Clinical trial results:
Phase IIa randomized, double blind, placebo controlled, parallel group, multiple dose study on ABX464 in combination with methotrexate (MTX), in patients with moderate to severe active Rheumatoid Arthritis who have inadequate response to MTX or/and to an anti- tumor necrosis factor alpha (TNF) therapy, or intolerance to anti-TNF therapy.

Summary

EudraCT number	2018-004677-27
Trial protocol	BE HU
Global end of trial date	27 April 2021

Results information

Result version number	v1 (current)
This version publication date	01 May 2022
First version publication date	01 May 2022

Trial information

Trial identification

Sponsor protocol code	ABX464-301

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, 75008
Public contact	VP Clinical Operations, Abivax, +33 0 15383 0961, paul.gineste@abivax.com
Scientific contact	VP Clinical Operations, Abivax, +33 0 15383 0961, 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	22 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 April 2021
Global end of trial reached?	Yes
Global end of trial date	27 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the safety of ABX464 given at two different doses (100mg and 50 mg) vs placebo in combination with MTX when administered once daily in patients with moderate to severe active Rheumatoid Arthritis.

Protection of trial subjects:

No specific protection

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 July 2019
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	Poland: 35
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Hungary: 12
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	35
From 65 to 84 years	25

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment started on August 2019 in France, Belgium, Poland and Hungary

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	60
Number of subjects completed	60

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, Carer, Assessor

Blinding implementation details:

Bliniding implemented through IWRS

Arms

Are arms mutually exclusive?	Yes
Arm title	ABX464 50mg

Arm description:

treatment with ABX464 50mg given once daily, orally

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

Dosage and administration details:

One capsule orally per day, in the morning

Arm title	ABX464 100mg

Arm description:

Treatment with ABX464 100 mg given once daily, orally

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

Dosage and administration details:

One capsule orally per day, in the morning

Arm title	Placebo

Arm description:

Matching Placebo given once daily, orally

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:

One capsule orally per day, in the morning

Number of subjects in period 1	ABX464 50mg	ABX464 100mg	Placebo
Started	21	19	20
Completed	18	6	19
Not completed	3	13	1
Consent withdrawn by subject	2	3	-
Adverse event, non-fatal	1	9	1
Protocol deviation	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	ABX464 50mg
Reporting group description:	
treatment with ABX464 50mg given once daily, orally	
Reporting group title	ABX464 100mg
Reporting group description:	
Treatment with ABX464 100 mg given once daily, orally	
Reporting group title	Placebo
Reporting group description:	
Matching Placebo given once daily, orally	

Reporting group values	ABX464 50mg	ABX464 100mg	Placebo
Number of subjects	21	19	20
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			
Mean Age value collected at baseline			
Units: years			
arithmetic mean	57.9	54.4	58.6
standard deviation	± 11.4	± 10.6	± 11.0
Gender categorical			
Number of female and male patients			
Units: Subjects			
Female	15	11	11
Male	6	8	9

Reporting group values	Total		
Number of subjects	60		
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			
Mean Age value collected at baseline			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Number of female and male patients			
Units: Subjects			
Female	37		
Male	23		

End points

End points reporting groups	
Reporting group title	ABX464 50mg
Reporting group description: treatment with ABX464 50mg given once daily, orally	
Reporting group title	ABX464 100mg
Reporting group description: Treatment with ABX464 100 mg given once daily, orally	
Reporting group title	Placebo
Reporting group description: Matching Placebo given once daily, orally	

Primary: number of treatment emergent adverse event	
End point title	number of treatment emergent adverse event
End point description: Number of Treatment-emergent Adverse Events in the ABX464 Treated Patients Versus Placebo	
End point type	Primary
End point timeframe: 12 weeks	

End point values	ABX464 50mg	ABX464 100mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	20	
Units: number of patients	18	18	14	

Statistical analyses

Statistical analysis title	analysis of all TEAEs 50 mg vs placebo
Comparison groups	ABX464 50mg v Placebo
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2212
Method	likelihood ratio chi-square test
Confidence interval	
level	90 %

Statistical analysis title	analysis of all TEAEs 100mg vs placebo
Comparison groups	ABX464 100mg v Placebo

Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0351
Method	likelihood ratio chi-square test

Secondary: ACR20/50/70 response

End point title	ACR20/50/70 response

End point description:

number of patients who achieved at least 20%, 50% or 70% improvement in the ACR response at week 12

End point type	Secondary

End point timeframe:

12 weeks

End point values	ABX464 50mg	ABX464 100mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	20	
Units: number of patients				
ACR20	9	3	4	
ACR50	5	2	1	
ACR70	4	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: C-Reactive Protein (CRP)

End point title	C-Reactive Protein (CRP)

End point description:

Mean CRP change from Baseline to Week 12

End point type	Secondary

End point timeframe:

12 weeks

End point values	ABX464 50mg	ABX464 100mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	20	
Units: mg/L				
arithmetic mean (standard deviation)	-4.31 (± 28.83)	0.62 (± 4.89)	-0.65 (± 18.74)	

Statistical analyses

No statistical analyses for this end point

Secondary: Tender Joint Count

End point title	Tender Joint Count

End point description:

Number of Tender Joint count (TJC) change from Baseline to week 12

End point type	Secondary

End point timeframe:

12 weeks

End point values	ABX464 50mg	ABX464 100mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	20	
Units: number				
arithmetic mean (standard deviation)	-6.8 (± 6.4)	-4.1 (± 6.6)	-2.9 (± 3.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Swollen Joint Count

End point title	Swollen Joint Count

End point description:

number of swollen Joint count (SJC) change from Baseline to Week 12

End point type	Secondary

End point timeframe:

12 weeks

End point values	ABX464 50mg	ABX464 100mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	20	
Units: number				
arithmetic mean (standard deviation)	-4.4 (± 4.2)	-3.2 (± 5.3)	-2.9 (± 3.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Pain-VAS

End point title	Pain-VAS

End point description:

Pain-Visaul Analog Scale change from baseline to Week 12

End point type	Secondary

End point timeframe:

12 weeks

End point values	ABX464 50mg	ABX464 100mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	20	
Units: number				
arithmetic mean (standard deviation)	-2.63 (± 2.43)	-0.89 (± 1.97)	-0.78 (± 2.36)	

Statistical analyses

No statistical analyses for this end point

Secondary: Patient global assessment of disease

End point title	Patient global assessment of disease

End point description:

Patient global assessment of disease (Pt-GA) change from Baseline to Week 12

End point type	Secondary

End point timeframe:

12 weeks

End point values	ABX464 50mg	ABX464 100mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	20	
Units: number				
arithmetic mean (standard deviation)	-1.44 (± 1.92)	-0.89 (± 1.93)	-0.36 (± 2.16)	

Statistical analyses

No statistical analyses for this end point

Secondary: Physician global assessment of disease

End point title	Physician global assessment of disease
End point description:	
Physician global assessment of disease (Pr-GA) change from baseline to week 12	
End point type	Secondary
End point timeframe:	
12 weeks	

End point values	ABX464 50mg	ABX464 100mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	20	
Units: number				
arithmetic mean (standard deviation)	-3.26 (± 2.7)	-1.89 (± 2.95)	-1.63 (± 2.38)	

Statistical analyses

No statistical analyses for this end point

Secondary: HAQ Functional Disability Index

End point title	HAQ Functional Disability Index
End point description:	
HAQ Functional Disability Index (HAQ-DI) change from Baseline to Week 12	
End point type	Secondary
End point timeframe:	
12 weeks	

End point values	ABX464 50mg	ABX464 100mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	20	
Units: number				
arithmetic mean (standard deviation)	-0.435 (± 0.618)	-0.105 (± 0.344)	-0.181 (± 0.482)	

Statistical analyses

No statistical analyses for this end point

Secondary: Erythrocyte Sedimentation Rate (ESR)

End point title	Erythrocyte Sedimentation Rate (ESR)
End point description: Change from Baseline in ESR	
End point type	Secondary
End point timeframe: 12 weeks	

End point values	ABX464 50mg	ABX464 100mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	20	
Units: number				
arithmetic mean (standard deviation)	-2.6 (± 19.3)	-0.3 (± 6.8)	-2.7 (± 16.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Disease activity score 28 joints (DAS28)

End point title	Disease activity score 28 joints (DAS28)
End point description: Change From Baseline in DAS28-CRP (C-reactive protein) and DAS28-ESR	
End point type	Secondary
End point timeframe: 12 weeks	

End point values	ABX464 50mg	ABX464 100mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	20	
Units: number				
arithmetic mean (standard deviation)				
DAS28-CRP	-1.41 (± 1.45)	-0.72 (± 1.13)	-0.60 (± 0.98)	
DAS28-ESR	-1.43 (± 1.39)	-0.74 (± 1.11)	-0.59 (± 1.00)	

Statistical analyses

No statistical analyses for this end point

Secondary: Simplified disease activity index score (SDAI)

End point title	Simplified disease activity index score (SDAI)
End point description: change from baseline in SDAI	
End point type	Secondary
End point timeframe: 12 weeks	

End point values	ABX464 50mg	ABX464 100mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	20	
Units: number				
arithmetic mean (standard deviation)	-20.21 (± 33.27)	-9.37 (± 14.44)	-7.58 (± 22.69)	

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Disease Activity Index Score (CDAI)

End point title	Clinical Disease Activity Index Score (CDAI)
End point description: Chnage from baseline in CDAI	
End point type	Secondary
End point timeframe: 12 weeks	

End point values	ABX464 50mg	ABX464 100mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	20	
Units: number				
arithmetic mean (standard deviation)	-15.89 (± 13.29)	-9.99 (± 15.85)	-6.93 (± 10.13)	

Statistical analyses

No statistical analyses for this end point

Secondary: DAS28-CRP EULAR response

End point title	DAS28-CRP EULAR response

End point description:

Numbe rof patients achieving categorical Disease Activity Score (DAS) DAS28-C-Reactive Protein (CRP) [DAS28-CRP] response measured as moderate/good European League Against Rheumatism (EULAR) response

End point type	Secondary

End point timeframe:

12 weeks

End point values	ABX464 50mg	ABX464 100mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	20	
Units: number of patients	14	6	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Low Disease Activity (LDA)

End point title	Low Disease Activity (LDA)

End point description:

Number of patients Achieving Low Disease Activity (LDA) defined as DAS28-ESR <=3.2

End point type	Secondary

End point timeframe:

12 weeks

End point values	ABX464 50mg	ABX464 100mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	20	
Units: number of patients	4	2	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Remission

End point title	Remission

End point description:

Number of patients achieving remmission:
DAS28-ESR remission is defined as DAS2-ESR < 2.6
SDAI remission is considered achieved if the SDAI score ≤ 3.3
CDAI remission is considered achieved if the CDAI score ≤ 2.8
ACR/EULAR boolean-based remission based on: Tender/painful Joint Count (28), Swollen Joint Count (28), C-Reactive Protein, patient global assessment of disease, All ≤ 1

End point type	Secondary

End point timeframe:

12 weeks

End point values	ABX464 50mg	ABX464 100mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	20	
Units: number of patients				
DAS28-ESR remission	2	0	0	
SDAI remission	1	0	0	
CDAI remission	3	0	0	
Boolean remission	1	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
15 weeks : 12 weeks treatment period + 3 weeks safety period	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups	
Reporting group title	ABX464 50 mg treatment
Reporting group description: -	
Reporting group title	ABX464 100 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	ABX464 50 mg treatment	ABX464 100 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	1 / 20 (5.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Atrial fibrillation	Additional description: atrial fibrillation reactive to hypokalemia secondary to diarrhea in the context of study drug treatment		
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 21 (0.00%)	0 / 19 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	ABX464 50 mg treatment	ABX464 100 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 21 (71.43%)	17 / 19 (89.47%)	5 / 20 (25.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 21 (38.10%)	10 / 19 (52.63%)	4 / 20 (20.00%)
occurrences (all)	19	16	6
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	5 / 21 (23.81%)	4 / 19 (21.05%)	1 / 20 (5.00%)
occurrences (all)	6	10	1
Diarrhoea			
subjects affected / exposed	4 / 21 (19.05%)	7 / 19 (36.84%)	1 / 20 (5.00%)
occurrences (all)	7	11	1
Dyspepsia			
subjects affected / exposed	1 / 21 (4.76%)	3 / 19 (15.79%)	0 / 20 (0.00%)
occurrences (all)	1	4	0
Vomiting			
subjects affected / exposed	2 / 21 (9.52%)	3 / 19 (15.79%)	0 / 20 (0.00%)
occurrences (all)	2	4	0
Abdominal pain			
subjects affected / exposed	2 / 21 (9.52%)	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences (all)	3	1	0
Nausea			
subjects affected / exposed	3 / 21 (14.29%)	9 / 19 (47.37%)	0 / 20 (0.00%)
occurrences (all)	4	12	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 21 (9.52%)	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences (all)	2	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 21 (0.00%)	2 / 19 (10.53%)	1 / 20 (5.00%)
occurrences (all)	0	3	1
Rheumatoid arthritis			

subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2	1 / 19 (5.26%) 1	1 / 20 (5.00%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 July 2019	Clarification on Data Safety Monitoring Board (DSMB) procedures Clarification on concomitant medication Clarfication about the infection exclusion criteria
24 October 2019	Addition of miR-124 assays and INR assessment Addition ofTruculture(R) samples for cytokines determination clarification of last dosing day procedure

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported