Clinical trial results:
Phase Ib/II Multicentric Study Combining Glasdegib with temozolomide in patients with newly diagnosed Glioblastoma, safety and preliminary efficacy for the combination.

Summary

EudraCT number	2017-002410-31
Trial protocol	ES
Global end of trial date	29 November 2023

Results information

Result version number	v1 (current)
This version publication date	27 February 2026
First version publication date	27 February 2026

Trial information

Trial identification

Sponsor protocol code	GEINO-1602

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03466450
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Grupo Español de Investigación en Neurooncología
Sponsor organisation address	Velazquez St, 7-3o, Madrid, Spain, 28001
Public contact	Federico Nepote, MFAR Clinical Research, +34 934344412, investigacion@mfar.net
Scientific contact	Federico Nepote, MFAR Clinical Research, +34 934344412, investigacion@mfar.net

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	29 April 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 November 2023
Global end of trial reached?	Yes
Global end of trial date	29 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Phase Ib: To determine the MTD and RDP2 are the primary endpoint of this part of the study. The MTD is defined as the dose at which one-third of patients experienced dose-limiting toxicity (DLT) from Glasdegib and/or TMZ using a standard "3+3" dose escalation determined from the toxicities during the first 12 weeks of therapy. The RDP2 is defined as the dose at which equal or fewer than one-sixth of patients experienced dose-limiting toxicity (DLT) form Glasdegib and/or TMZ using a standard "3+3" dose escalation determined from the toxicities during the first 12 weeks of therapy.
Phase II: To evaluate overall survival.

Protection of trial subjects:

All patient signed the informed consent. The project comply with the local regulations on data protection (GDPR).
The trial was approved by the competent authority in Spain (Agencia Española de Medicamentos y Productos Sanitarios; AEMPS) and the ethics committee from Hospital Ramon y Cajal. The trial was conducted in accordance with the ethics principles of the Declaration of Helsinki and with the Good Clinical Practice (GCP) guidelines defined by the International Council for Harmonisation (ICH).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2017
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: 79
Worldwide total number of subjects	79
EEA total number of subjects	79

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)	79
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	79
Number of subjects completed	74

Pre-assignment subject non-completion reasons

Reason: Number of subjects	did not received glasdegib: 1
Reason: Number of subjects	dose scalation phase at 100 mg/d: 4

Period 1

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

Blinding implementation details:

Not applicable. This is a single arm trial.

Arms

Arm title	Experimental arm

Arm description:

Patients receive Temozolamide (TMZ) at 75 mg/m2 /d concurrently with radiotherapy (RT) for a maximum of 42 days. At 4 weeks after RT completion, patients will start taking TMZ at 150 mg/m2/d for the first 5 days of a 28-day cycle. If first cycle is well tolerated, patients will receive TMZ at 200 mg/m2/d for the first 5 days of every subsequent 28-day cycle for another 5 cycles. Glasdegib will be continued until progression, unacceptable toxicity, non-compliance, consent withdrawal and/or 2 years of glasdegib administration.

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

Dosage and administration details:

Dose Levels of Glasdegib in Phase Ib:
100 mg / day
75 mg / day

Dose Level of Glasdegib in Phase II:
75 mg / day

Number of subjects in period 1[1]	Experimental arm
Started	74
Received glasdegib	74
Completed	74

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: Some patients were included in the Phase Ib (dose escalation phase)

Baseline characteristics

Reporting groups

Reporting group title	Phase II

Reporting group description: -

Reporting group values	Phase II	Total	
Number of subjects	74	74	
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 Units: years			
median	55		
full range (min-max)	28 to 78	-	
Gender categorical Units: Subjects			
Female	34	34	
Male	40	40	
Eastern Cooperative Oncology Group performance status (ECOG-PS)			
Scale validated by the World Health Organization (WHO) to assess the quality of life of cancer patients. The scale ranges from 0, patient fully active, to 5, patient dead.			
Units: Subjects			
ECOG 0	31	31	
ECOG 1	43	43	
Barthel index			
This is a test most commonly used to measure basic activities of daily living. The final score ranges from 0 to 100, with 100 being maximum independence and 0 being maximum dependence.			
Units: Subjects			
Score 100 - 90	52	52	
Score 90 - 0	8	8	
Missing	14	14	
Minimental index			
Mini-Mental is the most widely used cognitive screening test to assess suspected symptoms consistent with cognitive decline or dementia. It involves a series of questions and the performance of some actions by the person being assessed. It has a score range of 0 to 30, with higher values correlating with better function.			
Units: Subjects			
Score 30 - 27	56	56	
Score 27-0	8	8	

Missing	10	10	
Corticosteroids at inclusion			
Corticosteriods are commonly used for the management of neurological symptoms in patients with glioblastoma. Here we report the number of patients who were taken corticosteriods at the inclusion in the study.			
Units: Subjects			
Patients with corticosteroids	19	19	
Patients without corticosteroids	55	55	
Extent of resection			
All patients underwent a surgical resection of their tumor before study entry. Here we report the extent achieved by the resection, from the total removal of the tumor (complete resection), to the obtention of a partial small sample for diagnostic purposes (biopsy).			
Units: Subjects			
Biopsy	6	6	
Partial resection	12	12	
Subtotal resection	20	20	
Complete resection	36	36	
MGMT status			
MGMT promoter methylation is a favorable molecular biomarker in patients with glioblastoma who are exposed to alkylating agent chemotherapy, such as temozolomide.			
Units: Subjects			
Methylated	32	32	
Not methylated	40	40	
Not determined / Missing	2	2	
IDH status			
Mutations in IDH genes are the most common genetic alterations in low grade gliomas, but is uncommon in glioblastoma.			
Units: Subjects			
Mutated	1	1	
Not mutated	70	70	
Not determined / Missing	3	3	

End points

End points reporting groups

Reporting group title	Experimental arm

Reporting group description:

Patients receive Temozolamide (TMZ) at 75 mg/m2 /d concurrently with radiotherapy (RT) for a maximum of 42 days. At 4 weeks after RT completion, patients will start taking TMZ at 150 mg/m2/d for the first 5 days of a 28-day cycle. If first cycle is well tolerated, patients will receive TMZ at 200 mg/m2/d for the first 5 days of every subsequent 28-day cycle for another 5 cycles. Glasdegib will be continued until progression, unacceptable toxicity, non-compliance, consent withdrawal and/or 2 years of glasdegib administration.

Primary: Glasdegib Dose

End point title	Glasdegib Dose[1]

End point description:

For Phase Ib, The recommended dose for phase 2 (RDP2) of Glasdegib administered with temozolomide during and
after RT.

End point type	Primary

End point timeframe:

12 weeks

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: This is a single arm trial. No statistical comparisons are feasible

Statistical analyses

No statistical analyses for this end point

Primary: Overall Survival

End point title	Overall Survival[2]

End point description:

For Phase II, time between the start of treatment to death. Here we report the percentage of patients alive at 15 months after the start of treatment, estimated by Kaplan Meier method

End point type	Primary

End point timeframe:

15 months

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: This is a single arm trial. No statistical comparisons are feasible

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: Percentage of patients				
number (confidence interval 95%)	52.1 (41.7 to 65.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

Time between the start of treatment and progression of disease or death, whichever comes first. Here we report the median time to progression or death

End point type	Secondary

End point timeframe:

24 months

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: months				
median (confidence interval 95%)	7.1 (6.2 to 8.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Adverse events (safety)

End point title	Adverse events (safety)

End point description:

Based on the number and type of adverse events (AEs) reported since the start of treatment and throughout the study period. Here we report the number of patients who experienced adverse events.

End point type	Secondary

End point timeframe:

24 months

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: Patients				
Experienced AEs	72			
Did not experience AEs	2			

Statistical analyses

No statistical analyses for this end point

Secondary: AEs grade 3-5 (safety)

End point title	AEs grade 3-5 (safety)

End point description:

Based on the number and type of adverse events (AEs) reported since the start of treatment and throughout the study period. Here we report the number of patients who experienced adverse events.

End point type	Secondary

End point timeframe:

24 months

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: Patients				
Experienced AEs grade 3-5	39			
Did not experience AEs grade 3-5	35			

Statistical analyses

No statistical analyses for this end point

Secondary: AEs any grade related to study treatment (Safety)

End point title	AEs any grade related to study treatment (Safety)

End point description:

Based on the number and type of adverse events (AEs) reported since the start of treatment and throughout the study period. Here we report the number of patients who experienced adverse events.

End point type	Secondary

End point timeframe:

24 months

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: Patients				
Experienced AEs any grade related to study treatme	63			
Did not experienced AEs any grade related to study	11			

Statistical analyses

No statistical analyses for this end point

Secondary: AEs grade 3-5 related to study treatment (Safety)

End point title	AEs grade 3-5 related to study treatment (Safety)

End point description:

Based on the number and type of adverse events (AEs) reported since the start of treatment and throughout the study period. Here we report the number of patients who experienced adverse events.

End point type	Secondary

End point timeframe:

24 months

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: Patients				
Experienced AEs grade 3-5 related to study treatme	22			
Did not experienced AEs grade 3-5 related to study	52			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rate (ORR)

End point title	Objective response rate (ORR)

End point description:

Based tumor imaging scans locally assessed by the investigators following the response assessments in neurooncology (RANO) criteria. Here we report the best response achieved for each patient.

End point type	Secondary

End point timeframe:

24 months

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: Paients				
Complete response	1			
Partial response	2			
Stable disease	53			
Progression of the disease	16			
Not evaluable	2			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 24 months	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20

Reporting groups	
Reporting group title	Experimental arm

Reporting group description:

Patients receive Temozolamide (TMZ) at 75 mg/m2 /d concurrently with radiotherapy (RT) for a maximum of 42 days. At 4 weeks after RT completion, patients will start taking TMZ at 150 mg/m2/d for the first 5 days of a 28-day cycle. If first cycle is well tolerated, patients will receive TMZ at 200 mg/m2/d for the first 5 days of every subsequent 28-day cycle for another 5 cycles. Glasdegib will be continued until progression, unacceptable toxicity, non-compliance, consent withdrawal and/or 2 years of glasdegib administration.

Serious adverse events	Experimental arm		
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 74 (40.54%)		
number of deaths (all causes)	58		
number of deaths resulting from adverse events	4		
Vascular disorders			
Pulmonary thromboembolism			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thromboembolic event			
subjects affected / exposed	3 / 74 (4.05%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Brain tumor excision			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Planned surgery			

subjects affected / exposed	2 / 74 (2.70%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Surgical injury infection				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Brain abscess				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Depressed level of consciousness				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dysphasia				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Epileptic Crisis				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Epileptic seizures				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	1 / 74 (1.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ischemia cerebrovascular				

subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meningeal carcinomatosis			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Neurologic deterioration			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Seizure			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Clinical deterioration			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Death			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Fall			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Febrile syndrome			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Fever			
subjects affected / exposed	2 / 74 (2.70%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	2 / 74 (2.70%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Rectal hemorrhage			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumonia due to COVID-19 infection			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper respiratory infection			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Progressive disorientation			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary tract infection			

subjects affected / exposed	2 / 74 (2.70%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Lung infection			
subjects affected / exposed	1 / 74 (1.35%)		
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	Experimental arm		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	72 / 74 (97.30%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	5 / 74 (6.76%)		
occurrences (all)	5		
Nervous system disorders			
Dizziness			
subjects affected / exposed	10 / 74 (13.51%)		
occurrences (all)	10		
Dysphasia			
subjects affected / exposed	5 / 74 (6.76%)		
occurrences (all)	5		
Headache			
subjects affected / exposed	22 / 74 (29.73%)		
occurrences (all)	22		
Nervous system disorders			
subjects affected / exposed	31 / 74 (41.89%)		
occurrences (all)	31		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	7 / 74 (9.46%)		
occurrences (all)	7		
Lymphocyte count decreased			

subjects affected / exposed	5 / 74 (6.76%)		
occurrences (all)	5		
Neutrophil count decreased			
subjects affected / exposed	13 / 74 (17.57%)		
occurrences (all)	13		
Platelet count decreased			
subjects affected / exposed	22 / 74 (29.73%)		
occurrences (all)	22		
General disorders and administration site conditions			
Back pain			
subjects affected / exposed	5 / 74 (6.76%)		
occurrences (all)	5		
Fatigue			
subjects affected / exposed	40 / 74 (54.05%)		
occurrences (all)	40		
General disorders and administration site conditions			
subjects affected / exposed	5 / 74 (6.76%)		
occurrences (all)	5		
Eye disorders			
Eye disorders			
subjects affected / exposed	4 / 74 (5.41%)		
occurrences (all)	4		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	10 / 74 (13.51%)		
occurrences (all)	10		
Diarrhea			
subjects affected / exposed	6 / 74 (8.11%)		
occurrences (all)	6		
Dysgeusia			
subjects affected / exposed	26 / 74 (35.14%)		
occurrences (all)	26		
Nausea			
subjects affected / exposed	30 / 74 (40.54%)		
occurrences (all)	30		
Vomiting			

subjects affected / exposed	32 / 74 (43.24%)		
occurrences (all)	32		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 74 (6.76%)		
occurrences (all)	5		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	15 / 74 (20.27%)		
occurrences (all)	15		
Pruritus			
subjects affected / exposed	4 / 74 (5.41%)		
occurrences (all)	4		
Skin and subcutaneous tissue disorders			
subjects affected / exposed	12 / 74 (16.22%)		
occurrences (all)	12		
Psychiatric disorders			
Anorexia			
subjects affected / exposed	12 / 74 (16.22%)		
occurrences (all)	12		
Anxiety			
subjects affected / exposed	6 / 74 (8.11%)		
occurrences (all)	6		
Insomnia			
subjects affected / exposed	6 / 74 (8.11%)		
occurrences (all)	6		
Renal and urinary disorders			
Urinary tract infection			
subjects affected / exposed	4 / 74 (5.41%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders			
subjects affected / exposed	20 / 74 (27.03%)		
occurrences (all)	20		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 November 2018	- The indications received by the AEMPS on August 10, 2018 related to the query sent on August 7, 2018, by MFAR on behalf of the Sponsor, to determine the possible failure to include a patient in phase I. Along with this amendment, we sent the document "Study status report as of October 2018" as requested by the AEMPS on August 10, 2018. - This relevant amendment is used to introduce some changes to the Protocol and Patient Information Sheet and Informed Consent and to correct some errors in the documents.
12 July 2019	Change of Principal investigator in Hospital Universitario y Politécnico la Fe
05 August 2020	1. Substantial modification of Parts I and II due to the update of the Glasdegib Investigator's Manual and the safety information provided in the patient information sheet/informed consent. 2. Change of principal investigator at the Hospital Universitari i Politècnic La Fe in the new version of the protocol, this change was already reported to the local Authorities in the corresponding amendment No. 2, approved by the CEIm on July 12, 2019. 3. Modifications in the presentation of the medication, Glasdegib tablets go from being only Round White Film Coated Tablet 25 mg or Round Film Coated Tablets 100 mg to possibly also being Round Pale Orange Film Coated Tablet 25 mg. A new ATC code must be added in section D3.3, which will be L01XX63. 4. Incorporation of the AEMPS resolution into the evaluation of relevant amendment no. 3: "The definition of Dose Limiting Toxicity (DLT) should not vary throughout the study.
23 December 2021	• Substantial modification of Parts I and II due to the update of the Glasdegib Investigator's Manual and the safety information provided in the patient information sheet/informed consent. • Addition of an extra point in the protocol for the extraction of pharmacokinetic samples in patients in cycle 6 day 1 of the adjuvant phase of treatment. The informed consent has also been modified to reflect this point. • Typographical errors detected in the previous version have been corrected. • The description of the color indicated on the Glasdegib 25mg label has been homogenized according to the specifications of the SmPC; the color specified in the SmPC is yellow, instead of sepia.
27 April 2023	Substantial modification of Parts I and II due to update of the Glasdegib Investigator's Manual and safety information provided in the patient information sheet/informed consent.
28 June 2023	Change of principal invertigator in ICO Badalona

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.

Not applicable

Notes: