Clinical trial results:
Randomized, double-blind, placebo-controlled, 3-arm, 36 weeks parallel-group study to evaluate the safety and tolerability of ORY-2001 in patients with Relapsing-Remitting Multiple Sclerosis (RRMS) and Secondary Progressive Multiple Sclerosis (SPMS). SATEEN Study

Summary

EudraCT number	2017-002838-23
Trial protocol	ES
Global end of trial date	01 September 2020

Results information

Result version number	v1 (current)
This version publication date	06 December 2023
First version publication date	06 December 2023

Trial information

Trial identification

Sponsor protocol code	CL02-ORY-2001MS

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Oryzon Genomics S. A.
Sponsor organisation address	Carrer de Sant Ferran, 74, CORNELLA DE LLOBREGAT, Spain, 08940
Public contact	Douglas V. Faller, Oryzon Genomics S.A., 34 93 515 1313, dfaller@oryzon.com
Scientific contact	Douglas V. Faller, Oryzon Genomics S.A., 34 93 515 13 13, dfaller@oryzon.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	14 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 September 2020
Global end of trial reached?	Yes
Global end of trial date	01 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of two doses of vafidemstat (ORY-2001) compared to placebo in multiple sclerosis (MS) patients.

Protection of trial subjects:

In accordance with European Union RGPD 2016/679 of 27 April, 2016 the data were processed in accordance with the specifications outlined by the local law to ensure that requirements regarding personal data protection are met. If an external organization processed data on behalf of Oryzon, a contractual procedure was signed between Oryzon and the external organization to ensure compliance with the above-mentioned legislation. If applicable, the participation of patients in this study was reported to the appropriate local data protection agencies, in accordance with European Union RGPD 2016/679 of 27 April 2016 and Country-specific guidelines and laws (Spanish Organic Law 3/2018 of 5 December).

Patients were free to discontinue their participation in the study at any time. Withdrawal from the study did not affect or prejudice the patient’s further treatment. Patients could be withdrawn from study treatment and assessments at any time, if deemed necessary by the Investigator. In the event that a patient was to withdraw consent to participate in the study, the patient was asked, if possible, to return for a follow-up visit to document his clinical status. The data of this visit were only recorded in the patient's medical history. An independent Data Monitoring Committee (DMC) reviewed unblinded safety data throughout the study.

Background therapy: -

Evidence for comparator:

Placebo was the comparator in the Treatment period.

Actual start date of recruitment	24 January 2018
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: 18
Worldwide total number of subjects	18
EEA total number of subjects	18

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

Subject disposition

Recruitment

Recruitment details:

A total of 8 centers recruited patients in this study. A total of 25 patients were screened and 18 patients were randomized and treated. During the Treatment Period, 7 patients were randomized to and received vafidemstat 0.6 mg, 7 were randomized to and received vafidemstat 1.2 mg and 4 were randomized to and received placebo.

Pre-assignment

Screening details:

A Screening Period for up to 4 weeks before the Treatment Period was allowed. HIV antibody test and hepatitis testing including HBV surface antigen and HCV antibody were performed at the screening visit (Visit 0) for all patients. These tests were only used to determine patient eligibility for inclusion in the study.

Period 1

Period 1 title	Treatment Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Blinding implementation details:

To guarantee double-blind conditions, all the drugs were presented in identical capsules consisting of special opaque material for clinical studies, and the patients took the same number of capsules daily (one) during 5 consecutive days(total of 5 capsules) followed by 2 days off. The study randomisation was only to be broken for valid medical or safety reasons, for example, a serious adverse event.

Arms

Are arms mutually exclusive?	Yes
Arm title	Vafidemstat 0.6 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Vafidemstat 0.6 mg
Investigational medicinal product code	
Other name	ORY-2001
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Swedish orange colored size 3 capsules (hydroxypropyl methylcellulose shells) were loaded directly with 0.6 mg vafidemstat (ORY-2001) drug substance without addition of excipients, and by means of Xcelodose® filling technology. Study medication was to be taken orally, after overnight fasting conditions, early in the morning, five times per week, following a 5 days on / 2 days off schedule (i.e., fiw, once daily from Monday to Friday).

Arm title	Vafidemstat 1.2 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Vafidemstat 1.2 mg
Investigational medicinal product code	
Other name	ORY-2001
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Swedish orange colored size 3 capsules (hydroxypropyl methylcellulose shells) were loaded directly with 1.2 mg vafidemstat (ORY-2001) drug substance without addition of excipients, and by means of Xcelodose® filling technology. Study medication was to be taken orally, after overnight fasting

conditions, early in the morning, five times per week, following a 5 days on / 2 days off schedule (i.e., fiw, once daily from Monday to Friday).

Arm title	Placebo
Arm description: -	
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:

Swedish orange colored size 3 capsules (hydroxypropyl methylcellulose shells) were loaded directly with cellulose microcristalline by means of Xcelodose® filling technology. Study medication was to be taken orally, after overnight fasting conditions, early in the morning, five times per week, following a 5 days on / 2 days off schedule (i.e., fiw, once daily from Monday to Friday).

Number of subjects in period 1	Vafidemstat 0.6 mg	Vafidemstat 1.2 mg	Placebo
Started	7	7	4
Completed	5	6	3
Not completed	2	1	1
Withdrawal before W36 + No valid MRI assessment	1	-	-
No valid MRI assessment at W36	1	1	-
Any eligibility criteria not fulfilled + Major PD	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Vafidemstat 0.6 mg
Reporting group description: -	
Reporting group title	Vafidemstat 1.2 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Vafidemstat 0.6 mg	Vafidemstat 1.2 mg	Placebo
Number of subjects	7	7	4
Age categorical			
Only the FAS population results are available			
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)	7	7	4
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Only the FAS population results are available			
Units: years			
arithmetic mean	46.7	50.1	49.4
standard deviation	± 10.44	± 7.76	± 9.02
Gender categorical			
Units: Subjects			
Female	5	4	4
Male	2	3	0

Reporting group values	Total		
Number of subjects	18		
Age categorical			
Only the FAS population results are available			
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)	18		

From 65-84 years	0		
85 years and over	0		

Age continuous			
Only the FAS population results are available			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	13		
Male	5		

End points

End points reporting groups

Reporting group title	Vafidemstat 0.6 mg
Reporting group description: -	
Reporting group title	Vafidemstat 1.2 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Number of TEAEs

End point title	Number of TEAEs[1]
End point description:	
End point type	Primary
End point timeframe:	

Adverse events (AEs) were recorded during the study period from the signing of informed consent to the completion of the follow-up period (Visit FU2). Treatment emergent AEs (TEAEs) were defined as AEs which started after first intake of study drug.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The primary endpoints were assessments of safety and no statistical testing was performed.

End point values	Vafidemstat 0.6 mg	Vafidemstat 1.2 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	7	4	
Units: Units				
Overall number of TEAEs	17	21	17	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Serious TEAEs

End point title	Number of Serious TEAEs[2]
End point description:	
End point type	Primary
End point timeframe:	

Adverse events (AEs) were recorded during the study period from the signing of informed consent to the completion of the follow-up period (Visit FU2). Treatment emergent AEs (TEAEs) were defined as AEs which started after first intake of study drug.

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The primary endpoints were assessments of safety and no statistical testing was performed.

End point values	Vafidemstat 0.6 mg	Vafidemstat 1.2 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	7	4	
Units: Number				
Overall number of serious TEAEs	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Incidence of TEAEs

End point title	Incidence of TEAEs[3]

End point description:

End point type	Primary

End point timeframe:

Adverse events (AEs) were recorded during the study period from the signing of informed consent to the completion of the follow-up period (Visit FU2). Treatment emergent AEs (TEAEs) were defined as AEs which started after first intake of study drug.

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The primary endpoints were assessments of safety and no statistical testing was performed.

End point values	Vafidemstat 0.6 mg	Vafidemstat 1.2 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	7	4	
Units: unit(s)				
arithmetic mean (standard deviation)				
TEAEs per subject-years of follow-up	3.64 (± 2.45)	4.44 (± 2.67)	6.12 (± 4.13)	

Statistical analyses

No statistical analyses for this end point

Primary: Use of concomitant medication (most used)

End point title	Use of concomitant medication (most used)[4]

End point description:

Most used concomitant medications.

End point type	Primary

End point timeframe:

Concomitant medication at week 36.

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The primary endpoints were assessments of safety and no statistical testing was performed.

End point values	Vafidemstat 0.6 mg	Vafidemstat 1.2 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	7	4	
Units: Number				
Anti-inflammatory and Antirheumatic, Non-Steroids	4	5	2	
Other Analgesics And Antipyretics	2	3	3	
Antidepressants	1	2	1	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded during the study period from the signing of informed consent to the completion of the follow-up period (Visit FU2).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Vafidemstat 0.6 mg
Reporting group description: -	
Reporting group title	Vafidemstat 1.2 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Vafidemstat 0.6 mg	Vafidemstat 1.2 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Vafidemstat 0.6 mg	Vafidemstat 1.2 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 7 (85.71%)	7 / 7 (100.00%)	3 / 4 (75.00%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	3
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	3 / 4 (75.00%)
occurrences (all)	1	0	3
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	2 / 4 (50.00%)
occurrences (all)	0	0	2
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	2
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	2 / 4 (50.00%)
occurrences (all)	1	0	2
Constipation			
subjects affected / exposed	2 / 7 (28.57%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
Nausea			
subjects affected / exposed	0 / 7 (0.00%)	2 / 7 (28.57%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Abdominal pain upper			
subjects affected / exposed	1 / 7 (14.29%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	2
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	2 / 4 (50.00%)
occurrences (all)	1	0	3
Influenza			
subjects affected / exposed	0 / 7 (0.00%)	2 / 7 (28.57%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Urinary tract infection			

subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	1 / 7 (14.29%) 1	1 / 4 (25.00%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 December 2017	This amendment was regarded as "substantial" as it involved the following objectives: • Clarify and further detail the criteria for clinical observations that would require re-consent of the patient in the event that they appear for the first time, and a withdrawal of the patient in the event that they appear for the second time. • Clarify the duration of the open extension period of the trial. • Correct and / or clarify small inconsistencies between different sections of the protocol and small errors detected in the text. • Modify the information sheet for patients, consequently to the aforementioned changes in the protocol.
01 March 2018	This amendment was regarded as "substantial" since it involved the following objectives: • Specify some of the inclusion and exclusion criteria for patients in the trial. • Specify the type of antidepressant drugs not allowed in the trial. • Include blood and urine tests in the selection visit, which by mistake was not incorporated into the protocol as it was done for the rest of the follow-up visits. • Determine tuberculosis tests according to routine clinical practice. • Modify the calendar of meetings of the Data Monitoring Committee. • Administrative changes and correction of small errors in the text. • Modify the information sheet for patients, consequently to the aforementioned changes in the protocol.
09 July 2019	This amendment was considered as "substantial" since the following objectives were involved: • Add a second period of study extension in patients with Secondary Progressive Multiple Sclerosis (SPMS) • Correction of small errors in the text. • New specific patient information sheet for the second extension phase of the study in patients with SPMS.
16 October 2019	This amendment was considered as "substantial" since the following objectives were involved: • Clarify the period of time in which the concomitant medications established in the protocol would be prohibited in order to avoid possible drug interactions that may exist between vafidemstat and the prohibited concomitant medication. • Management of the patient in case of need for treatment with concomitant prohibited medication during the safety follow-up period.
12 November 2019	The approval of a substantial amendment to the protocol was requested to include the performance of a pharmacogenetic sub-study in order to evaluate whether individual genetic variability (polymorphisms and associated phenotypes) in the main genes related to ADME pathways in humans was associated with the pharmacokinetic response to vafidemstat.

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.

None reported.

Notes: