Clinical trial results:
A phase IIb, multicentre, randomised, double-blinded (DB), placebo-controlled, single-dose and multi-injection, parallel groups study to evaluate the efficacy and the safety of Ovasave (ovalbumin-specific autologous Treg cells (ova-Treg)) in patients with active refractory Crohn's Disease (Crohn's And Treg Study: CATS29)

Summary

EudraCT number	2014-001295-65
Trial protocol	BE DE AT IT
Global end of trial date	07 November 2016

Results information

Result version number	v1 (current)
This version publication date	03 February 2018
First version publication date	03 February 2018
Summary attachment (see zip file)	CATS29 CSR Synopsis (CSR CATS29_Summary.pdf)

Trial information

Trial identification

Sponsor protocol code	TXC-CD-002-2011

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02327221
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	TxCell
Sponsor organisation address	Allée de la Nertière, Valbonne Sophia-Antipolis, Les Cardoulines, France, 06560
Public contact	Clinical Department, TxCell, +33 (0) 497 218 301, contact@txcell.com
Scientific contact	Clinical Department, TxCell, +33 (0) 497 218 301, regulatory@txcell.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	06 October 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 November 2016
Global end of trial reached?	Yes
Global end of trial date	07 November 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Controlled versus placebo confirmation of the ability of a single intravenous (i.v.) injection of 1.10^6 cells dose of Ovasave (Ova-Treg cells) to induce a CDAI response (CDAI decrease ≥ 100 points) 6 weeks post administration compared to placebo in patients with moderately to severely active refractory Crohn's Disease (CD).

Protection of trial subjects:

Data and Safety Monitoring Board

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 December 2014
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	France: 10
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Germany: 7
Worldwide total number of subjects	26
EEA total number of subjects	26

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)	26
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study began on 03 Dec 2014.26 study centres were initiated, of which 11 were active site as follows: 4 centres in France, 3 in Belgium, 3 in Germany and 1 in Austria. 32 patients screened, 26 enrolled, and 7 randomised and received at least 1 administration of study treatment. The clinical trial was halted prematurely on 11 October 2016.

Pre-assignment

Screening details:

Patients were screened for eligibility against the inclusion criteria in the protocol at the Screening Visit (Visit 1). 32 patients were screened, 26 patients enrolled, and 7 patients were randomised and received at least 1 administration of the study treatment. The clinical trial was halted prematurely on 11 Oct 2016 following TxCell's decision.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	1.10e4

Arm description:

1.10e4 cells

Arm type	Experimental
Investigational medicinal product name	Ovasave
Investigational medicinal product code	
Other name	Ova-Treg
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Injection of 1x10e4 cells at Week 0 (visit 4) and Week 8 (visit 7)

Arm title	1.10e6

Arm description:

1.10e6 cells

Arm type	Experimental
Investigational medicinal product name	Ovasave
Investigational medicinal product code	
Other name	Ova-Treg
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Injection of 1x10e6 cells at Week 0 (visit 4) and Week 8 (visit 7)

Arm title	1.10e7

Arm description:

1.10e7 cells

Arm type	Experimental

Investigational medicinal product name	Ovasave
Investigational medicinal product code	
Other name	Ova-Treg
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Injection of 1x10e7 cells at Week 0 (visit 4) and Week 8 (visit 7)

Arm title	Placebo

Arm description:

Placebo

Arm type	Placebo
Investigational medicinal product name	Placebo for Ovasave
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Placebo for Ovasave injection at Week 0 and week 8

Number of subjects in period 1[1]	1.10e4	1.10e6	1.10e7
Started	2	1	2
Completed	2	1	2

Number of subjects in period 1[1]	Placebo
Started	2
Completed	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 32 subjects were screened and 26 were enrolled but only 7 were randomised and received treatment

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	7	7	
Age categorical 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)	7	7	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	3	3	
Male	4	4	

Subject analysis sets

Subject analysis set title	Full Analysis
Subject analysis set type	Full analysis

Subject analysis set description:

The analysis set includes all subjects who were randomised and received at least 1 administration of study treatment which is 7 subjects in total. The clinical trial was halted prematurely on 11 October 2016 following TxCell’s decision.

Reporting group values	Full Analysis		
Number of subjects	7		
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)	7		
From 65-84 years	0		
85 years and over	0		

Gender categorical Units: Subjects			
Female	3		
Male	4		

End points

End points reporting groups

Reporting group title	1.10e4
Reporting group description: 1.10e4 cells	
Reporting group title	1.10e6
Reporting group description: 1.10e6 cells	
Reporting group title	1.10e7
Reporting group description: 1.10e7 cells	
Reporting group title	Placebo
Reporting group description: Placebo	
Subject analysis set title	Full Analysis
Subject analysis set type	Full analysis

Subject analysis set description:

The analysis set includes all subjects who were randomised and received at least 1 administration of study treatment which is 7 subjects in total. The clinical trial was halted prematurely on 11 October 2016 following TxCell's decision.

Primary: CDAI response

End point title	CDAI response[1]

End point description:

The primary clinical efficacy endpoint was the percentage of patients with a CDAI response (CDAI decrease from baseline ≥100 points) in the active group of 1.10e6 Ova-Treg cells, 6 weeks after 1 Ovasave administration (Week 6 [Visit 6])

End point type	Primary

End point timeframe:

6 weeks after IMP administration

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: As the study was terminated early, planned statistical analyses were not carried out.

End point values	1.10e4	1.10e6	1.10e7	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	1	2	2
Units: number				
number (not applicable)	2	1	2	2

End point values	Full Analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: number				
number (not applicable)	7			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For Acute reactions - within 2 hours of IMP administration
For other general reactions - anytime throughout the study

Adverse event reporting additional description:

The type and incidence of adverse events (AEs) and serious adverse events (SAEs) were recorded at all visits and coded according to the medical dictionary for regulatory activities (MedDRA) criteria. Abnormal laboratory results constituted an AE, and were reported as such, if they are considered abnormal within the pathology of this study populatio

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	All Subjects

Reporting group description:

All subjects who were randomised and received at least 1 administration of study treatment.

Serious adverse events	All Subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 7 (57.14%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Immune system disorders			
Amyloidosis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anaphylactic reaction			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			

subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure	Additional description: Acute renal failure		
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	All Subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 7 (85.71%)		
Investigations			
Body temperature decreased			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Blood pressure increased			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Cardiac disorders			

Tachycardia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Feeling hot			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Sense of oppression			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Stomatitis	Additional description: Aphthous stomatis		
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			

Erythema subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 2 1 / 7 (14.29%) 1		
Metabolism and nutrition disorders Iron deficiency subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 February 2015	To propose changes concerning the quality of Ovasave
20 July 2015	To inform the NCAs and ECs of the 6 participating countries of a temporary halt of CATS29 study since 07 July 2015. This decision followed ANSM decision S15/217 (dated 07 July 2015) to suspend the manufacturing authorisation M14/298 granted to the TxCell Besançon site, the only site allowed to produce the IMP.
02 December 2015	To request the modification of the clinical study protocol while CATS29 study remained on hold. The main change was proposal of a new study design with 2 arms (Ovasave at the 1.10e6 cells dose versus placebo) instead of 4 arms (Ovasave at three doses of 1.10e4, 1.10e6, 1.10e7 cells versus placebo). The primary objective, study hypothesis and sample size calculations remained unchanged on the controlled assessment of the 1.10e6 cells dose versus placebo
25 February 2016	• To request the authorisation to restart the study • To modify the clinical study protocol • To produce the IMP by a new manufacturer with the quality section of the IMPD updated accordingly, and few quality related changes
14 April 2016	• To address the points raised by P-NCAs in the email dated 07 Apr 2016 while rejecting VHP555 SA4 • In addition to the changes already described in the Amendment 4, its clarified version addressed VHP concerns regarding the comparability between Ovasave batches manufactured at the initial and the new manufacturing site following manufacturer change

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date

07 July 2015	The study was temporarily halted on 07 July 2015 due to the decision of the Agence National de Sécurité du Médicament et des produits de santé (ANSM) to suspend the manufacturing authorisation of the only site used for production of clinical supplies for CATS29 (decision S15/217 dated 07 July 2015). National Competent Authorities (NCAs) and ECs were all informed about this temporary halt. The ANSM decision to suspend the manufacturing authorisation followed an ANSM inspection at TxCell's Besançon site in April 2015. The patients who had already received study treatment were followed as per protocol and all other patients were withdrawn from the study. TxCell decided to end the trial on 11 October 2016, due to challenges in Ovasave manufacturing (with suspension of the manufacturing site and transfer to a new manufacturing site), and a need to finalise and GMP-validate a more efficient manufacturing process prior to the conduct of clinical trials with Ovasave.	-

Notes:

Limitations and caveats

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

As well as countries listed in the summary, this trial additionally ran in FR & UK Due to manufacturing challenges and premature termination, the limited data obtained in this study does not allow for any firm conclusion on either efficacy or safety

Notes: