Clinical trial results:
A MULTICENTER, OPEN LABEL PHASE II STUDY OF CARFILZOMIB, CYCLOPHOSPHAMIDE AND DEXAMETHASONE IN NEWLY DIAGNOSED MULTIPLE MYELOMA PATIENTS

Summary

EudraCT number	2010-021111-17
Trial protocol	IT
Global end of trial date	31 May 2023

Results information

Result version number	v1 (current)
This version publication date	28 October 2023
First version publication date	28 October 2023

Trial information

Trial identification

Sponsor protocol code	IST-CAR-506

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01346787
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	STICHTING EUROPEAN MYELOMA NETWORK
Sponsor organisation address	Dr. Molewaterplein 40, ROTTERDAM, Netherlands, 3015 GD
Public contact	Clinical Trial Office, Fondazione EMN Italy Onlus, 0039 0110243236, clinicaltrialoffice@emnitaly.org
Scientific contact	Clinical Trial Office, Fondazione EMN Italy Onlus, 0039 0110243236, clinicaltrialoffice@emnitaly.org

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	31 May 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 May 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Determine whether the association of Carfilzomib, Cyclophosphamide and Dexamethasone (CCd) as induction treatment is safe and provides benefits in patients with newly diagnosed MM.

Protection of trial subjects:

The protocol for this study has been designed in accordance with the general ethical principles outlined in the Declaration of Helsinki. The review of this protocol by the IRB/EC and the performance of all aspects of the study, including the methods used for obtaining informed consent, must also be in accordance with principles enunciated in the declaration, as well as ICH Guidelines, Title 21 of the Code of Federal Regulations (CFR), Part 50 Protection of Human Subjects and Part 56 Institutional Review Boards.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 March 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 58
Worldwide total number of subjects	58
EEA total number of subjects	58

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)	1

From 65 to 84 years	56
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

This protocol is a phase II multicenter, international, non comparative, open label study designed to assess the safety and the efficacy of the association Carfilxomib with Cyclophosphamide and Deaxamethasone (CCd) as induction treatment in newly diagnosed MM patients.

Pre-assignment

Screening details:

The pre-treatment period includes screening visits, performed at study entry. After providing written informed consent to participate in the study, patients will be evaluated for study eligibility. The screening period includes the availability of inclusion criteria.

Period 1

Period 1 title	ITT (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	CCd arm

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Carflizomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Carfilzomib = 20 mg/m2 IV once daily on days 1, 2, of cycle 1 only followed by 36 mg/ m2 days 8, 9, 15, 16 in cycle 1, then for all subsequent doses 36 mg/ m2 IV once daily on days 1, 2, 8, 9, 15, 16, followed by 13-day rest period (day 17 through 28). Each cycle will be repeated every 28 days for a total of 9 courses.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Cyclophosphamide given orally at the dose of 300 mg/m2 on days 1, 8, 15.

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral drops, solution
Routes of administration	Oral use

Dosage and administration details:

Low dose Dexamethasone will be given orally at the dose of 40 mg on days 1, 8, 15, 22 or 20 mg on days 1-2, 8-9,15-16, 22-23

Number of subjects in period 1	CCd arm
Started	58
Completed	0
Not completed	58
Adverse event, serious fatal	4
Physician decision	1
Consent withdrawn by subject	7
Adverse event, non-fatal	22
Trial closured by sponsor	1
Lost to follow-up	2
Lack of efficacy	21

Baseline characteristics

Reporting groups	
Reporting group title	ITT

Reporting group description: -

Reporting group values	ITT	Total	
Number of subjects	58	58	
Age categorical Units: Subjects			
Adults (18-64 years)	1	1	
From 65-84 years	56	56	
85 years and over	1	1	
Age continuous Units: years			
median	71		
full range (min-max)	55 to 86	-	
Gender categorical Units: Subjects			
Female	31	31	
Male	27	27	
ISS Stage Units: Subjects			
ISS Stage I	16	16	
ISS Stage II	19	19	
ISS Stage III	23	23	
ECOG Units: Subjects			
ECOG 0	24	24	
ECOG 1	30	30	
ECOG 2	4	4	

Subject analysis sets	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:
ITT

Reporting group values	ITT		
Number of subjects	58		
Age categorical Units: Subjects			
Adults (18-64 years)	1		
From 65-84 years	56		
85 years and over	1		

Age continuous Units: years			
median	71		
full range (min-max)	55 to 86		
Gender categorical Units: Subjects			
Female	31		
Male	27		
ISS Stage Units: Subjects			
ISS Stage I	16		
ISS Stage II	19		
ISS Stage III	23		
ECOG Units: Subjects			
ECOG 0	24		
ECOG 1	30		
ECOG 2	4		

End points

End points reporting groups	
Reporting group title	CCd arm
Reporting group description: -	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: ITT	

Primary: PR Rate	
End point title	PR Rate
End point description: 	
End point type	Primary
End point timeframe: PR Rate	

End point values	CCd arm	ITT		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	58	58		
Units: subjects	49	49		

Statistical analyses

Statistical analysis title	No statistical analysis
Statistical analysis description: No statistical analysis	
Comparison groups	CCd arm v ITT
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0 [2]
Method	No statistical analysis
Parameter estimate	No statistical analysis
Point estimate	49
Confidence interval	
level	90 %
sides	2-sided
lower limit	49
upper limit	49
Variability estimate	Standard deviation
Dispersion value	0

Notes:
[1] - No statistical analysis
[2] - No statistical analysis

Secondary: Progression free survival

End point title	Progression free survival

End point description:

End point type	Secondary

End point timeframe:
Progression free survival

End point values	CCd arm	ITT		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	58	58		
Units: month				
median (confidence interval 95%)	35.5 (27.7 to 67)	35.5 (27.7 to 67)		

Statistical analyses

Statistical analysis title	No statistical analysis

Statistical analysis description:
No statistical analysis

Comparison groups	CCd arm v ITT
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0 [4]
Method	No statistical analysis
Parameter estimate	No statistical analysis
Point estimate	43
Confidence interval	
level	95 %
sides	2-sided
lower limit	43
upper limit	43
Variability estimate	Standard deviation
Dispersion value	0

Notes:
[3] - No statistical analysis
[4] - No statistical analysis

Secondary: Time to progression

End point title	Time to progression

End point description:

End point type	Secondary
End point timeframe:	
Time to progression	

End point values	CCd arm	ITT		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	58	58		
Units: month				
median (confidence interval 95%)	46.6 (34.5 to 72.4)	46.6 (34.5 to 72.4)		

Statistical analyses

Statistical analysis title	No statistical analysis
Statistical analysis description:	
No statistical analysis	
Comparison groups	CCd arm v ITT
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0 [6]
Method	No statistical analysis
Parameter estimate	No statistical analysis
Point estimate	46.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	46.6
upper limit	46.6
Variability estimate	Standard error of the mean

Notes:

[5] - No statistical analysis

[6] - No statistical analysis

Secondary: Time to next therapy

End point title	Time to next therapy
End point description:	

End point type	Secondary
End point timeframe:	
Time to next therapy	

End point values	CCd arm	ITT		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	58	58		
Units: month				
median (confidence interval 95%)	43 (28 to 55.1)	43 (28 to 55.1)		

Statistical analyses

Statistical analysis title	No statistical analysis
Statistical analysis description:	
No statistical analysis	
Comparison groups	CCd arm v ITT
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	= 0 [8]
Method	No statistical analysis
Parameter estimate	No statistical analysis
Point estimate	43
Confidence interval	
level	95 %
sides	2-sided
lower limit	43
upper limit	43
Variability estimate	Standard deviation
Notes:	
[7] - No statistical analysis	
[8] - No statistical analysis	

Secondary: Overall survival

End point title	Overall survival
End point description:	
End point type	Secondary
End point timeframe:	
Overall survival	

End point values	CCd arm	ITT		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	58	58		
Units: month				
median (confidence interval 95%)	78 (52.1 to 78)	78 (52.1 to 78)		

Statistical analyses

Statistical analysis title	No statistical analysis
Statistical analysis description:	
No statistical analysis	
Comparison groups	CCd arm v ITT
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other[9]
Method	No statistical analysis
Parameter estimate	No statistical analysis
Point estimate	78
Confidence interval	
level	95 %
sides	2-sided
lower limit	78
upper limit	78
Variability estimate	Standard deviation
Dispersion value	0

Notes:

[9] - No statistical analysis

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Per protocol	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24

Reporting groups	
Reporting group title	Per Protocol

Reporting group description: -

Serious adverse events	Per Protocol		
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 58 (36.21%)		
number of deaths (all causes)	30		
number of deaths resulting from adverse events	7		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasma cell leukemia			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Lung adenocarcinoma			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal neoplasm			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastric cancer			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Investigations			

Blood creatine increased				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Head injury				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Ischaemia				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Cardiac failure congestive				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	1 / 1			
Myocardial ischaemia				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Acute myocardial infarction				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorder	Additional description: decompensation cardiac			

subjects affected / exposed	2 / 58 (3.45%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Bundle branch block left				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Nervous system disorders				
Neuropathy peripheral				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral ischaemia				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Presyncope				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				

subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Chest pain			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ileal perforation			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Nausea			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Epistaxis			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute pulmonary oedema			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary oedema			
subjects affected / exposed	2 / 58 (3.45%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	1 / 1		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Oliguria			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary retention			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Infections and infestations			
Pneumonia			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 1		
Septic shock			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Klebsiella infection			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Per Protocol		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 58 (89.66%)		
Investigations			
Blood creatinine increased			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	58		
Alanine aminotransferase increased			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	58		
Vascular disorders			
Hypertension			
subjects affected / exposed	7 / 58 (12.07%)		
occurrences (all)	58		
Nervous system disorders			

Headache subjects affected / exposed occurrences (all) Neuropathy peripheral subjects affected / exposed occurrences (all)	 5 / 58 (8.62%) 58 3 / 58 (5.17%) 58		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all)	 38 / 58 (65.52%) 58 22 / 58 (37.93%) 58 21 / 58 (36.21%) 58		
General disorders and administration site conditions Pain subjects affected / exposed occurrences (all) Oedema subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all)	 11 / 58 (18.97%) 58 8 / 58 (13.79%) 58 8 / 58 (13.79%) 58 5 / 58 (8.62%) 58		
Gastrointestinal disorders Pyrexia subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	 19 / 58 (32.76%) 58 10 / 58 (17.24%) 58		

Diarrhoea subjects affected / exposed occurrences (all)	10 / 58 (17.24%) 58		
Vomiting subjects affected / exposed occurrences (all)	9 / 58 (15.52%) 58		
Constipation subjects affected / exposed occurrences (all)	4 / 58 (6.90%) 58		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	9 / 58 (15.52%) 58		
Dyspnoea subjects affected / exposed occurrences (all)	5 / 58 (8.62%) 58		
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all)	4 / 58 (6.90%) 58		
Rash subjects affected / exposed occurrences (all)	4 / 58 (6.90%) 58		
Pruritus subjects affected / exposed occurrences (all)	3 / 58 (5.17%) 58		
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	5 / 58 (8.62%) 58		
Insomnia subjects affected / exposed occurrences (all)	4 / 58 (6.90%) 58		
Anxiety subjects affected / exposed occurrences (all)	3 / 58 (5.17%) 58		

Agitation subjects affected / exposed occurrences (all)	3 / 58 (5.17%) 58		
Musculoskeletal and connective tissue disorders Muscle spasms subjects affected / exposed occurrences (all)	4 / 58 (6.90%) 58		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Pneumonia subjects affected / exposed occurrences (all)	5 / 58 (8.62%) 58 3 / 58 (5.17%) 58		
Metabolism and nutrition disorders Hyperglycaemia subjects affected / exposed occurrences (all) Hypocalcaemia subjects affected / exposed occurrences (all)	8 / 58 (13.79%) 58 3 / 58 (5.17%) 58		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 November 2011	Substantial Amendment n.1: It was necessary to update the informed consent, following the update of the Investigator's Brochure of the drug Carfilzomib. Furthermore, the consent in the paragraph "Appendix on the protection of confidentiality" has been corrected and the paragraph relating to insurance has been updated.
12 February 2018	Substantial Amendment n.2: The Amendment was necessary to update the contacts of the Sponsor and the Principal Investigator of the study, as well as update the criteria for evaluating the disease response. With this amendment, the new documents relating to the drug Carfilzomib are transmitted, as it will be imported, labelled, packaged, released and distributed directly by Amgen Europe B.V., in Breda, and no longer by Fisher. Following this transition, the labels for Carfilzomib were updated. The side effects of Carfilzomib and the appendix on the protection of confidentiality have been updated on the Information Sheet and Informed Consent Form.
11 February 2019	Substantial Amendment n.3: The Amendment was necessary to update the following aspects: • Update on the side effects of the drug Carfilzomib on the Informed Consent • Privacy update according to new EU Regulation 2016/679
16 September 2019	Substantial Amendment n.4: The Amendment was necessary to update the side effects of the drug Carfilzomib on the Informed Consent
10 February 2020	Substantial Amendment n.5: The Amendment was necessary to update the side effects of the drug Carfilzomib on the Informed Consent
30 April 2021	Substantial Amendment n.6: The request for a substantial amendment concerns the change of the promoter of the study from HOVON Foundation to STICHTING EUROPEAN MYELOMA NETWORK (EMN) and the updating of the side effects of the drug Carfilzomib, based on what is reported in the Investigator's Brochure v.20.0 and v .20.1. The labels of the drug carfilzomib have been updated in order to meet the requirements of the cytotoxicity regulation. This review was made to align with the EMA/CHMP request to review the information on the marketed product. The risk classification for the drug carfilzomib did not change with the introduction of the cytotoxicity statement. There has been no new toxicity data or regulations since the drug Kyprolis gained approval. Furthermore, the requirements for handling and destroying the drug have not changed, so such changes will not have a significant impact on the safety or physical or mental integrity of clinical trial participants, or on the conduct or management of the trial.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported