Clinical trial results:
An exploratory, open-label, multicenter study to evaluate the safety and efficacy of a two-dose regimen of ATIR101, a T-lymphocyte enriched leukocyte preparation depleted ex vivo of host alloreactive T-cells (using photodynamic treatment), in patients with a hematologic malignancy, who received a CD34-selected hematopoietic stem cell transplantation from a haploidentical donor

Summary

EudraCT number	2015-002821-20
Trial protocol	BE DE PT HR
Global end of trial date	17 December 2018

Results information

Result version number	v1 (current)
This version publication date	02 January 2021
First version publication date	02 January 2021

Trial information

Trial identification

Sponsor protocol code	CR-AIR-008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02500550
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Kiadis Pharma
Sponsor organisation address	Paasheuvelweg 25A, Amsterdam, Netherlands, 1105BP
Public contact	Clinical Trial Information, Kiadis Pharma Netherlands B.V., +31 203140250, clinicaltrials@kiadis.com
Scientific contact	Clinical Trial Information, Kiadis Pharma Netherlands B.V., +31 203140250, clinicaltrials@kiadis.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	25 September 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of the study is to study the safety and efficacy of a repeat dose administration of ATIR101 in patients with a hematologic malignancy who received a T-cell depleted haploidentical HSCT.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki (and all amendments thereof) and that are consistent with the International Conference on Harmonization (ICH) Guideline for Good Clinical Practice (Topic E6 [R1]) as well as the applicable regulatory requirements.

The investigator/sub-investigator was responsible for explaining the nature and purpose of the study as well as other study-related matters to patients and donors, using the written information, and for obtaining their full understanding and written consent to participate in the study at their own free will. No patient/donor was to be subjected to undue influence, such as compulsory enrollment into the study. Informed consent had to be obtained prior to performing the first observations/examinations of the screening period (use of assessments which were performed before signing informed consent was subject of informed consent).

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	02 September 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Germany: 1
Worldwide total number of subjects	15
EEA total number of subjects	8

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	15
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

T-lymphocyte enriched leukocyte preparation depleted ex vivo of host alloreactive T-cells (using photodynamic treatment). Two intravenous infusions with 2x10E6 viable T-cells/kg approximately 42 days apart (unless the second dose is reduced or halted for safety reasons).

Period 1

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

Arms

Arm title	ATIR101

Arm description: -

Arm type	Experimental
Investigational medicinal product name	ATIR101
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

The first four ATIR101-treated patients were infused with two doses of 2.0×10e6 viable T-cells/kg (based on the patient weight at screening).
As decided in consultation with the IDMC, the next two patients were infused with a first dose 2.0×10e6 viable T-cells/kg and a second dose of 1.0×10e6 viable T-cells/kg. As recommended by the IDMC the remaining
patients were infused with a single ATIR101 dose of 2.0×10e6 viable T-cells/kg.

The first ATIR101 dose was infused at a median of 28.0 days (range 27-46) after the HSCT and the second ATIR101 dose (if given) was infused at a median of 73.5 days (range 71-77) after the HSCT.

Number of subjects in period 1	ATIR101
Started	15
Completed	8
Not completed	7
Adverse event, serious fatal	7

Baseline characteristics

End points

End points reporting groups

Reporting group title	ATIR101

Reporting group description: -

Primary: incidence of grade III/IV acute GVHD up to 180 days after HSCT.

End point title	incidence of grade III/IV acute GVHD up to 180 days after HSCT.[1]

End point description:

End point type	Primary

End point timeframe:

The primary endpoint was the incidence of grade III/IV acute GVHD up to 180 days after HSCT. Therefore, the primary analysis was based on the data at 180 days after the HSCT.

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: Overall in the study, four ATIR101-treated patients met the primary endpoint, grade III/IV acute GVHD within 180 days after HSCT: two (33.3%) in the double-dose group and two (22.2%) in the single-dose group

End point values	ATIR101			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: number of patients	15			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 1-year post HSCT	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	19
Reporting groups	
Reporting group title	ATIR101

Reporting group description: -

Serious adverse events	ATIR101		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 15 (46.67%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events	7		
Immune system disorders			
cGVHD			
subjects affected / exposed	7 / 15 (46.67%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 7		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	ATIR101		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 15 (53.33%)		
Investigations			
Cytomegalovirus test positive			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Immune system disorders			
aGVHD			
subjects affected / exposed	7 / 15 (46.67%)		
occurrences (all)	7		
cGVHD			

subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2		

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? No

Limitations and caveats

None reported