Clinical trial results:
Double-blind Randomized Clinical Trial, Placebo-controlled to Assess the Efficacy of Montelukast in Mild-moderate Respiratory Symptoms in Patients With Long-COVID: E-SPERANZA COVID PROJECT

Summary

EudraCT number	2021-000605-24
Trial protocol	ES
Global end of trial date	28 August 2023

Results information

Result version number	v1 (current)
This version publication date	19 September 2024
First version publication date	19 September 2024
Summary attachment (see zip file)	E-SPERANZA COVID Final report_ICH E3 (E-SPERANZA COVID_Informe final.pdf)

Trial information

Trial identification

Sponsor protocol code	ESPERANZA_COVID

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04695704
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	IDIAP Jordi Gol
Sponsor organisation address	Gran Via de les Corts 587, Barcelona, Spain, 08007
Public contact	Unitat d'Estudi del Medicament (UEM), IDIAP Jordi Gol, 34 934824124, rmonfa@idiapjgol.info
Scientific contact	Unitat d'Estudi del Medicament (UEM), IDIAP Jordi Gol, 34 638686961, rmonfa@idiapjgol.info

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	03 July 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 July 2023
Global end of trial reached?	Yes
Global end of trial date	28 August 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective is to evaluate the efficacy of montelukast versus placebo to improve the quality of life associated with respiratory symptoms at day 28.

Protection of trial subjects:

Not applicable. Low risk intervention trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 August 2021
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: 86
Worldwide total number of subjects	86
EEA total number of subjects	86

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)	85
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients 18 to 80 years old with SARS-CoV-2 infectiontreated in Primary Health Care, with persistent respiratory symptoms (more than 1 and <12 months of evolution) and mild-moderate dyspnea: score at the beginning of the study according to the modified Medical Research Council (mMRC) scale from 0 to 3.

Pre-assignment period milestones

Number of subjects started	86
Number of subjects completed	86

Period 1

Period 1 title	overall trial (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:

Unblinding process done when final results were available.

Arms

Are arms mutually exclusive?	Yes
Arm title	Montelukast

Arm description:

10 mg oral montelukast once daily for 28 days

Arm type	Experimental
Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	Pluralais
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

10 mg oral montelukast once daily for 28 days

Arm title	Placebo

Arm description:

10 mg oral placebo once daily for 28 days

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

Dosage and administration details:

10 mg oral montelukast once daily for 28 days

Number of subjects in period 1	Montelukast	Placebo
Started	43	43
Completed	38	37
Not completed	5	6
Adverse event, non-fatal	2	-
Lost to follow-up	3	6

Baseline characteristics

Reporting groups	
Reporting group title	Montelukast
Reporting group description:	
10 mg oral montelukast once daily for 28 days	
Reporting group title	Placebo
Reporting group description:	
10 mg oral placebo once daily for 28 days	

Reporting group values	Montelukast	Placebo	Total
Number of subjects	43	43	86
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)	43	42	85
From 65-84 years	0	1	1
85 years and over	0	0	0
Age continuous Units: years			
median	45.00	51.00	
inter-quartile range (Q1-Q3)	38.50 to 49.00	41.50 to 56.50	-
Gender categorical Units: Subjects			
Female	36	32	68
Male	7	11	18

End points

End points reporting groups

Reporting group title	Montelukast
Reporting group description:	
10 mg oral montelukast once daily for 28 days	
Reporting group title	Placebo
Reporting group description:	
10 mg oral placebo once daily for 28 days	
Subject analysis set title	Study completed population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The Wilcoxon test was used for the comparison of quantitative variables and the chisquare test for the comparison of qualitative variables (or the Fisher test in case of extreme distributions in the crossed tables). In all comparisons, the statistical significance was set at 5%. Outcome measures were described and compared between the montelukast and placebo groups using the same statistics.	

Primary: Primary

End point title	Primary
End point description:	
Quality of life of respiratory symptoms according to COPD Assessment Test (CAT The COPD Assessment Test (CAT) is a questionnaire for people with COPD, designed to measure the impact of COPD on a person's life, and how this changes over time.Quality of life of respiratory symptoms according to COPD Assessment Test (CAT). This is a validated self-administered scale to quantify and monitor the impact of COPD on well-being and daily life. It consists of 8 items (from 0 to 5 points), and a total score of 0-40 (0-9 mild, 10-20 moderate, 21-30 severe and 31-40 very severe), being higher scores worse outcome. A difference of 2 or more points in health status is considered clinically significant.	
End point type	Primary
End point timeframe:	
Day 28	

End point values	Montelukast	Placebo	Study completed population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	43	43	86	
Units: [0-40]				
median (inter-quartile range (Q1-Q3))	17.00 (11.50 to 19.50)	12.00 (8.00 to 16.50)	13.00 (8.00 to 18.00)	

Statistical analyses

Statistical analysis title	Primary endpoint
Comparison groups	Montelukast v Placebo

Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Timeframe for reporting adverse events: Day 7, Day 14, Day 21, Day 28 and Day 56

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Montelukast

Reporting group description:

10 mg oral montelukast once daily for 28 days

Reporting group title	Placebo

Reporting group description:

10 mg oral placebo once daily for 28 days

Serious adverse events	Montelukast	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (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	Montelukast	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 43 (18.60%)	7 / 43 (16.28%)	
Nervous system disorders			
Insomnia			
subjects affected / exposed	0 / 43 (0.00%)	2 / 43 (4.65%)	
occurrences (all)	0	2	
Headache			
subjects affected / exposed	2 / 43 (4.65%)	2 / 43 (4.65%)	
occurrences (all)	2	2	
Gastrointestinal disorders			

Diarrhea			
subjects affected / exposed	2 / 43 (4.65%)	2 / 43 (4.65%)	
occurrences (all)	2	2	
Abdominal pain			
subjects affected / exposed	4 / 43 (9.30%)	1 / 43 (2.33%)	
occurrences (all)	4	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 September 2021	Adaptation of the protocol to the current long-covid profile patients associated with respiratory symptoms. Exclusion criteria related to a maximum of 3 months with symptomatology was extended until 12 months.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported