Clinical trial results:
An open-label phase II single-centre study investigating the safety and efficacy of LTX-315 and adoptive T-cell therapy in patients with advanced/metastatic soft tissue sarcoma

Summary

EudraCT number	2017-002877-20
Trial protocol	DK
Global end of trial date	11 October 2021

Results information

Result version number	v1 (current)
This version publication date	05 January 2023
First version publication date	05 January 2023
Summary attachment (see zip file)	Exploratory endpoints results (Summary sheet_exploratory endpoints.pdf)

Trial information

Trial identification

Sponsor protocol code	C17-315-04

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03725605
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Lytix Biopharma AS
Sponsor organisation address	Sandakerveien 138, Oslo, Norway, 0484
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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	15 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 July 2021
Global end of trial reached?	Yes
Global end of trial date	11 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

* To determine the ability of LTX-315 to induce T-cell infiltration prior to TIL expansion in advanced/metastatic soft tissue sarcoma
* To determine the safety of LTX-315 as part of adoptive T-cell therapy in advanced/metastatic soft tissue sarcoma

Protection of trial subjects:

The study was performed in accordance with the CSP version 2.0 and 3.0, and the current revision of the Declaration of Helsinki, as well as with the Note for Guidance on Good Clinical Practice and applicable regulatory requirements.
Prophylactic treatment (antihistamines and a leukotriene antagonist) was initiated in all patients prior to administration of LTX-315.
For T-cell therapy, prophylactic treatment included i.v. administration of cyclophosphamide as well as supportive treatment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2018
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	Denmark: 6
Worldwide total number of subjects	6
EEA total number of subjects	6

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	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All subjects were treated at the CCIT, Herlev Hospital, Denmark. The majority of the subjects were recruited in Denmark, while 1 subject was identified in Norway and referred to Denmark for screening procedures and treatment.

Pre-assignment

Screening details:

A total of 7 subjects were screened and 6 subjects were enrolled in the study.

Period 1

Period 1 title	LTX-315 treatment (Step 1)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	LTX-315 treatment (Step 1)

Arm description:

This is a one-arm study where all subjects received LTX-315 during Step 1.

Arm type	Experimental
Investigational medicinal product name	LTX-315
Investigational medicinal product code	
Other name	Ruxotemitide
Pharmaceutical forms	Solution for injection
Routes of administration	Intratumoral use

Dosage and administration details:

- LTX-315 was administered on dosing days (i.e., Step 1, Days 1, 2, 3 and 8 were mandatory, Days 15 and 22 were optional)
- The index tumour lesion for injection needed to have a minimum LD of 1 cm as measured by ultrasound or calliper
- The LTX-315 dose was 5 mg (10 mg/ml concentration) at each injection time point
- The number of LTX-315 injections to a single lesion on an LTX-315 dosing day could vary depending on the volume of that lesion:
  - Lesions (< 3cm LD) could receive up to 4 injections per day (i.e., a total daily dose of up to 20 mg)
  - Lesions (> 3cm LD) could receive up to 12 injections per day (i.e., a total maximum daily dose of 60 mg)

Number of subjects in period 1	LTX-315 treatment (Step 1)
Started	6
LTX-315 injections (W1-3)	6
Lesion tumour surgery (W3-5)	6
Completed	6

Period 2

Period 2 title	Adoptive T-cell therapy (Step 2)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Adoptive T-cell therapy (Step 2)

Arm description:

This is a one-arm study where subjects underwent TIL infusion and received chemotherapy and interleukin treatment during Step 2.

Arm type	Experimental
Investigational medicinal product name	Tumour Infiltrating Lymphocytes (TILs)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Subjects with successful TIL expansion received TIL infusion. The infusion was performed on one single day. The number of T-cells in the product depended on the achieved level of in vitro expansion and the number of TILs infused varied between subjects, ranging from 44x10^9 TILs to 63x10^9 TILs.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Cyclophosphamide was given as an intravenous infusion for 2 consecutive days in a dose of 60 mg per kg of body weight.

Investigational medicinal product name	Fludarabine phosphate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Fludarabine phosphate was given as an intravenous infusion for 5 consecutive days in a dose of 25 mg per m2 body surface (starting the day after the last dose of cyclophosphamide).

Investigational medicinal product name	Interleukin 2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Injection

Dosage and administration details:

Daily subcutaneous injections with IL-2 (2 MIU) were administered from Day 1 to 14.

Number of subjects in period 2	Adoptive T-cell therapy (Step 2)
Started	6
Completed	4
Not completed	2
Unsuccessful TIL expansion	2

Baseline characteristics

Reporting groups	
Reporting group title	LTX-315 treatment (Step 1)

Reporting group description: -

Reporting group values	LTX-315 treatment (Step 1)	Total	
Number of subjects	6	6	
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)	5	5	
From 65-84 years	1	1	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	2	2	
Male	4	4	
Race			
Race was recorded as White, American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, Black or African American, or Other			
Units: Subjects			
White	5	5	
Asian	1	1	
American Indian or Alaska Native	0	0	
Native Hawaiian or other Pacific Islander	0	0	
Black or African American	0	0	
Other	0	0	
Ethnic Origin			
Ethnic origin was recorded as Hispanic/Latino or Not Hispanic/Not Latino			
Units: Subjects			
Hispanic/Latino	0	0	
Not Hispanic/Not Latino	6	6	

End points

End points reporting groups

Reporting group title	LTX-315 treatment (Step 1)
Reporting group description:	
This is a one-arm study where all subjects received LTX-315 during Step 1.	
Reporting group title	Adoptive T-cell therapy (Step 2)
Reporting group description:	
This is a one-arm study where subjects underwent TIL infusion and received chemotherapy and interleukin treatment during Step 2.	

Primary: Change in total T-cell level in tumour tissues from Baseline (Step 1, Week 1, Day 1) to end of Step 1 (Step 1, Week 3)

End point title	Change in total T-cell level in tumour tissues from Baseline (Step 1, Week 1, Day 1) to end of Step 1 (Step 1, Week 3)[1]
End point description:	
The primary efficacy endpoint was change in total T-cell level in tumour tissues from baseline (Step 1, Week 1, Day 1) to end of Step 1. In Step 1 the total T-cell level was measured at baseline and end of Step 1. Absolute values and change from baseline (Step 1, Week 1, Day 1) for T-cell level were listed for the FAS. Change from baseline was listed as absolute change. Data are presented as the arithmetic mean value for the factor increase (+) or decrease (-) in number of cells/mm2 from baseline to end of Step 1.	
End point type	Primary
End point timeframe:	
15 to 42 days (Step 1, W1, D1 to end of Step 1)	

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 formal hypothesis testing was planned for this study due to the low number of subjects included. A total of 6 patients were enrolled of whom 3 were included using the CSP v2.0 and 3 patients were included using the CSP v3.0. The 2 versions differ in amount and timepoints of visits and IMP administrations. CSP v3.0 also allowed the inclusion of subjects that were in stable disease at baseline, and therefore, data from patients enrolled using different protocols cannot be compared.

End point values	LTX-315 treatment (Step 1)			
Subject group type	Reporting group			
Number of subjects analysed	5[2]			
Units: factor change in CD3+ cells/square mm				
arithmetic mean (full range (min-max))	1.9 (-0.6 to 6.9)			

Notes:

[2] - For 1 subject evaluation was not possible due to complete necrosis of the injected lesion

Statistical analyses

No statistical analyses for this end point

Primary: Adverse events (AE) related to LTX-315 or to the combination of LTX-315 and adoptive T-cell therapy from Baseline (Step 1, Week 1, Day 1) to end of treatment (EoT) (Step 2, Week 7)

End point title	Adverse events (AE) related to LTX-315 or to the combination of LTX-315 and adoptive T-cell therapy from Baseline (Step 1, Week 1, Day 1) to end of treatment (EoT) (Step 2, Week 7)[3]

End point description:

The primary safety endpoint was AEs related to LTX-315 or to the combination of LTX-315 and adoptive T-cell therapy from baseline (Step 1, Week 1, Day 1) to end of treatment (Step 2, Week 7).
AEs were events occurring during or after administration of the IMP. AEs were coded using MedDRA version 21.1 and were classified by System Organ Class (SOC), Preferred Term (PT) and Lowest Level Term (LLT).
Adverse events related to LTX-315 were events where causality to LTX-315 was marked on the adverse events page.
Adverse events related to the combination of LTX-315 and adoptive T-cell therapy were events where both causality to LTX-315 and at least one of the other IMPs (TILs, Sendoxan®, Fludara® and Proleukin®) were marked on the adverse event page.

End point type	Primary

End point timeframe:

Up to 133 days (from Step 1, Week 1, Day 1 to Step 2, Week 7)

Notes:

[3] - 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 formal hypothesis testing was planned for this study due to the low number of subjects included. A total of 6 patients were enrolled of whom 3 were included using the CSP v2.0 and 3 patients were included using the CSP v3.0. The 2 versions differ in amount and timepoints of visits and IMP administrations. CSP v3.0 also allowed the inclusion of subjects that were in stable disease at baseline, and therefore, data from patients enrolled using different protocols cannot be compared.

End point values	LTX-315 treatment (Step 1)	Adoptive T-cell therapy (Step 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	4		
Units: events				
AEs (LTX-315 + adoptive T-cell therapy)	0	0		
AEs (LTX-315)	14	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in CD3+ T-cell and CD3+CD8+ T cell density in non-injected tumour tissues from Baseline (Step 1, Week 1, Day 1) to EoT (Step 2, Week 7)

End point title	Change in CD3+ T-cell and CD3+CD8+ T cell density in non-injected tumour tissues from Baseline (Step 1, Week 1, Day 1) to EoT (Step 2, Week 7)

End point description:

The change in CD3+CD8+ T-cells from baseline to end of Step 2 could only be evaluated for 1 subject. The change is described as factor increase.

End point type	Secondary

End point timeframe:

133 days (from Step 1, Week 1, Day 1 to end of Step 2, Week 7).

End point values	Adoptive T-cell therapy (Step 2)			
Subject group type	Reporting group			
Number of subjects analysed	1[4]			
Units: factor change in CD8+ cells/square mm				
arithmetic mean (full range (min-max))	3.3 (3.3 to 3.3)			

Notes:

[4] - Data was only available for 1 subject

Statistical analyses

No statistical analyses for this end point

Secondary: Total number of CD3+CD8+ T-cells in TIL infusion product

End point title	Total number of CD3+CD8+ T-cells in TIL infusion product

End point description:

TIL expansion took place between Step 1 and Step 2 for a period of 41-49 days. The composition of the TIL infusion product was evaluated for the 4 subjects for whom it was possible to grow TILs. For 2 subjects it was not possible to meet the criteria of 4x10^7 cells as described in the IMPD.

End point type	Secondary

End point timeframe:

TIL expansion took place between Step 1 and Step 2, i.e., during a period of 41-49 days.

End point values	LTX-315 treatment (Step 1)			
Subject group type	Reporting group			
Number of subjects analysed	4[5]			
Units: million CD8+ cells				
arithmetic mean (full range (min-max))	8032 (210 to 23177)			

Notes:

[5] - The TIL infusion product was evaluated for the 4 subjects for whom it was possible to grow TILs.

Statistical analyses

No statistical analyses for this end point

Secondary: % CD3+CD8+ T-cells of total CD3+ in TIL infusion product

End point title	% CD3+CD8+ T-cells of total CD3+ in TIL infusion product

End point description:

TIL expansion took place between Step 1 and Step 2 for a period of 41-49 days. The composition of the TIL infusion product was evaluated for the 4 subjects for whom it was possible to grow TILs. For 2 subjects it was not possible to meet the criteria of 4x10^7 cells as described in the IMPD.

End point type	Secondary

End point timeframe:

TIL expansion took place between Step 1 and Step 2, i.e., during a period of 41-49 days.

End point values	LTX-315 treatment (Step 1)			
Subject group type	Reporting group			
Number of subjects analysed	4[6]			
Units: %CD8+ of total CD3+ T-cells in the TILs				
arithmetic mean (full range (min-max))	17 (1 to 52)			

Notes:

[6] - The TIL infusion product was evaluated for the 4 subjects for whom it was possible to grow TILs.

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rate

End point title	Objective response rate

End point description:

The ORR was defined as the proportion of subjects who according to RECIST 1.1 achieved complete response or partial response at EoT (Step 2, Week 7) and up to 15 months after EoT.

End point type	Secondary

End point timeframe:

Endpoint evaluated at EoT (Step 2, Week 7) and up to 15 months after EoT.

End point values	Adoptive T-cell therapy (Step 2)			
Subject group type	Reporting group			
Number of subjects analysed	4[7]			
Units: percent				
number (not applicable)				
ORR at EoT (Step 2, Week 7) ORR at up to 15 months after EoT	0 0			

Notes:

[7] - ORR was evaluated for the 4 subjects who progressed to Step 2.

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical benefit rate

End point title	Clinical benefit rate

End point description:

The CBR was defined as proportion of subjects who according to RECIST 1.1 had achieved complete response, partial response or stable disease at EoT (Step 2, Week 7) and up to 15 months after EoT. CBR was evaluated at Step 2, Week 7 and Week 13.

End point type	Secondary

End point timeframe:

Endpoint evaluated at at EoT (Step 2, Week 7) and up to Week 13.

End point values	Adoptive T-cell therapy (Step 2)			
Subject group type	Reporting group			
Number of subjects analysed	4[8]			
Units: percent				
number (not applicable)				
CBR at EoT (Step2, Week7)	75			
CBR at up to 15 months after EoT (Week 13)	25			

Notes:

[8] - The endpoint was evaluated for the 4 subjects who progressed to Step 2.

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall tumour response

End point title	Best overall tumour response

End point description:

BOR was defined in the CSP as the best response recorded from the start of the treatment until disease progression/recurrence (taking as reference for PD the smallest measurements recorded since the treatment started).

End point type	Secondary

End point timeframe:

Assessed at Visit 25 (Step 2, Week 7, Day 42).

End point values	Adoptive T-cell therapy (Step 2)			
Subject group type	Reporting group			
Number of subjects analysed	4[9]			
Units: subject(s)				
Stable disease	3			
Progressive disease	1			

Notes:

[9] - Evaluated for the 4 subjects who progressed to Step 2.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival

End point title	Progression free survival

End point description:

PFS was calculated as number of days from date of screening (Baseline) until date of progressive disease or up to 15 months after EoT.

End point type	Secondary

End point timeframe:

From screening (Baseline) until date of progressive disease or up to 15 months after EoT.

End point values	Adoptive T-cell therapy (Step 2)			
Subject group type	Reporting group			
Number of subjects analysed	4[10]			
Units: Days				
arithmetic mean (full range (min-max))	153 (72 to 208)			

Notes:

[10] - Endpoint evaluated for the 4 subjects who progressed to Step 2.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 133 days

Adverse event reporting additional description:

AEs were events occurring during or after administration of IMP. AEs were coded using the MedDRA version 21.1 and were classified by SOC, PT and LLT.
AEs were collected from the time the patient signed the informed consent form to end of study (Step 2, Week 7, Day 42)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	All subjects

Reporting group description:

AEs are presented overall, i.e., from Step 1, Week 1, Day 1 to end of Step 2, Week 7, Day 42

Serious adverse events	All subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Fascial rupture			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			

Bacteraemia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 6 (16.67%)		
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	All subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Blood alkaline phosphatase decreased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Blood magnesium decreased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Blood potassium decreased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Blood sodium drecreased			

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
C-reactive protein increased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
International normalised ratio increased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Neutrophil count decreased			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	3		
Platelet count decreased			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	3		
Transaminases decreased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Weight increased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Nervous system disorders			
Fascial paresis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	4 / 6 (66.67%)		
occurrences (all)	8		
Neutropenia			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	4		
Thrombocytopenia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chills			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	3		
Injection site erythema			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Injection site pain			
subjects affected / exposed	4 / 6 (66.67%)		
occurrences (all)	9		
Localised oedema			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Oedema			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Pyrexia			
subjects affected / exposed	4 / 6 (66.67%)		
occurrences (all)	6		
Gastrointestinal disorders			

Diarrhoea subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 4		
Nausea subjects affected / exposed occurrences (all)	4 / 6 (66.67%) 6		
Abdominal pain subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 2		
Constipation subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2		
Dry mouth subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2		
Gastric disorder subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Vomiting subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 3		
Skin and subcutaneous tissue disorders			
Dry skin subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 3		
Pruritus subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Rash subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 3		
Renal and urinary disorders			

Haematuria subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Infections and infestations Oral fungal infection subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Metabolism and nutrition disorders Electrolyte imbalance subjects affected / exposed occurrences (all) Hypocalcaemia subjects affected / exposed occurrences (all) Hypoglycaemia subjects affected / exposed occurrences (all) Hypomagnesaemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1 1 / 6 (16.67%) 3 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 September 2018	A non-substantial amendment (Amendment#01) was issued 05 September 2018 and included: • Adding how to handle pregnancies • Clarifications of adverse event reporting procedures • Elaboration of definitions (Clinical Significant laboratory adverse events, not related causality, severity, Common Terminology Criteria for Adverse Events) • Change of pharmacovigilance Contract Research Organisation • Change of serious adverse event reporting to be via electronic case report form and paper as back-up • Updates of project managers and medical personnel (KLIFO A/S and Lytix Biopharma A/S)
31 March 2021	A substantial amendment (Amendment#02) was issued 31 March 2021 and included: • Change/update of inclusion criteria 1, 2, 3 and 11 • Follow-up period shortened from 2 years to 15 months • IrRC obsolete, only RECIST will be measured. • Secondary endpoints updated to conform with secondary objectives • Stable disease (SD) included that change the table 6.1 • Reference 51 updated with RECIST publication • Treatment time (days) when IMP is given, changed • Safety update • Personnel changes (including tasks) at Lytix A/S and KLIFO A/S • Appendix IV updated with RECIST • Added table with Key changes to the protocol • Updated abbreviation list • Study design graph updated • Table 5 updated

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.

TIL infusion during Step 2 of the study depended on TIL expansion being successful. Successful TIL expansion was achieved for 4/6 subjects hence secondary efficacy endpoints were evaluable for only 4 subjects.

Notes: