Clinical trial results:
Abscopal Effect of Radiotherapy and Nivolumab in anti-PD1 Pretreated Relapsed or Refractory classical Hodgkin Lymphoma - An international multicenter Phase II trial

Summary

EudraCT number	2017-003334-82
Trial protocol	DE NO NL AT
Global end of trial date	04 May 2024

Results information

Result version number	v1 (current)
This version publication date	21 May 2025
First version publication date	21 May 2025

Trial information

Trial identification

Sponsor protocol code	Uni-Koeln-3140

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03480334
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Cologne
Sponsor organisation address	Albertus-Magnus-Platz , Cologne, Germany, 50923
Public contact	German Hodgkin Study Group (GHSG), Trial Coordination Center, +49 22147888200, ghsg@uk-koeln.de
Scientific contact	German Hodgkin Study Group (GHSG), Trial Coordination Center, +49 22147888200, ghsg@uk-koeln.de

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	01 November 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 May 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary aim of this international, prospective, multicenter phase II proof-of-concept trial is to demonstrate the efficacy of the experimental treatment strategy. The combination of immune checkpoint inhibition with nivolumab and immunogenic radiotherapy is expected to act synergistically, offering a well-tolerated and effective therapeutic approach in patients with relapsed or refractory Hodgkin lymphoma previously treted with an anti-pD1 antibody. The study is specifically designed to assess the abscopal effect of localized radiotherapy directed at a single lesion.

Protection of trial subjects:

Participants give their written informed consent to participate in the trial. They may discontinue trial treatment at any time at their own request. Protocol treatment must be stopped in the event of pregnancy in a female participant, unless re-consent for continuation is obtained. Treatment may also be terminated at the discretion of the treating physician in cases of unacceptable toxicity, disease progression (PD), or serious comorbid conditions.

Early termination of the entire trial may be initiated by the trial chairman if:
- the formal stopping criterion regarding the primary endpoint is met,
- participant safety is at risk,
- the risk-benefit ratio for patients changes significantly,
- the trial medication can no longer be justifiably used,
- the sponsor (represented by the trial chairman) deems discontinuation necessary for safety reasons,
- the trial proves unfeasible due to low recruitment or major shifts in the treatment landscape or sequencing for relapsed/refractory Hodgkin lymphoma (rrHL).

An independent Data Monitoring Committee (DMC) oversees trial progress and patient safety. The GHSG Trial Coordination Center ensures that the DMC receives all necessary information. Regular safety analyses are conducted for all patients (FAS) to monitor:

- Study eligibility,
- Disease progression, relapse, and mortality during and after treatment,
- Adverse events (AEs) and serious adverse events (SAEs).
- Cases of early treatment discontinuation are documented and analyzed for safety assessment and to identify patients who may need to be replaced in the Abscopal Response Analysis Set (ARAS).

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	05 December 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Austria: 5
Country: Number of subjects enrolled	Germany: 15
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)	20
From 65 to 84 years	5
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

A total of 26 patients were enrolled at 15 European sites before the trial was closed to recruitment on September 30, 2023. Originally, 29 evaluable patients were planned, but after positive interim results and changes in clinical practice during the COVID-19 pandemic, recruitment slowed considerably.

Pre-assignment

Screening details:

1 patient had a screening failure and could not be included in the trial

Period 1

Period 1 title	Stage-2 (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Stage-2

Arm description:

This trial is a single-arm two-stage phase II study.

Arm type	single-arm
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Therapy began as soon as possible after the patient has been enrolled and preferably started on a Wednesday (w1d1) to allow timely initiation of RT on day 6 of treatment week 1 (w1d6). Patients received 240 mg nivolumab i.v. in 2-weekly intervals usually in an outpatient setting. The first infusion was administered over 60 minutes while consecutive infusions were administered over 30 minutes if no infusion related reaction was observed. Subjects were dosed no less than 12 days from the previous dose of drug and subsequent infusions should not have been delayed unnecessarily or without medical reasons. The patient should have been observed for 60 minutes following the first infusion of nivolumab. During this observation period, the i.v. line should have remained patent to allow administration of i.v. drugs if necessary. In case an infusion-related reaction have occured after reduction to 30 minutes infusion duration, the following nivolumab infusions had to be administered over 60 min.

Number of subjects in period 1[1]	Stage-2
Started	25
Completed	25

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: One patient could not be included in the trial due to a screening failure.

Baseline characteristics

Reporting groups	
Reporting group title	Stage-2

Reporting group description:

The reporting group consists of all patients evaluated in the final analysis. This corresponds to the Full Analysis Set (FAS), which includes all patients who qualify for enrollment into the trial and received at least 1 dose of the study drug. The FAS contains 25 patients.

Reporting group values	Stage-2	Total	
Number of subjects	25	25	
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)	20	20	
From 65-84 years	4	4	
85 years and over	1	1	
Not recorded	0	0	
Age continuous Units: years			
median	37		
full range (min-max)	25 to 90	-	
Gender categorical Units: Subjects			
Female	10	10	
Male	15	15	
Not recorded	0	0	
Stage Units: Subjects			
Stage I	0	0	
Stage II	3	3	
Stage III	11	11	
Stage IV	11	11	
B-Symptoms Units: Subjects			
Weight loss > 10%	3	3	
Unclear fever > 38°	0	0	
Night sweats	1	1	
not recorded	21	21	
GHSG stage Units: Subjects			
IIA	2	2	
IIB	1	1	

IIIA	9	9	
IIIB	2	2	
IVA	11	11	
ECOG performance status Units: Subjects			
normal activity, no symptoms	16	16	
able to work, symptoms apparent	6	6	
able to care for her-/himself	3	3	
Concomitant disease			
Any clinically relevant concomitant diseases?			
Units: Subjects			
yes	22	22	
no	3	3	
Body mass index (BMI) Units: kg/m²			
median			
full range (min-max)		-	

Subject analysis sets

Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set (FAS) consists of all patients who qualify for enrollment into the trial and receive at least one dose of study drug.

Subject analysis set title	Abscopal response analysis set (ARAS)
Subject analysis set type	Per protocol

Subject analysis set description:

The ARAS consists of all FAS subjects who meet all evaluability criteria and none of the exclusion criteria stated below:
Evaluability Criteria: Patient received one initial nivolumab dose before and at least 3 doses after the first fraction of RT, RT was timed and performed according to protocol.
Exclusion Criteria: First Nivolumab dose more than 6 weeks after the scheduled treatment-interval of the last anti-PD1 infusion outside the trial, Less than 4 Nivolumab doses before week 12, RT start before the first nivolumab dose, RT start after the second nivolumab dose, >3 calendar days between any two consecutive RT treatment days, Less than 9 or more than 12 single RT doses, No Non-RTL outside the 10% isodose of RT, Start of non-study treatment before completion of RE-6 examinations.
One patient withdrew informed consent and had no post-baseline assessment and was excluded from the ARAS.

Reporting group values	Full Analysis Set (FAS)	Abscopal response analysis set (ARAS)	
Number of subjects	25	24	
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)	20	19	
From 65-84 years	4	4	
85 years and over	1	1	

Not recorded	0	0	

Age continuous			
Units: years			
median	37	37	
full range (min-max)	25 to 90	25 to 90	
Gender categorical			
Units: Subjects			
Female	10	10	
Male	15	14	
Not recorded	0	0	
Stage			
Units: Subjects			
Stage I	0	0	
Stage II	3	3	
Stage III	11	10	
Stage IV	11	11	
B-Symptoms			
Units: Subjects			
Weight loss > 10%	3	3	
Unclear fever > 38°	0	0	
Night sweats	1	1	
not recorded	21	21	
GHSG stage			
Units: Subjects			
IIA	2	2	
IIB	1	1	
IIIA	9	8	
IIIB	2	2	
IVA	11	11	
ECOG performance status			
Units: Subjects			
normal activity, no symptoms	16	15	
able to work, symptoms apparent	6	6	
able to care for her-/himself	3	3	
Concomitant disease			
Any clinically relevant concomitant diseases?			
Units: Subjects			
yes	22	22	
no	3	2	
Body mass index (BMI)			
Units: kg/m²			
median	23.3	23.3	
full range (min-max)	17.7 to 41.9	17.7 to 41.9	

End points

End points reporting groups

Reporting group title	Stage-2

Reporting group description:

This trial is a single-arm two-stage phase II study.

Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set (FAS) consists of all patients who qualify for enrollment into the trial and receive at least one dose of study drug.

Subject analysis set title	Abscopal response analysis set (ARAS)
Subject analysis set type	Per protocol

Subject analysis set description:

The ARAS consists of all FAS subjects who meet all evaluability criteria and none of the exclusion criteria stated below:
Evaluability Criteria: Patient received one initial nivolumab dose before and at least 3 doses after the first fraction of RT, RT was timed and performed according to protocol.
Exclusion Criteria: First Nivolumab dose more than 6 weeks after the scheduled treatment-interval of the last anti-PD1 infusion outside the trial, Less than 4 Nivolumab doses before week 12, RT start before the first nivolumab dose, RT start after the second nivolumab dose, >3 calendar days between any two consecutive RT treatment days, Less than 9 or more than 12 single RT doses, No Non-RTL outside the 10% isodose of RT, Start of non-study treatment before completion of RE-6 examinations.
One patient withdrew informed consent and had no post-baseline assessment and was excluded from the ARAS.

Primary: Abscopal response rate (ARR)

End point title	Abscopal response rate (ARR)

End point description:

The primary objective was to assess the ARR to localized RT combined with 4–6 doses of the study drug. An ARR ≤5% was considered insignificant, while an ARR of around 30% suggested a promising systemic effect in heavily pre-treated HL patients. Efficacy benchmarks were evaluated using Simon's optimal two-stage design. The null hypothesis (H0: ARR-6 < 5%) was tested against a one-sided alternative with a significance level of 5%. The probability of not rejecting H0 when the true ARR-6 was 30% was controlled at <5%. In stage 2, the UMVUE and two-sided 90% confidence limits for ARR-6 were calculated according to Koyama and Chen. The one-sided 95% confidence interval was obtained by setting the upper limit to 1. H0 was rejected if the lower limit exceeded 5%. Based on stage-1 results, the test had 100% power regardless of the final number of evaluable patients in stage 2.

End point type	Primary

End point timeframe:

Prerequisite of primary endpoint assessment is the first restaging which was performed and documented between weeks 12 – 14, after the last nivolumab dose administered before week 12 after start of treatment.

End point values	Full Analysis Set (FAS)	Abscopal response analysis set (ARAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	24		
Units: point estimate (95% CIs)				
yes	11	11		
no	13	13		
not applicable	1	0		

Statistical analyses

Statistical analysis title	Primary efficacy endpoint analysis
Comparison groups	Abscopal response analysis set (ARAS) v Full Analysis Set (FAS)
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	point estimate (UMVUE)
Point estimate	45.8
Confidence interval	
level	95 %
sides	1-sided
lower limit	31.5

Notes:

[1] - The primary endpoint (ARR-6) was estimated using the uniformly minimum variance unbiased estimator (UMVUE) according to Koyama and Chen (2008), consistent with Simon's optimal two-stage design. A one-sided 95% CI with an upper limit of 1 was also calculated as required for hypothesis testing.

Secondary: Remission status

End point title	Remission status

End point description:

The overall remission status (CR, PR, SD, PD) was listed for each subject and summarized per investigator.

End point type	Secondary

End point timeframe:

Consecutive restaging examination over the course of therapy with nivolumab doses (RE-6)

End point values	Abscopal response analysis set (ARAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: subjects				
Complete remission (CR)	1			
Partial remission (PR)	8			
Stable disease (SD)	6			
Progressive disease (PD)	9			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR)

End point title	Duration of response (DOR)

End point description:

For subjects who survive without PD, the DOR was censored on the date of their last tumor assessment. Subjects who started subsequent therapy without a prior reported PD were censored at the last tumor assessments prior to initiation of the subsequent anticancer therapy. This endpoint will only be evaluated in subjects with CR or PR.

End point type	Secondary

End point timeframe:

DOR was defined as the time from first response (CR or PR) to the date of first objectively documented disease progression (PD) or death due to any cause, whichever occurs first.

End point values	Full Analysis Set (FAS)	Abscopal response analysis set (ARAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	24		
Units: subjects				
median (full range (min-max))	10.7 (2.8 to 19.4)	10.7 (2.8 to 19.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Failure-free survival (FFS)

End point title	Failure-free survival (FFS)

End point description:

Failure-free survival (FFS) was calculated as time between the initiation of treatment with nivolumab within the trial and the date of first progression, relapse, death, or administration of any anti-cancer drug other than nivolumab or radiotherapy. If none of these events have occurred, FFS was censored on the date of the last documented staging or follow-up.

End point type	Secondary

End point timeframe:

One-year FFS (as reported) and 18-months FFS rates

End point values	Full Analysis Set (FAS)	Abscopal response analysis set (ARAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	24		
Units: percent				
number (confidence interval 95%)	6.4 (2.7 to	6.4 (2.7 to		

11.3)	11.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS)

End point description:

Progression-free survival (PFS) was calculated for each as time between the initiation of treatment with nivolumab within the trial and the date of first progression, relapse or death. In cases of continuing response, PFS will be censored at the date of the last documented follow-up.

End point type	Secondary

End point timeframe:

One-year PFS rates (as reported) and 18-months PFS rates

End point values	Full Analysis Set (FAS)	Abscopal response analysis set (ARAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	24		
Units: percent				
number (confidence interval 95%)	8.3 (3.4 to 13.2)	8.3 (3.4 to 13.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

Overall survival (OS) was calculated for each patient as time between the initiation of treatment with nivolumab within the trial and the date of death. In patients alive by the time of analysis, OS was censored at the date of the last documented information on survival status.

End point type	Secondary

End point timeframe:

One-year OS rates (as reported) and 18-months OS rates

End point values	Full Analysis Set (FAS)	Abscopal response analysis set (ARAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	24		
Units: percent				
number (confidence interval 95%)	19.9 (14.7 to 27.4)	19.9 (14.7 to 27.4)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All events from first dose up to 125 days after treatment end must be reported. Events beyond 125 days must be reported only if a causal relationship to study treatment is suspected.

Adverse event reporting additional description:

During the period, every adverse event has to be documented, independent of the investigator’s opinion whether there is a causative relation with therapy or not.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.1

Reporting groups

Reporting group title	Safety analysis set (SAS)

Reporting group description:

The safety analysis set (SAS) consists of all patients of the FAS who had at least one valid post-baseline safety assessment. In this trial all patients who were included in the FAS were also included in the SAS (N=25).

Serious adverse events	Safety analysis set (SAS)		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 25 (24.00%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Blood and lymphatic disorders	Additional description: Includes Neutropenia		
subjects affected / exposed	2 / 25 (8.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
General disorders	Additional description: Includes: Malaise, reduced general condition, Migraine with aura		
subjects affected / exposed	3 / 25 (12.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrointestinal disorder	Additional description: Includes: SAPO virus infection, diarrhea, nausea, exicosis		
subjects affected / exposed	5 / 25 (20.00%)		
occurrences causally related to treatment / all	3 / 8		
deaths causally related to treatment / all	0 / 0		

Infections and infestations			
Infections and infestations	Additional description: Includes: lung infection, fever		
subjects affected / exposed	4 / 25 (16.00%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Safety analysis set (SAS)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 25 (96.00%)		
Cardiac disorders			
Cardiac disorders			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	2		
Nervous system disorders			
Nervous system disorders	Additional description: Includes: Neuropathy		
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	3		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	27		
Leukopenia			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	33		
Neutropenia			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Thrombocytopenia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	3		
General disorders and administration site conditions			
Allergic reaction			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Toothache			

subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Gastrointestinal disorders	Additional description: Includes: Nausea, vomiting		
subjects affected / exposed	5 / 25 (20.00%)		
occurrences (all)	21		
Mucositis			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	21		
Hepatobiliary disorders			
Hepatobiliary disorders			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	22		
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	8		
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders			
subjects affected / exposed	11 / 25 (44.00%)		
occurrences (all)	36		
Renal and urinary disorders			
Renal and urinary tract disorders			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			
Muscle, bone and joint disorders			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	19		
Infections and infestations			
Fever			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Infections			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	6		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 August 2019	Amendment to the protocol, Amendment to other documents appended to the initial application form, Amendment to other documents or information (SmPC-Update), SmPC-Update with effect on the ICF: Correction of the laboratory address for the accompanying program
17 February 2020	Amendment of the protocol, Amendment of other documents or information (SmPC-Update): - The quality of life (QoL) analyses, originally planned as secondary endpoints, were added as secondary objectives - The procedure for the assessment and reporting of adverse events was clarified - The anticipated end of the study was added - The definition of women of childbearing potential (WOCBP) and postmenopausal women was specified - An incorrect description of the patient population was corrected
29 July 2020	Amendment to the protocol, Amendment to other documents or information (SmPC-Update and Informed Consent Form): - incorrect definition of postmenopausal status for distinguishing WOCBP was corrected - potential study termination for feasibility reasons was clarified - Information on DMC involvement in the decision to proceed to stage 2 recruitment was added - planned publication process was clarified - clinical relevance of a potentially positive study outcome was described - treatment schedule including possible delays in the initiation of radiotherapy (RT) was detailed - Compliance with current GCP and European data protection regulations was elaborated - reference to the respective patient information sheet regarding details of the scientific support program was added - Information on patient insurance coverage abroad was added
18 June 2021	Amendment to the protocol, Amendment to other documents or information (SmPC-Update): - continuation of study recruitment in phase 2 (previously reported in 05/2020) - relevant inclusion criterion was adjusted - interval between the last anti-PD1 dose outside and the first dose within the study was modified - Inclusion of patients with well-controlled HIV infection under adequate antiretroviral therapy was allowed
30 August 2022	Amendment to the protocol, Amendment to other documents or information: - Adjustment of timelines - Revision of inclusion/exclusion criteria - General wording of the medication supply - Editorial and organizational adjustments
06 February 2023	Amendment to information in the CT application form, Amendment to the protocol, Amendment to other documents appended to the initial application form (Informed Consent Form update, SmPC Update,Additional Information for patients who have already been briefed): - adverse reaction eosinophilia was listed with a changed frequency (occasional instead of rare) - adverse reaction "renal failure (including acute renal failure)" was replaced in the OPDIVO® October 2022 prescribing information by "renal failure (including acute kidney injury)

17 January 2024	Amendment to the protocol, Amendment to other documents appended to the initial application form (SmPC-Update, Additional Information for patients who have already been briefed): - Adjustment of timelines due to the shortened study duration - Revision of the statistical section based on the actual sample size of 26 patients - Editorial adjustments

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported