Clinical trial results:
A phase 2/3, randomized, double blind, placebo-controlled study to evaluate the efficacy and the safety of ABX464 in treating inflammation and preventing COVID-19 associated acute respiratory failure in patients aged 65 and patients aged 18 with at least one additional risk factor who are infected with SARS-CoV-2. (the MiR-AGE study).

Summary

EudraCT number	2020-001673-75
Trial protocol	FR DE GB ES BE IT
Global end of trial date	16 April 2021

Results information

Result version number	v1 (current)
This version publication date	30 January 2022
First version publication date	30 January 2022

Trial information

Trial identification

Sponsor protocol code	ABX464-401

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Abivax
Sponsor organisation address	5 rue de la Baume, Paris, France,
Public contact	CLINICAL OPERATIONS, ABIVAX, Paul.Gineste@abivax.com
Scientific contact	CLINICAL OPERATIONS, ABIVAX, Paul.Gineste@abivax.com

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	25 November 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 April 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to determine the efficacy of ABX464 50mg to prevent respiratory failure or death in study patients.

Protection of trial subjects:

An independent Data and Safety Monitoring Board (DSMB), with expertise and experience in virology, immunology, and biostatistics, and without direct involvement in the conduct of the trial, will be set up specifically to guarantee effective protection of patients, ensure the ethical conduct of the trial, benefit/risk ratio of the trial, and to ensure the independent review of the scientific results during the trial and at the end of the trial.
All safety data will be thoroughly reviewed by the DSMB. Part of the DSMB duties is to review occurrence of adverse events which character, severity or frequency is new in comparison to the existing risk profile. In such case, recommendations from the DSMB may lead the either additional stopping rules up to study discontinuation.
The DSMB will meet first after the 20 first patients are enrolled and treated for at least 4 weeks (D28) and then every month after this first meeting.
The DSMB will oversee the adequate balance of baseline characteristics (i.e. gender, disease duration, previous and concomitant CD medication) among the treatment groups and will review safety and efficacy data.
Furthermore, all potential causally-related Serious Adverse Events within 7 days of the initial notification by an investigating site. Every grade 3 or higher adverse event will be reported within 24 hours to the DSMB for causality assessment.
The DSMB has a consultative role. It will inform the Sponsor who will decide whether the DSMB recommendation will be followed. Besides, the DSMB may recommend the early termination of the trial at any time if an unacceptable toxicity occurs.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 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: 39
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	France: 32
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Italy: 31
Country: Number of subjects enrolled	Brazil: 352
Country: Number of subjects enrolled	Peru: 31

Country: Number of subjects enrolled	Mexico: 15
Worldwide total number of subjects	509
EEA total number of subjects	110

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)	361
From 65 to 84 years	148
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment period: 01-Jul-2020 to 05-Mar-2021

Pre-assignment

Screening details:

Adult (≥ 18 years old) men or women, hospitalized or not hospitalized, diagnosed for SARS-CoV-2 infection by PCR or Rapid Antigen tests, with at least one associated risk factor: Age ≥ 65 years/Obesity defined as BMI ≥ 30/Recent history of uncontrolled High Blood Pressure/Treated diabetes (type I or II)/History of ischemic cardiovascular disease

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

Arms

Are arms mutually exclusive?	Yes
Arm title	ABX464 + Standard of care

Arm description:

ABX464 50 mg once a day (oral capsule) for 28 days + Standard of Care (SOC)

Arm type	Active comparator
Investigational medicinal product name	ABX464
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

50 mg once a day during 28 days

Arm title	Placebo + Standard of care

Arm description:

Placebo 50 mg once a day (oral capsule) for 28 days + Standard of Care (SOC)

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:

50 mg once a day during 28 days

Number of subjects in period 1	ABX464 + Standard of care	Placebo + Standard of care
Started	339	170
Interim Analysis	203	102
Completed	188	99
Not completed	151	71
Adverse event, serious fatal	6	4
Consent withdrawn by subject	24	8
Adverse event, non-fatal	11	2
Lost to follow-up	5	4
Protocol deviation	1	-
Study terminated by sponsor+data missing in eCRF	104	53

Baseline characteristics

Reporting groups	
Reporting group title	ABX464 + Standard of care
Reporting group description:	
ABX464 50 mg once a day (oral capsule) for 28 days + Standard of Care (SOC)	
Reporting group title	Placebo + Standard of care
Reporting group description:	
Placebo 50 mg once a day (oral capsule) for 28 days + Standard of Care (SOC)	

Reporting group values	ABX464 + Standard of care	Placebo + Standard of care	Total
Number of subjects	339	170	509
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)	241	120	361
From 65-84 years	98	50	148
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	54.9	54.4	
standard deviation	± 15.36	± 15.05	-
Gender categorical Units: Subjects			
Female	160	84	244
Male	179	86	265

End points

End points reporting groups

Reporting group title	ABX464 + Standard of care
Reporting group description:	
ABX464 50 mg once a day (oral capsule) for 28 days + Standard of Care (SOC)	
Reporting group title	Placebo + Standard of care
Reporting group description:	
Placebo 50 mg once a day (oral capsule) for 28 days + Standard of Care (SOC)	

Primary: Rate of Patients With no Invasive or Non-invasive Mechanical Ventilation (IMV and NIV, Respectively), But Excluding Simple Nasal/Mask Oxygen Supplementation, and Who Are Alive

End point title	Rate of Patients With no Invasive or Non-invasive Mechanical Ventilation (IMV and NIV, Respectively), But Excluding Simple Nasal/Mask Oxygen Supplementation, and Who Are Alive

End point description:

Efficacy analysis was done at time of interim analysis.
The data from the interim analysis shows that ratio of responders in active group was less than in the control group.
After 305 randomized patients completed the Day 28 assessment or reached the end of study- the estimated conditional power was 0.0% and study met the predefined stopping criterion for futility. This result was presented in DSMB meeting. DSMB recommended study early termination for futility, which led to stopping recruitment.

End point type	Primary

End point timeframe:

At the end of the 28-day treatment period

End point values	ABX464 + Standard of care	Placebo + Standard of care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	102		
Units: participants				
Responder	169	87		
Non-responder	24	7		
Missing	10	8		

Statistical analyses

Statistical analysis title	.Analysis of Primary Efficacy Endpoint

Statistical analysis description:

The number and percentage of patients without respiratory failure or death prevented (RFDP), estimate of common
risk difference, the corresponding CI and the p-value will be presented. The primary endpoint will also be analyzed
using logistic regression analysis with all stratification factors and treatment.

Comparison groups	ABX464 + Standard of care v Placebo + Standard of care
Number of subjects included in analysis	305
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.001
Method	Mantel-Haenszel

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
4 months	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24

Reporting groups	
Reporting group title	ABX464 + Standard of care
Reporting group description:	
ABX464 50 mg once a day (oral capsule) for 28 days + Standard of Care (SOC)	
Reporting group title	Placebo + Standard of care
Reporting group description:	
Placebo 50 mg once a day (oral capsule) for 28 days + Standard of Care (SOC)	

Serious adverse events	ABX464 + Standard of care	Placebo + Standard of care	
Total subjects affected by serious adverse events			
subjects affected / exposed	36 / 335 (10.75%)	20 / 170 (11.76%)	
number of deaths (all causes)	2	4	
number of deaths resulting from adverse events			
Investigations			
Oxygen saturation decreased			
subjects affected / exposed	1 / 335 (0.30%)	2 / 170 (1.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Shock			
subjects affected / exposed	0 / 335 (0.00%)	1 / 170 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 335 (0.30%)	0 / 170 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			

subjects affected / exposed	0 / 335 (0.00%)	1 / 170 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 335 (0.30%)	0 / 170 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 335 (0.00%)	1 / 170 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 335 (0.30%)	0 / 170 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	2 / 335 (0.60%)	0 / 170 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	1 / 335 (0.30%)	0 / 170 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 335 (0.30%)	0 / 170 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroduodenal haemorrhage			
subjects affected / exposed	0 / 335 (0.00%)	1 / 170 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pancreatitis			
subjects affected / exposed	0 / 335 (0.00%)	1 / 170 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	2 / 335 (0.60%)	0 / 170 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 335 (0.30%)	0 / 170 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic artery embolism			
subjects affected / exposed	1 / 335 (0.30%)	0 / 170 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	3 / 335 (0.90%)	2 / 170 (1.18%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	2 / 335 (0.60%)	0 / 170 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	2 / 335 (0.60%)	0 / 170 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 335 (0.00%)	1 / 170 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory failure			
subjects affected / exposed	1 / 335 (0.30%)	3 / 170 (1.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 335 (0.30%)	0 / 170 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Coronavirus infection			
subjects affected / exposed	0 / 335 (0.00%)	1 / 170 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	5 / 335 (1.49%)	5 / 170 (2.94%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 1	
Septic shock			
subjects affected / exposed	0 / 335 (0.00%)	1 / 170 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Severe acute respiratory syndrome			
subjects affected / exposed	1 / 335 (0.30%)	1 / 170 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	10 / 335 (2.99%)	2 / 170 (1.18%)	
occurrences causally related to treatment / all	0 / 10	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Metabolism and nutrition disorders			
Diabetic metabolic decompensation			

subjects affected / exposed	2 / 335 (0.60%)	0 / 170 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 335 (0.00%)	1 / 170 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	ABX464 + Standard of care	Placebo + Standard of care	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	115 / 335 (34.33%)	27 / 170 (15.88%)	
Nervous system disorders			
Headache			
subjects affected / exposed	49 / 335 (14.63%)	19 / 170 (11.18%)	
occurrences (all)	51	19	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	32 / 335 (9.55%)	5 / 170 (2.94%)	
occurrences (all)	34	5	
Diarrhoea			
subjects affected / exposed	30 / 335 (8.96%)	6 / 170 (3.53%)	
occurrences (all)	31	6	
Nausea			
subjects affected / exposed	20 / 335 (5.97%)	6 / 170 (3.53%)	
occurrences (all)	21	7	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	23 / 335 (6.87%)	4 / 170 (2.35%)	
occurrences (all)	24	4	

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

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

DSMB recommended study early termination for futility based on the interim analysis. Therefore, further efficacy analysis were not performed.

Notes: