Clinical trial results:
Phase II trial of Tisagenlecleucel in Elderly Patients with First-Relapsed or Primary Refractory Agressive B-cell Non-Hodgkin Lymphoma

Summary

EudraCT number	2019-002930-35
Trial protocol	DE
Global end of trial date	24 February 2023

Results information

Result version number	v1 (current)
This version publication date	20 July 2023
First version publication date	20 July 2023

Trial information

Trial identification

Sponsor protocol code	Uni-Koeln-3903

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04161118
WHO universal trial number (UTN)	-
Other trial identifiers	ClinicalTrials.gov: NCT04161118

Notes:

Sponsors

Sponsor organisation name	University of Cologne
Sponsor organisation address	Albertus-Magnus-Platz, Köln, Germany, 50923
Public contact	Cologne Lymphoma Working Group (C-LWG), University Hospital Cologne, 0049 22147896533, TIGER-CTL019-Studienteam@uk-koeln.de
Scientific contact	Cologne Lymphoma Working Group (C-LWG), University Hospital Cologne, 0049 22147896533, TIGER-CTL019-Studienteam@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	19 June 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 February 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to estimate efficacy of treatment with tisagenlecleucel in elderly patients with relapsed or refractory aggressive B-cell non-Hodgkin lymphoma (r/r aNHL).

Protection of trial subjects:

Written informed consent before study entry, central response evaluation

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 August 2021
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: 3
Worldwide total number of subjects	3
EEA total number of subjects	3

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)	0
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

We enrolled 3 participants from 3 trial sites between 02 Aug 2021 and 28 Oct 2021.

Pre-assignment

Screening details:

Main entry criteria were histologically confirmed first relapse of aNHL within 365 days after rituximab- and anthracycline-containing first-line immunochemotherapy or refractory to respective 1st-line therapy, ineligibility for either autologous or allogeneic SCT, age <= 80 years

Period 1

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

Arms

Arm title	TIGER-CTL019

Arm description:

Patients received a single tisagenlecleucel infusion in a range of 0.6 – 6.0 x 108 CAR-positive viable T cells.

Arm type	Experimental
Investigational medicinal product name	Tisagenlecleucel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The recommended dose consists of a single IV infusion of 0.6 – 6.0 x 10^8 CAR-positive viable T cells. The viability of the entire cells has to be not less than 70%.
Tisagenlecleucel infusion was to start 2 - 8 days after completion of LD chemotherapy. Vital signs were monitored before, during, and following tisagenlecleucel infusion.

Number of subjects in period 1	TIGER-CTL019
Started	3
Completed	3

Baseline characteristics

Reporting groups	
Reporting group title	Enrollment

Reporting group description: -

Reporting group values	Enrollment	Total	
Number of subjects	3	3	
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)	0	0	
From 65-84 years	3	3	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	2	2	
Male	1	1	

End points

End points reporting groups

Reporting group title	TIGER-CTL019

Reporting group description:

Patients received a single tisagenlecleucel infusion in a range of 0.6 – 6.0 x 108 CAR-positive viable T cells.

Primary: Complete metabolic response rate

End point title	Complete metabolic response rate[1]

End point description:

The following special cases should be considered:
- If in the restaging after 4 weeks a PET/CT is performed and a CMR is reached according to central review, the patient will count as responder for the primary endpoint irrespective of their response after 12 weeks.
- If in the restaging after 4 weeks no PET/CT is performed, images are not available for central review, or no CMR has been reached according to central review, the response in the restaging after 12 weeks is used for determination of the primary endpoint.
- If the restaging after 12 weeks is not performed or images are not available for panel review and the patient did not already reach a CMR by central review in the restaging after 4 weeks, the patient will count as failure for the primary endpoint.

Patients will be excluded from analysis of the primary endpoint if their diagnosis of r/r aNHL is disconfirmed or if they did not receive any investigational drug for any reasons.

End point type	Primary

End point timeframe:

Efficacy will be determined using the complete metabolic response (CMR) rate, which is the proportion of patients with a Deauville score of 1–3 according to central review up until the restaging 12 weeks after treatment with tisagenlecleucel.

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: The TIGER-CTL019 trial was prematurely closed on 24 Feb 2023 with a total of 3 patients enrolled. Therefore, the statistical analyses planned in the trial protocol were not done, as stated in the statistical analysis plan.

End point values	TIGER-CTL019			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: subjects				
CMR	2			
Non-CMR	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs that occured from the time of signing the ICF up to the end of the trial had to be reported.

Adverse event reporting additional description:

AEs were assessed on the regular trial CRFs. SAEs were additionally assessed on specific forms. SAEs may thus be reported twice; non-serious AEs might contain SAEs; non-serious and SAEs might not add up to a total number of AEs.
All AEs of CTCAE grade >=1 will be reported.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.1

Reporting groups

Reporting group title	TIGER-CTL019

Reporting group description:

Patients received a single tisagenlecleucel infusion in a range of 0.6 – 6.0 x 108 CAR-positive viable T cells.

Serious adverse events	TIGER-CTL019		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Disease progression			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Tachyarrhythmia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			

Pituitary tumour removal			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Neurotoxicity			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sepsis			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cytokine release syndrome			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	TIGER-CTL019		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	4		
Other general disorders and administration site conditions			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Immune effector cell-associated neurotoxicity syndrome			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Psychiatric disorders			
Psychiatric disorders			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Cardiac disorders			
Cardiac disorders			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Nervous system disorders			
Nervous system disorders			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	3		

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 3 (100.00%)		
occurrences (all)	16		
Thrombocytopenia			
subjects affected / exposed	3 / 3 (100.00%)		
occurrences (all)	15		
Leukopenia			
subjects affected / exposed	3 / 3 (100.00%)		
occurrences (all)	18		
Other blood and lymphatic system disorders			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	3		
Eye disorders			
Eye disorders			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	3		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Other gastrointestinal disorders			
subjects affected / exposed	3 / 3 (100.00%)		
occurrences (all)	6		
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Renal and urinary disorders			
Renal and urinary disorders			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Endocrine disorders			

Hypothyroidism subjects affected / exposed occurrences (all) Other endocrine disorders subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1 1 / 3 (33.33%) 1		
Musculoskeletal and connective tissue disorders Musculoskeletal and connective tissue disorders subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Infections and infestations Infections and infestations subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
24 February 2023	Premature termination of the trial	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The trial was prematurely closed with 3 patients enrolled. Therefore, the statistical analyses planned in the trial protocol were not done, as stated in the SAP V1.0.

Notes: