

**Clinical trial results:****A Phase 1-2 Study of Ti-061 Alone and in combination with other anti-cancer agents in Patients with Advanced Malignancies****Summary**

EudraCT number	2016-004372-22
Trial protocol	GB
Global end of trial date	02 August 2017

**Results information**

Result version number	v1 (current)
This version publication date	08 August 2018
First version publication date	08 August 2018

**Trial information****Trial identification**

Sponsor protocol code	Ti-061-101
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**Additional study identifiers**

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

Notes:

**Sponsors**

Sponsor organisation name	Tioma Therapeutics, Inc.
Sponsor organisation address	2000 Sierra Point Parkway, Suite 700, Brisbane, United States, CA 94005
Public contact	Clinical Trial Information Desk, Tioma Therapeutics, Inc., 001 4156714027, clinical@tiomatx.com
Scientific contact	Clinical Trial Information Desk, Tioma Therapeutics, Inc., 001 4156714027, clinical@tiomatx.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	29 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 August 2017
Global end of trial reached?	Yes
Global end of trial date	02 August 2017
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

- To evaluate the safety and tolerability of Ti-061 in adult patients with advanced malignancies
- To evaluate the safety and tolerability of Ti-061 combined with pembrolizumab in adult patients with advanced malignancies.

Protection of trial subjects:

A DRC was established to monitor and evaluate the safety of patients and to maintain oversight of study data and monitoring process.

If an infusion related reaction occurred, patients would be monitored until complete resolution of symptoms and treated as clinically indicated, including interruption and/or slowing of infusion rate as necessary.

During the first treatment period, patients provided with a study information card to be carried at all times until completion of the follow-up visit.

Background therapy:

None

Evidence for comparator:

No comparator used

Actual start date of recruitment	15 April 2017
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	United Kingdom: 1
Worldwide total number of subjects	1
EEA total number of subjects	1

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	1
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Recruitment was initiated in the UK on 23 May 2017. Only one patient was recruited in the UK on 24 May 2017.

### Pre-assignment

Screening details: -

### Pre-assignment period milestones

Number of subjects started	2 <sup>[1]</sup>
Number of subjects completed	1

### Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screen failure: 1
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Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The pre-assignment period includes the patient numbers for the screening period – i.e. the number of patients who entered screening. The worldwide number enrolled in the trial is the number of patients who passed screening and were then enrolled into the trial.

### Period 1

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

Blinding implementation details:

Open, no blinding

### Arms

Arm title	Part A - Ti-061
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Arm description:

Escalating repeat doses of Ti-061 monotherapy by intravenous administration to identify the maximum tolerated dose and recommended phase 2 dose, followed by expansion into 4 or more specific tumor type cohorts to examine preliminary efficacy and further document tolerability in patients with advanced malignancies

Arm type	Experimental
Investigational medicinal product name	Humanized monoclonal antibody targeting the CD47 cell surface protein
Investigational medicinal product code	Ti-061
Other name	None
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ti-061 was to be administered IV over at least 1 hour at escalating doses of 1 to 20 mg/kg weekly on days 1, 8 and 15 of each 3-week cycle or every 2 weeks on days 1 and 15 of each 4-week cycle in the exploratory Q2W cohort.

<b>Number of subjects in period 1</b>	Part A - Ti-061
Started	1
Completed	1

## Baseline characteristics

### Reporting groups

Reporting group title	Treatment period
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Reporting group description:

Ti-061 monotherapy

Reporting group values	Treatment period	Total	
Number of subjects	1	1	
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	1	1	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	73		
full range (min-max)	73 to 73	-	
Gender categorical			
Units: Subjects			
Female	1	1	
Male	0	0	

## End points

### End points reporting groups

Reporting group title	Part A - Ti-061
Reporting group description: Escalating repeat doses of Ti-061 monotherapy by intravenous administration to identify the maximum tolerated dose and recommended phase 2 dose, followed by expansion into 4 or more specific tumor type cohorts to examine preliminary efficacy and further document tolerability in patients with advanced malignancies	

### Primary: Safety and tolerability of Ti-061 alone and in combination with pembrolizumab.

End point title	Safety and tolerability of Ti-061 alone and in combination with pembrolizumab. <sup>[1]</sup>
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#### End point description:

Safety and tolerability of Ti-061 alone and in combination with pembrolizumab - the primary analysis of safety was a comprehensive evaluation of AEs and/or toxicity, presented by dose, regimen and tumor type cohort and overall, based on:

- Recording of AEs by CTCAE V4
- Recording of IRRs
- Results of monitoring vital signs
- Occurrence of late or cumulative AEs
- Occurrence of autoimmune AEs
- Results of clinical chemistry, hematology/coagulation, and urine analysis tests
- ECG results
- Changes in physical examination
- Markers of inflammation and immunogenicity
- Need for concomitant medications

End point type	Primary
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#### End point timeframe:

Ti-061 administered at escalating doses of 1-20mg/kg weekly on d1, 8 & 15 of each 3-wk cycle or every 2 wks on d1 & 15 of each 4-wk cycle in the exploratory Q2W cohort. If no MTD established 20mg/kg dose, higher doses up to 40mg/kg may have been explored

#### 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: Statistical analysis was not appropriate for this end point, so was therefore not performed.

End point values	Part A - Ti-061			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: mg/kg	0			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs (including abnormal laboratory test results) will be collected from the time of signing the informed consent until 30 days after the last Ti-061 dose.

Adverse event reporting additional description:

Only AEs/abnormalities occurring after the first dose of Ti-061 will be considered treatment-emergent.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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### Reporting groups

Reporting group title	Part A - Ti-061
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Reporting group description:

Escalating repeat doses of Ti-061 monotherapy by intravenous administration to identify the maximum tolerated dose and recommended phase 2 dose, followed by expansion into 4 or more specific tumor type cohorts to examine preliminary efficacy and further document tolerability in patients with advanced malignancies

<b>Serious adverse events</b>	Part A - Ti-061		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Vascular disorders			
Red blood cell agglutination			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		

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

<b>Non-serious adverse events</b>	Part A - Ti-061		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
Investigations			
Transaminitis (transaminase increase)			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 May 2017	Notification of Substantial Amendment Number 1- Temporary halt of the trial

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
24 May 2017	Only one patient was enrolled and treated in the trial; the patient completed the first study drug infusion but died on cycle 1, day 2, and the study was discontinued as a precautionary measure in light of this event.	-

Notes:

### Limitations and caveats

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

One patient enrolled, primary cause of death characterized as red cell agglutination. Sponsor considers this an important aspect, Sponsor would suggest that other aspects contributed to the patient's death, including intravascular hemolytic anemia.

Notes: