

**Clinical trial results:****Phase II trial of Tisagenlecleucel in Elderly Patients with First-Relapsed or Primary Refractory Aggressive 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
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**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  $\leq$  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

<b>Arm title</b>	TIGER-CTL019
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Arm description:

Patients received a single tisagenlecleucel infusion in a range of  $0.6 - 6.0 \times 10^8$  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  $0.6 - 6.0 \times 10^8$  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.

<b>Number of subjects in period 1</b>	TIGER-CTL019
Started	3
Completed	3

## Baseline characteristics

### Reporting groups

Reporting group title	Enrollment
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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 10 <sup>8</sup> CAR-positive viable T cells.	

### Primary: Complete metabolic response rate

End point title	Complete metabolic response rate <sup>[1]</sup>
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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
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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 occurred 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  $\geq 1$  will be reported.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	10.1
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### Reporting groups

Reporting group title	TIGER-CTL019
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Reporting group description:

Patients received a single tisagenlecleucel infusion in a range of 0.6 – 6.0 x 10<sup>8</sup> 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 occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 3 (33.33%) 0 / 1 0 / 0		
Nervous system disorders Neurotoxicity subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 3 (33.33%) 2 / 2 0 / 0		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 3 (33.33%) 1 / 1 0 / 0		
Musculoskeletal and connective tissue disorders Muscular weakness subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 3 (33.33%) 1 / 1 0 / 0		
Infections and infestations Sepsis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 3 (33.33%) 0 / 1 0 / 1		
Cytokine release syndrome subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 3 (33.33%) 1 / 1 0 / 0		
Metabolism and nutrition disorders Dehydration subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 3 (33.33%) 0 / 1 0 / 0		

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

<b>Non-serious adverse events</b>	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 occurrences (all)  Other general disorders and administration site conditions subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 4  1 / 3 (33.33%) 2		
Immune system disorders Cytokine release syndrome subjects affected / exposed occurrences (all)  Immune effector cell-associated neurotoxicity syndrome subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2  2 / 3 (66.67%) 3		
Respiratory, thoracic and mediastinal disorders Respiratory, thoracic and mediastinal disorders subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Psychiatric disorders Psychiatric disorders subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Cardiac disorders Cardiac disorders subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Nervous system disorders Nervous system disorders subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 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)	1 / 3 (33.33%) 1		
Other endocrine disorders subjects affected / exposed occurrences (all)	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

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### 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: