Clinical trial results:
A Novel Phase I/IIa Open label Study of IMM 101 in Combination with Selected Standard of Care (SOC) Regimens in Patients with Metastatic Cancer or Unresectable Cancer at Study Entry.

Summary

EudraCT number	2016-001459-28
Trial protocol	GB
Global end of trial date	30 August 2017

Results information

Result version number	v1 (current)
This version publication date	21 March 2019
First version publication date	21 March 2019

Trial information

Trial identification

Sponsor protocol code	IMM-101-011

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03009058
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Immodulon Therapeutics Ltd
Sponsor organisation address	6-9 The Square, Stockley Park, Uxbridge, United Kingdom, UB11 1FW
Public contact	Clinical Trial Information Desk, Immodulon Therapeutics Ltd, info@immodulon.com
Scientific contact	Clinical Trial Information Desk, Immodulon Therapeutics Ltd, info@immodulon.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	26 October 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 August 2017
Global end of trial reached?	Yes
Global end of trial date	30 August 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to provide safety data for IMM-101 in combination with a number of selected chemotherapy regimens in patients with unresectable or metastatic cancer.
Secondary objectives included safety data for the combination of IMM-101 with anti-programmed death-1 (anti-PD-1) (pembrolizumab, nivolumab) regimens and with anti-cytotoxic T lymphocyte-associated antigen 4 (anti-CTLA-4) (ipilimumab) regimens and preliminary data regarding the activity of IMM-101 (in terms of response to treatment) in combination with selected SOC regimens in a number of different tumour types.
Only two patients were enrolled into the study before the study was terminated early by the Sponsor, after a review of the resources required to complete the study concluded that sufficient funding for completion of the study could not be guaranteed. Hence, no formal analysis could be conducted and the objectives of the study could not be met.

Protection of trial subjects:

This clinical study was conducted in compliance with the study protocol, and in accordance with the provisions of the guidelines of the WMA Declaration of Helsinki, as amended by the 64th World Medical Association (WMA) General Assembly, Fortaleza, Brazil, October 2013, the guidelines of ICH-GCP (CPMP/ICH/135/95), designated standard operating procedures (SOPs), and with local laws and regulations relevant to the use of new therapeutic agents.
An internal safety review committee reviewed the clinical safety data twice during the course of the study.

Background therapy:

Specified tumour types and standard care regimes were allowed per protocol. Patients could only be considered for entry into the study when they were commencing a new line of standard care. Patients were to be enrolled into different cohorts depending on their tumour type and standard of care. Only 2 patients were enrolled; both into the cohort receiving anti-PD-1 (nivolumab) alongside IMM-101.

Evidence for comparator: -

Actual start date of recruitment	31 May 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: 2
Worldwide total number of subjects	2
EEA total number of subjects	2

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)	1
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Two patients were enrolled before the study was terminated early by the Sponsor. Both patients were enrolled into the cohort for patients with advanced melanoma receiving standard of care anti-PD-1 (nivolumab).

Pre-assignment

Screening details:

Patients aged ≥18 years were eligible for the study if they had metastatic or unresectable cancer and were considered by their physician to be indicated for a new line of standard care therapy as specified in the protocol. Three patients were screened and two were eligible and enrolled into the study.

Period 1

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

Arms

Arm title	Metastatic melanoma and IMM-101 + nivolumab

Arm description:

Patients with metastatic melanoma receiving nivolumab + IMM-101

Arm type	Experimental
Investigational medicinal product name	Heat killed Mycobacterium obuense NCTC13365 (IMM-101)
Investigational medicinal product code	UPI EMA/569517 (IMM-101)
Other name	IMM-101
Pharmaceutical forms	Suspension for injection
Routes of administration	Intradermal use

Dosage and administration details:

IMM-101 (10 mg/mL) administered as a single 0.1 mL intradermal injection into the skin overlying the deltoid muscle, with the arm being alternated between each dose. The first three patients receiving anti-PD-1 (nivolumab) received one dose of IMM-101 every 4 weeks throughout. In the absence of safety signals, subsequent patients treated with anti-PD-1 would be dosed with the standard IMM-101 dosing regimen which comprised: one dose given every 2 weeks for the first three doses followed by a rest period of 4 weeks, then one dose every 2 weeks for the next three doses followed by a dose every 4 weeks thereafter. Dosing was to be continued to a maximum of 28 weeks in the Treatment Phase. A Maintenance Phase of ongoing treatment with IMM-101 approximately every 4 weeks (starting from Week 28) for up to 4.5 years was also planned.In practice, only 2 patients were enrolled, both into the cohort receiving anti-PD-1 (nivolumab).

Number of subjects in period 1	Metastatic melanoma and IMM-101 + nivolumab
Started	2
Completed	0
Not completed	2
study terminated by Sponsor	2

Baseline characteristics

Reporting groups	
Reporting group title	Study period
Reporting group description:	
All enrolled patients. Both enrolled patients received study drug (IMM-101) and nivolumab	

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

End points

End points reporting groups

Reporting group title	Metastatic melanoma and IMM-101 + nivolumab

Reporting group description:

Patients with metastatic melanoma receiving nivolumab + IMM-101

Primary: Safety assessment

End point title	Safety assessment[1]

End point description:

It was planned to assess AEs, related AEs and SAEs according to the proportion of patients having at least one event, by coded terms, and by severity. Adverse events leading to withdrawal or death would have been assessed. As the study terminated early with only 2 patients enrolled, no statistical assessment of safety could be made.

End point type	Primary

End point timeframe:

Adverse events were recorded from the time of informed consent. All adverse events were followed until resolution, death or 30 days after the End of Study/Withdrawal

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 study terminated early when only 2 patients had been enrolled so the planned statistical analyses and data presentations described in the study protocol were therefore not carried out. The data collected were listed only and not tabulated or analysed further.

End point values	Metastatic melanoma and IMM-101 + nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: patients with adverse events	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Tumour response

End point title	Tumour response

End point description:

The activity of IMM-101 was planned to be assessed for each standard of care by tumour type by assessing the response rate after the tenth patient in each standard of care/tumour type cohort reached the Week 28 visit.
A CT/MRI scan was performed at baseline (either a scan performed in the 30 days prior to screening or a scan performed at screening) and the first post-baseline scan was planned at Week 12. Due to the early termination of the study, both enrolled patients had their only post-baseline scan at their end of study visit which was approximately 11 weeks following first dose of IMM-101. The response to treatment according to immune-related Response Criteria (irRC) was assessed. A response was defined according to irRC as either immune-related partial response or immune-related complete response.

End point type	Secondary

End point timeframe:

A CT/MRI scan was performed at baseline (either a scan performed in the 30 days prior to screening or a scan performed at screening) and the post-baseline scan was at approximately 11 weeks following first dose of IMM-101.

End point values	Metastatic melanoma and IMM-101 + nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Patients with a response	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded from the time of informed consent. All adverse events were followed until resolution, death or 30 days after the End of Study/Withdrawal.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20

Reporting groups

Reporting group title	Safety population

Reporting group description:

All patients in the safety population, i.e. all patients receiving at least one dose of IMM-101, the investigational medicinal product.

Serious adverse events	Safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)		
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Endocrine disorders			

Hyperthyroidism subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1		
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 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? No

Limitations and caveats

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

Due to the early termination of this study, the objectives of the study could not be met and no meaningful assessment of safety and efficacy could be made.

Notes: