COVID-19 infection in early stages compared to the current treatment standard.
-To compare the baseline clinical and biological parameters, including serum IL-6, of the intervention population against historical controls, to search for possible markers that identify candidates for treatment with subcutaneous IL-6 inhibitors and attempt an approximation to the time frame of "window of opportunity".

Protection of trial subjects:

The trial was approved by the AEMPS and the Research Ethics Committee of the HUP on April 9th, 2020 (Reference number 4078) and was conducted in accordance with the principles of the Declaration of Helsinki and the Good Clinical Practice guidelines of the International Conference on Harmonization.

Background therapy:

Sarilumab (SAR) is a human monoclonal antibody that binds membrane-bound and soluble IL-6 receptors to inhibit IL-6 signaling, licensed in a subcutaneous route administration for the treatment of Rheumatoid Arthritis. At a moment where the health system was overrun, especially emergency and intensive care unit (ICU) facilities, with real concern about TCZ shortages, we conceived that subcutaneous administration of SAR could facilitate the administration of an IL-6 inhibitor in all settings, including wards and overloaded emergency rooms. Additionally, the safety and maximum pharmacodynamic effects of a single 200 mg dose of subcutaneous SAR are known through the results of two open randomized controlled trials. Data were similar to those obtained with single doses of 4 and 8 mg/kg intravenous TCZ, with a longer effect of TCZ in the second week. Our hypothesis was that the use of 2 subcutaneous SAR injections and early intervention (window of opportunity) could prevent higher oxygenation requirements through non-invasive (NI) and invasive mechanical ventilation (IMV) and reduce death rate. Thus, we proposed an open pilot pragmatic RCT to evaluate the efficacy and safety of a single 400 mg subcutaneous dose of SAR, in patients with moderate to early severe COVID-19, compared to standard care (SC).

Evidence for comparator:

The pharmacodynamic effect and safety of a single dose of sarilumab s.c (150 and 200 mg) and of tocilizumab i.v. (4 and 8 mg / kg) were evaluated in two open, randomized trials, in Japanese (n = 30) (PDY14191 [NCT02404558]) and non-Japanese (n = 101) (6R88-RA-1309 [NCT02097524]) population of patients with RA. Although there were differences in the baseline pharmacodynamic parameters between both studies, the onset of the effect on the absolute neutrophil count, C-reactive protein (CRP), serum levels of IL-6 and the soluble IL-6 receptor, during the first week after a single dose, it was similar regardless of drug, dose, or route of administration. The maximum effects on neutrophil count nadir and CRP, and on serum peaks of IL-6 and soluble IL-6 receptor were comparable in both studies for sarilumab and tocilizumab. The pharmacodynamic response was longer for i.v. tocilizumab. and there were no substantial differences in safety.

Actual start date of recruitment	13 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	Spain: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	18
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted in the Hospital Universitario de La Princesa in Patients older than 18 attending the emergency room of this hospital in need for hospitalization by COVID-19. All patients or their legal representatives provided oral informed consent according to the AEMPS exceptional measures applicable for COVID19 studies.

Pre-assignment

Screening details:

Patients 18 and <80-years attending the emergency room with confirmed pneumonia by COVID-19. at least 2 of the following additional criteria needed to be fulfilled: Fever ≥ 37.8°C; IL-6 in serum ≥ 25 pg/mL or PCR> 5mg/dL; Lymphocytes <600/mm3; Ferritin > 300 µg/L and LDH > 250, or D-dimer > 1 mg/L.

Period 1

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

Blinding implementation details:

This is an open label phase II pragmatic RCT (randomized clinical trial) to evaluate the efficacy and safety of a single 400 mg subcutaneous dose of SAR, in patients with moderate to early severe COVID-19, compared to standard care (SC). This study was open for investigators and patients.

Arms

Are arms mutually exclusive?	Yes
Arm title	Sarilumab plus Standard of Care

Arm description:

Sarilumab Kevzara 200 mg, 2 sc injections in pre-filled syringe or pen, 400 mg single dose. The patients of this arm also received drugs, including corticosteroids, or full supportive care according to the best SC updated in the local protocol for COVID-19.
Sarilumab (ATC code L04AC14) is a fully human anti-IL-6R monoclonal IgG1 antibody that binds to both membrane bound and soluble interleukin 6 (IL-6) receptor forms, thus blocking the cis- and trans-inflammatory signalling cascades of IL-6.

Arm type	Experimental
Investigational medicinal product name	Sarilumab
Investigational medicinal product code	SAR153191
Other name	Kevzaras
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

The pharmacodynamic and safety characteristics of a single dose of 150 and 200 mg sarilumab s.c. are known, which do not differ significantly from those obtained with single doses of 4 and 8 mg / kg of tocilizumab i.v. The administration of 2 injections s.c. of sarilumab and in earlier stages (moderate COVID-19 pneumonia or early severe disease), it was expected that it could increase the initial concentration peak and compensate for the somewhat shorter duration of its pharmacodynamic effects, described for a single 200 mg dose.

Arm title	Standard Care

Arm description:

Patients in standard care (SC) will received drugs, including corticosteroids, or full supportive care according to the best SC updated in the local protocol for COVID-19. Patients in the standard care (SC) were given the option to receive intravenous Tocilizumab (TCZ) after randomization if they worsened at investigator discretion, as this agent had become the SC in our centre when the protocol was designed.

Arm type	Active comparator

Investigational medicinal product name	Standard Care
Investigational medicinal product code	
Other name	Could use tozilizumab
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Intravenous use

Dosage and administration details:

Patients in the standard care (SC) were given the option to receive intravenous TCZ after randomization if they worsened at investigator discretion, as this agent had become the SC in our centre when the protocol was designed

Number of subjects in period 1	Sarilumab plus Standard of Care	Standard Care
Started	20	10
Completed	20	10

Baseline characteristics

Reporting groups	
Reporting group title	Sarilumab plus Standard of Care

Reporting group description:

Sarilumab Kevzara 200 mg, 2 sc injections in pre-filled syringe or pen, 400 mg single dose. The patients of this arm also received drugs, including corticosteroids, or full supportive care according to the best SC updated in the local protocol for COVID-19.
Sarilumab (ATC code L04AC14) is a fully human anti-IL-6R monoclonal IgG1 antibody that binds to both membrane bound and soluble interleukin 6 (IL-6) receptor forms, thus blocking the cis- and trans-inflammatory signalling cascades of IL-6.

Reporting group title	Standard Care

Reporting group description:

Patients in standard care (SC) will received drugs, including corticosteroids, or full supportive care according to the best SC updated in the local protocol for COVID-19. Patients in the standard care (SC) were given the option to receive intravenous Tocilizumab (TCZ) after randomization if they worsened at investigator discretion, as this agent had become the SC in our centre when the protocol was designed.

Reporting group values	Sarilumab plus Standard of Care	Standard Care	Total
Number of subjects	20	10	30
Age categorical			
Age> 18 years			
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)	12	6	18
From 65-84 years	8	4	12
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	5	5	10
Male	15	5	20
Race			
Race			
Units: Subjects			
Wihte	10	4	14
Asian	0	1	1
Hispanic or latino	10	5	15
Oxygen support at randomization (7-category ordinal scale)			
Oxygen support at randomization (7-category ordinal scale) n (%). Supplemental low flow oxygen therapy: O2 flow ≤ 15l/min e.g., by face mask, nasal cannula (NC); High flow supplemental oxygen therapy or NIV (noninvasive ventilation): O2 flow >15l/min, e.g., by face mask, 'High Flow' devices (e.g. HFNC), CPAP or NIV including BiPAP and other device.			
Units: Subjects			
5. No supplemental oxygen therapy	4	0	4

4. Supplemental low flow oxygen therapy	12	10	22
3. High flow supplemental oxygen therapy or NIV	4	0	4
Coexisting disorders			
Coexisting disorders at inclusion visit			
Units: Subjects			
Yes	14	5	19
No	6	5	11
Median days from symptom onset to randomization			
Median days from symptom onset to randomization (IQR)			
Units: day			
median	10.5	16	
inter-quartile range (Q1-Q3)	8 to 12.5	12 to 23	-
Median days from admission to randomization			
Median days from admission to randomization (IQR)			
Units: day			
median	2	3	
inter-quartile range (Q1-Q3)	1 to 4	1 to 6	-
Median body temperature at randomization			
Median body temperature at randomization (IQR) in grade centigrade			
Units: ºC			
median	37.1	36.5	
inter-quartile range (Q1-Q3)	36.6 to 38.1	36.3 to 37.2	-
PaO2/Fi02: partial pressure of arterial oxygen/fraction of inspired oxygen			
Median PaO2/Fi02 mmHg (IQR) at randomization. PaO2/Fi02: partial pressure of arterial oxygen/fraction of inspired oxygen			
Units: mmHg			
median	298	341	
inter-quartile range (Q1-Q3)	223 to 348	261 to 404	-

End points

End points reporting groups

Reporting group title	Sarilumab plus Standard of Care

Reporting group description:

Sarilumab Kevzara 200 mg, 2 sc injections in pre-filled syringe or pen, 400 mg single dose. The patients of this arm also received drugs, including corticosteroids, or full supportive care according to the best SC updated in the local protocol for COVID-19.
Sarilumab (ATC code L04AC14) is a fully human anti-IL-6R monoclonal IgG1 antibody that binds to both membrane bound and soluble interleukin 6 (IL-6) receptor forms, thus blocking the cis- and trans-inflammatory signalling cascades of IL-6.

Reporting group title	Standard Care

Reporting group description:

Patients in standard care (SC) will received drugs, including corticosteroids, or full supportive care according to the best SC updated in the local protocol for COVID-19. Patients in the standard care (SC) were given the option to receive intravenous Tocilizumab (TCZ) after randomization if they worsened at investigator discretion, as this agent had become the SC in our centre when the protocol was designed.

Primary: Change in Clinical Status Assessment

End point title	Change in Clinical Status Assessment

End point description:

Score ranges 1-7
1. Death;
2. Hospitalized, requiring invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO);
3. Hospitalized, requiring non-invasive ventilation or high flow oxygen devices;
4. Hospitalized, requiring supplemental oxygen;
5. Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise)
6. Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care
7. Not hospitalized

No significant differences were seen in the median change [IQR] in clinical status on the 7-category ordinal scale at day 7 between SAR and SC (2 [0-3] vs 3 [0-3], p 0.32)

Chart: Evolution of clinical status in COVID-19 patients from baseline to day 14 according to the 7-category ordinal scale. Data are shown as the percentage of patients at each ordinal point in the sarilumab + standard care (SAR; n=20) and standard care (SC; n=10) groups, displayed as boxes with the different hues ranging

End point type	Primary

End point timeframe:

Day 7 After Randomisation

End point values	Sarilumab plus Standard of Care	Standard Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	10		
Units: Ordinal Scale				
median (inter-quartile range (Q1-Q3))	2 (0 to 3)	3 (0 to 3)		

Attachments (see zip file)	Evolution of clinical status in COVID-19 patients /Figure 2.jpeg

Statistical analyses

Statistical analysis title	Statistical Methods Change in clinical status 7 d
Comparison groups	Sarilumab plus Standard of Care v Standard Care
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Log hazard ratio

Primary: Duration of Hospitalisation

End point title	Duration of Hospitalisation
End point description: Median days to discharge on SAR and SC were similar (HR 0.65, SD 0.26; p 0.27)	
End point type	Primary
End point timeframe: 30 days form enrolment	

End point values	Sarilumab plus Standard of Care	Standard Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	10		
Units: day				
median (inter-quartile range (Q1-Q3))	7 (6 to 11)	6 (4 to 12)		

Statistical analyses

Statistical analysis title	Statistical Methods Duration of hospitalization
Comparison groups	Sarilumab plus Standard of Care v Standard Care

Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.05
Method	Kruskal-wallis
Parameter estimate	Hazard ratio (HR)

Primary: Death (30-day mortality)

End point title	Death (30-day mortality)

End point description:

Regarding 30-day mortality, 2/20 (10%) patients died in the SAR arm while no events (0/10) were found in SC. Those results were identical for in hospital mortality. Two deaths occurred in patients with previous grade III chronic kidney disease (CKD) and NIMV at randomization.

End point type	Primary

End point timeframe:

30 days from enrolment

End point values	Sarilumab plus Standard of Care	Standard Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	10		
Units: Number of patients	2	0		

Statistical analyses

Statistical analysis title	Death Statistical Analysis Death
Comparison groups	Standard Care v Sarilumab plus Standard of Care
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Log hazard ratio

Secondary: Time to Become Afebrile

End point title	Time to Become Afebrile

End point description:

Time to become afebrile for a minimum period of 48 hours, without antipyretics

End point type	Secondary

End point timeframe:

30 days from enrolment

End point values	Sarilumab plus Standard of Care	Standard Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	10		
Units: day				
median (inter-quartile range (Q1-Q3))	3 (3 to 6)	4 (4 to 8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progresion to Mechanical Ventilation

End point title	Progresion to Mechanical Ventilation

End point description:

In SAR, 4/20 (20%) and 3/20 (15%) patients required No-Invasive Mechanical Ventilation (NIMV) and Invasive Mechanical Ventilation (IMV) respectively vs none in the SC. Notably, 2/3 patients progressing to IMV were not receiving corticosteroids at randomization. The median time to oxygen withdrawal was similar between groups

End point type	Secondary

End point timeframe:

30 days from enrolment

End point values	Sarilumab plus Standard of Care	Standard Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	10		
Units: Number of patients				
Non-Invasive Mechanical Ventilation (NIMV)	4	0		
Invasive Mechanical Ventilation (IMV)	3	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Independence From Supplementary Oxygen Therapy

End point title	Time to Independence From Supplementary Oxygen Therapy

End point description:

Days from enrolment to supplementary oxygen therapy withdrawal. Evolution of partial pressure of arterial oxygen/fraction of inspired oxygen (PaO2/FiO2) throughout study visits (Chart, panel A) showed

no significant differences between both allocated interventions at day 1, 2, and 7 after randomization, nor at discharge.

Chart: Evolution of partial pressure of arterial oxygen/fraction of inspired oxygen (PaO2/FiO2) throughout study visits. Patients are grouped depending on: A) allocated interventions: standard care (SC) or sarilumab (SAR) and B) level of serum interleukin-6 (IL-6) at randomization (cut-off for high levels ≥ 30 pg/ml). Two patients died and their last observed value was carried forward. IL-6 levels at randomization were available only in 24 patients; high IL-6 levels were observed in 3 patients from the SAR group and 1 patient from the SC group. Data are shown as interquartile ranges (p75 upper edge of box, p25 lower edge, p50 midline) as well as the p95 & P5.

End point type	Secondary

End point timeframe:

30 days from enrolment

End point values	Sarilumab plus Standard of Care	Standard Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	10		
Units: day				
median (inter-quartile range (Q1-Q3))	5.5 (3 to 13)	4.5 (2 to 12)		

Attachments (see zip file)	Evolution of PaO2/FiO2/Figure 3.jpeg

Statistical analyses

No statistical analyses for this end point

Secondary: Evolution of laboratory parameters

End point title	Evolution of laboratory parameters

End point description:

Regarding surrogate inflammatory markers and laboratory parameters, no significant differences were observed between arms at baseline nor along the study, except for significant reductions of LDH levels after day 2 from randomization (Chart) in patients allocated to SC. The time plot decline of median CRP levels was consistent with previously reported data for sarilumab after a single 200 mg subcutaneous injection with a maximum decrease in day 7, but we did not observe a steeper decrease with 400 mg SAR on days 1,2, 4-5 after randomization compared to the control group (Chart, panel A)

Chart: Evolution of laboratory parameters throughout study visits. Patients from standard care (SC; white boxes) and sarilumab (SAR; gray boxes). Only values available at each time-point are shown and results are displayed as interquartile range (p75 upper edge of box, p25 lower edge, p50 midline) as well as the p95 (line above box) and p5 (line below). Dots represent outliers.

End point type	Secondary

End point timeframe:

30 days from enrolment-

End point values	Sarilumab plus Standard of Care	Standard Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	10		
Units: Please see chart	0	0		

Attachments (see zip file)	Evolution of laboratory parameters /Figure 4.jpeg

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Clinical Status Assessment (14 days)

End point title	Change in Clinical Status Assessment (14 days)

End point description:

Scale ranges 1-7:
1. Death
2. Hospitalized, with mechanical ventilation or extracorporeal membrane oxygenation (ECMO).
3. Hospitalized, with non-invasive mechanical ventilation, a mask with a reservoir or oxygen with high flow nasal goggles.
4. Hospitalized with oxygen supplement
5. Hospitalized, without oxygen supplement, but in need of continued medical care (related or not with COVID)
6. Hospitalized, without oxygen supplement and without the need for continued medical care
7 Not hospitalized

End point type	Secondary

End point timeframe:

14 days from enrolment

End point values	Sarilumab plus Standard of Care	Standard Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	10		
Units: Ordinal Scale				
median (inter-quartile range (Q1-Q3))	3 (3 to 3)	4 (2 to 4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Discontinuation Due to Adverse Reactions

End point title	Discontinuation Due to Adverse Reactions

End point description:

Number of adverse reactions that requires discontinuation of any drug in the study

End point type	Secondary

End point timeframe:
30 days after enrolment

End point values	Sarilumab plus Standard of Care	Standard Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	10		
Units: Number of patients	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

14 days post hospital discharge

Adverse event reporting additional description:

At the beginning of each visit, the patients were asked about the possible appearance of any adverse effect. The adverse events described spontaneously by the patients were also reported. Each adverse event was described temporarily. Adverse Events were defined as Definite, Probable, Posible, Unlikely or Conditional and Unrelated acoording to the c

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24

Reporting groups

Reporting group title	Sarilumab plus Standard of Care

Reporting group description:

Sarilumab Kevzara 200 mg, 2 sc injections in pre-filled syringe or pen, 400 mg single dose. The patients of this arm also received drugs, including corticosteroids, or full supportive care according to the best SC updated in the local protocol for COVID-19.
Sarilumab (ATC code L04AC14) is a fully human anti-IL-6R monoclonal IgG1 antibody that binds to both membrane bound and soluble interleukin 6 (IL-6) receptor forms, thus blocking the cis- and trans-inflammatory signalling cascades of IL-6.

Reporting group title	Standard Care

Reporting group description:

Patients in standard care (SC) will received drugs, including corticosteroids, or full supportive care according to the best SC updated in the local protocol for COVID-19. Patients in the standard care (SC) were given the option to receive intravenous Tocilizumab (TCZ) after randomization if they worsened at investigator discretion, as this agent had become the SC in our centre when the protocol was designed.

Serious adverse events	Sarilumab plus Standard of Care	Standard Care	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 20 (20.00%)	0 / 10 (0.00%)	
number of deaths (all causes)	2	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Organ failure	Additional description: 1 respiratory failure, and 2 fatal cases with failure of 2 organs (lung and kidney).		
subjects affected / exposed	2 / 20 (10.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Secondary bacterial infection	Additional description: 2 Secondary respiratory bacterial infections by Achromobacter xylosoxidans and Stafilococus aureus		

subjects affected / exposed	2 / 20 (10.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Sarilumab plus Standard of Care	Standard Care	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 20 (50.00%)	4 / 10 (40.00%)	
Hepatobiliary disorders			
Increased liver enzymes			
subjects affected / exposed	5 / 20 (25.00%)	3 / 10 (30.00%)	
occurrences (all)	0	0	
Endocrine disorders			
Steroid diabetes	Additional description: Steroid-induced hyperglycemia		
subjects affected / exposed	4 / 20 (20.00%)	1 / 10 (10.00%)	
occurrences (all)	0	0	
Infections and infestations			
Bacterial infection	Additional description: Invarive Bacterial or Fungal Infection		
subjects affected / exposed	2 / 20 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 April 2020	Positive serology (IgG/gM by ICT or IgM/IgA by ELISA) is included in the detection of Covid-19, in addition to the PCR already included in the original protocol. Study treatment defined, Kevzara 200 mg, 2 sc injections in prefilled syringe or autoinjector, 400 mg single dose. The original protocol established 400 mg or 300 mg based on the number of neutrophils.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This is a pilot study and the small sample size is the main limitation of the study. A full analysis of the limitations of the study is included in the publication in Frontiers of medicine doi: 10.3389/fmed.2022.819621.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32907638

http://www.ncbi.nlm.nih.gov/pubmed/34228774

http://www.ncbi.nlm.nih.gov/pubmed/35280907