Clinical trial results:
A phase Ib/II, open label study of siremadlin monotherapy and in combination with donor lymphocyte infusion as a treatment for patients with acute myeloid leukemia postallogeneic stem cell transplantation who are in complete remission but at high risk for relapse.

Summary

EudraCT number	2021-003596-34
Trial protocol	ES DE IT
Global end of trial date	26 October 2023

Results information

Result version number	v1 (current)
This version publication date	21 September 2024
First version publication date	21 September 2024

Trial information

Trial identification

Sponsor protocol code	CHDM201K12201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05447663
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma, AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma, AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma, AG, 41 613241111, novartis.email@novartis.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	26 October 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 October 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine the dose and schedule of siremadlin monotherapy that are tolerable without unacceptable toxicities (recommended dose for Part 2) [Part 1 - siremadlin monotherapy].

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 February 2023
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	Germany: 5
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Spain: 1
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)	5
From 65 to 84 years	3

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

38 participants were planned to be enrolled; 12 participants in Part 1 and 26 participants in Part 2; however, due to permanent recruitment halt, the enrollment was stopped after the 1st dose escalation meeting. The study was conducted in 6 centers in 3 countries: Germany, Italy and Spain.

Pre-assignment

Screening details:

Prior to dosing at Cycle 1 Day 1, participants who fulfilled all the inclusion/exclusion criteria were enrolled via IRT and a treatment number was provided for the study treatment siremadlin.

Period 1

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

Arms

Arm title	Siremadlin (HDM201) 30mg

Arm description:

Participants with AML post allogeneic stem cell transplantation (allo-SCT) received 30mg siremadlin monotherapy in part 1

Arm type	Experimental
Investigational medicinal product name	Siremadlin
Investigational medicinal product code	HDM201
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

10 mg, 20mg and 30 mg* (During the study, siremadlin (HDM201) 30mg capsule was included as additional strength which was globally supplied), administered orally (PO).

Number of subjects in period 1	Siremadlin (HDM201) 30mg
Started	8
Entered post-treatment follow-up	7
Did not enter post-treatment follow -up	1
Completed	0
Not completed	8
Adverse event, serious fatal	2
Consent withdrawn by subject	1
Study terminated by Sponsor	5

Baseline characteristics

Reporting groups	
Reporting group title	Siremadlin (HDM201) 30mg
Reporting group description:	
Participants with AML post allogeneic stem cell transplantation (allo-SCT) received 30mg siremadlin monotherapy in part 1	

Reporting group values	Siremadlin (HDM201) 30mg	Total	
Number of subjects	8	8	
Age categorical Units: Subjects			
Adults (18-64 years)	5	5	
From 65-84 years	3	3	
Age Continuous Units: years			
arithmetic mean	52.0		
standard deviation	± 17.96	-	
Sex: Female, Male Units: Participants			
Female	3	3	
Male	5	5	
Race/Ethnicity, Customized Units: Subjects			
Not Hispanic or Latino	7	7	
Hispanic or Latino	1	1	

End points

End points reporting groups

Reporting group title	Siremadlin (HDM201) 30mg
Reporting group description:	
Participants with AML post allogeneic stem cell transplantation (allo-SCT) received 30mg siremadlin monotherapy in part 1	
Subject analysis set title	Siremadlin (HDM201) 10mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with AML post allogeneic stem cell transplantation (allo-SCT) received 10mg siremadlin monotherapy in part 1	
Subject analysis set title	Seremadlin (HDM201) 30mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with AML post allogeneic stem cell transplantation (allo-SCT) received 30mg siremadlin monotherapy in part 1	
Subject analysis set title	Siremadlin (HDM201) 30mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with AML post allogeneic stem cell transplantation (allo-SCT) received 30mg siremadlin monotherapy in part 1	
Subject analysis set title	Siremadlin (HDM201) 10mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with AML post allogeneic stem cell transplantation (allo-SCT) received 10mg siremadlin monotherapy in part 1	
Subject analysis set title	Siremadlin (HDM201) 30mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with AML post allogeneic stem cell transplantation (allo-SCT) received 30mg siremadlin monotherapy in part 1	

Primary: Rate of Dose Limiting Toxicities (DLTs) with siremadlin monotherapy in part 1 (dose confirmation with siremadlin monotherapy)

End point title	Rate of Dose Limiting Toxicities (DLTs) with siremadlin monotherapy in part 1 (dose confirmation with siremadlin monotherapy)[1]
End point description:	
To determine the dose and schedule of siremadlin monotherapy that are tolerable without unacceptable toxicities as defined by the incidence of DLT during the first cycle of treatment in part 1. 'A dose-limiting toxicity (DLT) is defined as an adverse event or abnormal laboratory value assessed, by the Investigator, to be at least possibly related to study treatment (siremadlin monotherapy and/or siremadlin in combination with DLI), and as unrelated to disease, disease progression, inter-current illness, or concomitant medications, that occurs during the DLT observation period and meets severity criteria as per protocol.	
End point type	Primary
End point timeframe:	
from cycle 1 day 1 (C1D1) to end of Cycle 1 (cycle = 28days)	

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: No analysis was done for this endpoint

End point values	Siremadlin (HDM201) 30mg			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Count of Participants	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Participants who are alive and maintained CR or CRi with no evidence of hematologic relapse

End point title	Participants who are alive and maintained CR or CRi with no evidence of hematologic relapse

End point description:

This involves evaluating the preliminary efficacy of siremadlin monotherapy at the recommended dose for part 2 on prevention of hematologic relapse

End point type	Secondary

End point timeframe:

Over 6 months from start of siremadlin monotherapy (part 1)

End point values	Siremadlin (HDM201) 30mg			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: Participants				
number (not applicable)				

Notes:

[2] - No participant was analyzed for this endpoint

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Graft versus Host Disease (GvHD)

End point title	Incidence of Graft versus Host Disease (GvHD)

End point description:

Incidence of grade III or IV acute GvHD, and moderate to severe chronic GvHD in part 1 and 2.

End point type	Secondary

End point timeframe:

From start of study treatment to up to 24 months from last patient first treatment

End point values	Siremadlin (HDM201) 30mg			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: Participants				
number (not applicable)				

Notes:

[3] - No participant was analyzed for this endpoint

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with permanent study treatment discontinuation due to GvHD or other adverse events

End point title	Percentage of participants with permanent study treatment discontinuation due to GvHD or other adverse events

End point description:

Percentage of participants with permanent discontinuation of study treatment due to GvHD or other adverse events in part 1 and 2.

End point type	Secondary

End point timeframe:

From start of study treatment to up to 24 months from last patient first treatment

End point values	Siremadlin (HDM201) 30mg			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Count of Participants	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Time from start of study treatment to the date of death from any cause

End point title	Time from start of study treatment to the date of death from any cause

End point description:

Assessment of Overall survival (OS) in part 2

End point type	Secondary

End point timeframe:

From start of study treatment to up to 36 months from last patient first treatment

End point values	Siremadlin (HDM201) 30mg			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: months				
number (not applicable)				

Notes:

[4] - No participant was analyzed for this endpoint

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative incidence of AML relapse

End point title	Cumulative incidence of AML relapse

End point description:

Cumulative incidence of Acute Myeloid Leukemia (AML) relapse at one year and 2 years after the start of study treatment in part 1 and 2. Cumulative incidence of relapse (CIR) is defined as the time from start of study treatment to the date of first documented hematologic relapse. CIR was to be analyzed in the FAS population who initiated priming phase at siremadlin recommended dose (RD) in Part 2 and participants at the RD in Part 1.

End point type	Secondary

End point timeframe:

at 1 year and at 2 years after start of study treatment

End point values	Siremadlin (HDM201) 30mg			
Subject group type	Reporting group			
Number of subjects analysed	0[5]			
Units: Participants				
number (not applicable)				

Notes:

[5] - No participant was analyzed for this endpoint

Statistical analyses

No statistical analyses for this end point

Secondary: Time from start of study treatment to the date of first documented occurrence or worsening of treatment emergent grade III or IV acute GvHD, or chronic GvHD requiring initiation of systemic immunosuppressive treatment

End point title	Time from start of study treatment to the date of first documented occurrence or worsening of treatment emergent grade III or IV acute GvHD, or chronic GvHD requiring initiation of systemic immunosuppressive treatment

End point description:

Assessment of GvHD-free/relapse-free survival (GRFS) in part 1 and 2.

End point type	Secondary

End point timeframe:

From start of treatment to up to 36 months from last patient first treatment

End point values	Siremadlin (HDM201) 30mg			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: months				
number (not applicable)				

Notes:

[6] - No participant was analyzed for this endpoint

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) characteristic AUC of siremadlin

End point title	Pharmacokinetic (PK) characteristic AUC of siremadlin

End point description:

AUC is the area under the concentration vs. time curve in part 1. Part 2 did not open for enrollment due to recruitment halt and so no data was analyzed.

End point type	Secondary

End point timeframe:

From Cycle 1 Day 1 to Cycle 1 Day 5 in part 1 [each cycle is 28 days for monotherapy]

End point values	Siremadlin (HDM201) 10mg	Seremadlin (HDM201) 30mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1	7		
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)				
AUClast: Cycle 1 Day 1	1497 (± 999)	3077 (± 39.7)		
AUC0-8hr: Cycle 1 Day 1	446 (± 999)	1187.1 (± 39.8)		
AUClast: Cycle 1 Day 5 (n = 0, 6)	999 (± 999)	1880.7 (± 31.2)		
AUC0-8hr: Cycle 1 Day 5 (n = 0, 6)	999 (± 999)	1894 (± 30.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK characteristic Cmax of siremadlin

End point title	PK characteristic Cmax of siremadlin

End point description:

The maximum (peak) observed plasma, blood, serum or other body fluid drug concentration following drug administration (mass x volume^-1) in part 1. Part 2 did not open for enrollment due to recruitment halt and so no data was analyzed.

End point type	Secondary

End point timeframe:

From Cycle 1 Day 1 to Cycle 1 Day 5 in part 1 [each cycle is 28 days for monotherapy]

End point values	Siremadlin (HDM201) 10mg	Siremadlin (HDM201) 30mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1	7		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	73.6 (± 999)	207.68 (± 36.2)		
Cycle 1 Day 5 (n = 0, 6)	999 (± 999)	296.92 (± 30.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK characteristic Ctrough of siremadlin

End point title	PK characteristic Ctrough of siremadlin

End point description:

Concentration that is just prior to the beginning of, or at the end of a dosing interval; corresponding to the pre-dose concentration in part 1 and 2.

End point type	Secondary

End point timeframe:

From Cycle 1 Day 1 to Cycle 24 Day 1 in part 1 or from Cycle 1 Day 1 safety confirmation to Cycle 21 Day 1 maintenance in part 2; [each cycle is 28 days for monotherapy, and 42 days for combination]

End point values	Siremadlin (HDM201) 30mg			
Subject group type	Reporting group			
Number of subjects analysed	0[7]			
Units: ng/ml				
geometric mean (geometric coefficient of variation)	()			

Notes:

[7] - No participant was analyzed for this endpoint

Statistical analyses

No statistical analyses for this end point

Secondary: PK characteristic Tmax of siremadlin

End point title	PK characteristic Tmax of siremadlin

End point description:

The time to reach maximum (peak) plasma, blood, serum or other body fluid drug concentration after drug administration (time) in part 1. Part 2 did not open for enrollment due to recruitment halt and so no data was analyzed.

End point type	Secondary

End point timeframe:

From Cycle 1 Day 1 to Cycle 1 Day 5 in part 1 [each cycle is 28 days for monotherapy]

End point values	Siremadlin (HDM201) 10mg	Siremadlin (HDM201) 30mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1	7		
Units: hour (hr)				
median (full range (min-max))				
Cycle 1 Day	3.00 (3.00 to 3.00)	5.95 (2.02 to 6.03)		
Cycle 1 Day 5 (n = 0, 6)	999 (999 to 999)	4.50 (1.92 to 7.75)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from first dose of study treatment to 30 days after last dose of study treatment (on-treatment). Subjects remaining in the study after endo of treatment (EOT) (responders and non-responders, regardless of when treatment was d

Adverse event reporting additional description:

Any sign or symptom that occurs during the conduct of the trial and safety follow-up. Deaths in the post treatment survival follow-up are not considered Adverse Events.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	SIREMADLIN 30 mg

Reporting group description:

SIREMADLIN 30 mg

Serious adverse events	SIREMADLIN 30 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oesophagitis			

subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abdominal infection			
subjects affected / exposed	1 / 8 (12.50%)		
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	SIREMADLIN 30 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 8 (37.50%)		
occurrences (all)	3		
Mucosal inflammation			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	3		
Immune system disorders			
Chronic graft versus host disease			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Acute graft versus host disease			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	3		
Reproductive system and breast			

disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Endometrial thickening			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Alanine aminotransferase increased			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Blood bilirubin increased			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Upper limb fracture			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Lumbar vertebral fracture			

subjects affected / exposed occurrences (all) Fall subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1 1 / 8 (12.50%) 1		
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1		
Nervous system disorders Psychomotor hyperactivity subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all)	 3 / 8 (37.50%) 4 1 / 8 (12.50%) 3 6 / 8 (75.00%) 7 7 / 8 (87.50%) 9		
Ear and labyrinth disorders External ear pain subjects affected / exposed occurrences (all) Vertigo subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1		
Eye disorders			

Corneal exfoliation subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Dry eye subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Eyelid oedema subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	4 / 8 (50.00%) 4		
Nausea subjects affected / exposed occurrences (all)	4 / 8 (50.00%) 5		
Vomiting subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	3 / 8 (37.50%) 3		
Pruritus subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Dry skin subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Dermatitis subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Infections and infestations			
Rhinitis subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Oral herpes			

subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Clostridium difficile infection			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Clostridium difficile colitis			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
COVID-19			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hyperuricaemia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Hypoglycaemia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 July 2022	As the release of this amendment, no sites had been initiated, and no subject had been screened or had received study treatment in this trial. The main purpose of this amendment was to comply with health authority's request to modify the protocol as follows: To modify the study design by adding a siremadlin monotherapy dose confirmation part (Part 1) with at least 6 evaluable participants to evaluate the safety and tolerability of siremadlin monotherapy and determine the recommended dose before commencing the treatment strategy part (Part 2), which includes siremadlin/donor lymphocyte infusion (DLI) combination as well as priming and maintenance with siremadlin monotherapy; To specify that after the recommended siremadlin dose was determined in Part 1, enrollment in Part 2 would start after obtaining Health Authority's approval as applicable. Enrollment in Part 2 would not have been applicable to the participating sites in the United States; To implement a larger dose reduction to 20% of siremadlin (instead of 30%) of the total planned dose when administered concomitantly with strong CYP3A inhibitors in the initial treatment cohort(s). Following the first safety review meeting and based on safety and siremadlin total exposure data, this could have changed to a dose reduction to 30% of the planned siremadlin dose with concomitant use of strong CYP3A inhibitors; To clarify that pre-allo-SCT participants with AML in morphologic complete remission at time of transplant but with evidence of residual leukemia had been removed from inclusion criteria 4. The assessment of this pre-transplant risk factor was based on retrospective test results and could not fulfill regulatory requirements of a MRD assay; To clarify that the decision about DLI administration in eligible participants in Part 2 would have been at the discretion of the treating investigator per the standard of practice.
18 November 2022	At the time of release of this amendment, no sites had been initiated, and no subject had been screened or received study treatment in this trial. The main purpose of this amendment was to restrict the participation of the German sites to Part 1 of the study. The protocol specified that the participating sites in Germany will enroll patients only in Part 1 with siremadlin monotherapy. The German sites were not permitted to enroll patients in Part 2, which included Donor Lymphocyte Infusion (DLI) in combination with siremadlin.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported