Clinical trial results:
Treatment of autologous mesenchymal stem cells derived from bone marrow as a potential therapeutic strategy for the treatment of multiple sclerosis

Summary

EudraCT number	2012-000734-19
Trial protocol	ES
Global end of trial date	27 November 2019

Results information

Result version number	v1 (current)
This version publication date	21 April 2022
First version publication date	21 April 2022
Summary attachment (see zip file)	Treatment of autologous mesenchymal stem cells derived from bone marrow as a potential therapeutic strategy for the treatment of multiple sclerosis (SYNOPSIS (multiple sclerosis).pdf)

Trial information

Trial identification

Sponsor protocol code	XCEL-MS-02

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Banc de Sang i Teixits
Sponsor organisation address	Passeig Taulat 116, Barcelona, Spain,
Public contact	Ruth Coll, Banc de Sang i Teixits, 34 93557 35 00, rucoll@bst.cat
Scientific contact	Ruth Coll, Banc de Sang i Teixits, 34 93557 35 00, rucoll@bst.cat

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	27 November 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 November 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1 - To evaluate the safety and tolerability of XCEL-MC-ALPHA by:
a. Overall incidence of adverse events by treatment
b. Incidence of adverse events by organ system preferred term, by treatment.
c. Severity of adverse events per treatment.
d. Intensity of adverse events per treatment.
e. Causation by treatment.

Protection of trial subjects:

There were no specific procedure. BM extraction were performed under local anaesthesia and sedation, and were discharged few hours later.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 March 2014
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: 8
Worldwide total number of subjects	8
EEA total number of subjects	8

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)	8
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The recruitment period was from May 11th, 2015 to August 23trd, 2016. All patients were included in a single center (Hospital Vall d'Hebron) in Barcelona.

Pre-assignment

Screening details:

All screened patients (8) were compliant with inclusion/exclusion details and all entered the trial. All patients were diagnosed with Relapsing-Remitting Multiple Sclerosis (RRMS) or Secondary Progressive Multiple Sclerosis (SPMS).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	XCEL-MC-ALPHA/Placebo

Arm description:

Autologous adult mesenchymal stem cells from bone marrow expanded and cryopreserved in saline solution balanced with electrolytes (ViafloPlasmalyte, Baxter, S.L) and 2% v/v of human serum albumin (Instituto Grifols, S.A. Suspension for injection)]. Dose: 106±20% cells/kg. Mode of administration: Intravenous use. Infusion duration: 10 minutes

Arm type	Experimental
Investigational medicinal product name	XCEL-MC-ALPHA
Investigational medicinal product code	
Other name	BM-MSC cryopreserved
Pharmaceutical forms	Infusion
Routes of administration	Intravascular use

Dosage and administration details:

Dose: 106±20% cells/kg (0.8x106 to 1.2x106 cells/kg). Mode of administration: Intravenous use. Infusion duration: 10 minutes.

Arm title	Placebo/XCEL-MC-ALPHA

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravascular use

Dosage and administration details:

Dose: NA. Mode of administration: Intravenous use. Infusion duration: 10 minutes.

Number of subjects in period 1	XCEL-MC-ALPHA/Placebo	Placebo/XCEL-MC-ALPHA
Started	4	4
Completed	4	4

Baseline characteristics

Reporting groups

Reporting group title	Period 1

Reporting group description: -

Reporting group values	Period 1	Total	
Number of subjects	8	8	
Age categorical			
Demography and Baseline Characteristics: Mean (SD) age = 43.3 (5.6), 50% men, mean (SD) of years since the first outbreak = 15.7 (8.3), mean (SD) of outbreaks in the last year = 1.0 (0.5) and mean (SD) of baseline EDSS score = 3.0 (0.7). No significant differences were observed on demography and baseline characteristics, medical history and concurrent illnesses between the two groups at randomisation (U Mann-Whitney test, p>0.05 and Fisher's exact test, p>0.05).			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	8	8	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	4	4	
Male	4	4	

Subject analysis sets

Subject analysis set title	Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

Includes all eligible patients who have received the study treatment.

Subject analysis set title	Efficacy
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients in the safety population who have not incurred in any major protocol violation and have at least one baseline and one subsequent primary efficacy endpoint assessment of each treatment period. It will be the reference population for the efficacy analyses.

Reporting group values	Safety	Efficacy	
Number of subjects	8	8	
Age categorical			
Demography and Baseline Characteristics: Mean (SD) age = 43.3 (5.6), 50% men, mean (SD) of years since the first outbreak = 15.7 (8.3), mean (SD) of outbreaks in the last year = 1.0 (0.5) and mean (SD) of baseline EDSS score = 3.0 (0.7). No significant differences were observed on demography and baseline characteristics, medical history and concurrent illnesses between the two groups at randomisation (U Mann-Whitney test, p>0.05 and Fisher's exact test, p>0.05).			

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)	8		
From 65-84 years	0		
85 years and over	0		
Gender categorical			
Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	XCEL-MC-ALPHA/Placebo

Reporting group description:

Autologous adult mesenchymal stem cells from bone marrow expanded and cryopreserved in saline solution balanced with electrolytes (ViafloPlasmalyte, Baxter, S.L) and 2% v/v of human serum albumin (Instituto Grifols, S.A. Suspension for injection)]. Dose: 106±20% cells/kg. Mode of administration: Intravenous use. Infusion duration: 10 minutes

Reporting group title	Placebo/XCEL-MC-ALPHA

Reporting group description: -

Subject analysis set title	Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

Includes all eligible patients who have received the study treatment.

Subject analysis set title	Efficacy
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients in the safety population who have not incurred in any major protocol violation and have at least one baseline and one subsequent primary efficacy endpoint assessment of each treatment period. It will be the reference population for the efficacy analyses.

Primary: Safety

End point title	Safety

End point description:

The safety and tolerability were evaluated by:
a. Overall incidence of adverse events by treatment.
b. Incidence of adverse events by system organ class and preferred term, by treatment.
c. Severity of adverse events per treatment.
d. Intensity of adverse events per treatment.
e. Causatlity assessment.

End point type	Primary

End point timeframe:

Week 24 and week 48

End point values	XCEL-MC-ALPHA/Placebo	Placebo/XCEL-MC-ALPHA	Safety	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	4	4	8	
Units: number	4	4	8	

Statistical analyses

Statistical analysis title	Descriptive

Statistical analysis description:

Descriptive statistics:
- Categorical variables: frequencies and category percentages.
- Continuous variables: Mean and Standard Deviation (SD); Median and 25th and 75th

percentiles of the distribution; number of cases; minimum and maximum value.

Comparison groups	Placebo/XCEL-MC-ALPHA v XCEL-MC-ALPHA/Placebo
Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 1
Method	Fisher exact

Notes:
[1] - Descriptive

Secondary: Efficacy: Lesions that enhance with gadolinium T1 in sequence MRI

End point title	Efficacy: Lesions that enhance with gadolinium T1 in sequence MRI

End point description:

End point type	Secondary

End point timeframe:
Week 24

End point values	XCEL-MC-ALPHA/Placebo	Placebo/XCEL-MC-ALPHA	Efficacy	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	4	4	8	
Units: number	4	4	8	

Statistical analyses

Statistical analysis title	Enhanced lesions with gadolinium T1
Comparison groups	XCEL-MC-ALPHA/Placebo v Placebo/XCEL-MC-ALPHA
Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0
Method	Fisher exact

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Week 24	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0
Reporting groups	
Reporting group title	XCEL-MC-ALPHA/Placebo
Reporting group description: -	
Reporting group title	Placebo/XCEL-MC-ALPHA
Reporting group description: -	

Serious adverse events	XCEL-MC-ALPHA/Placebo	Placebo/XCEL-MC-ALPHA	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (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: 0 %

Non-serious adverse events	XCEL-MC-ALPHA/Placebo	Placebo/XCEL-MC-ALPHA	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	4 / 4 (100.00%)	
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Nervous system disorders			
Neuralgia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Otitis externa			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Excessive cerumen production			
subjects affected / exposed	0 / 4 (0.00%)	2 / 4 (50.00%)	
occurrences (all)	0	2	
Vertigo			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Rhinitis allergic			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Gastroenteritis viral			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Tooth abscess			

subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 4 (25.00%)	2 / 4 (50.00%)	
occurrences (all)	1	2	
Periodontitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	

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

None reported