Clinical trial results:
A Phase 2, Open-Label, Multi-cohort Study of PD-L1 Probody™ Therapeutic CX-072 in Combination With Other Anticancer Therapy in Adults With Solid Tumors (PROCLAIM-CX-072-002)

Summary

EudraCT number	2019-000999-42
Trial protocol	GB ES NL
Global end of trial date	21 May 2020

Results information

Result version number	v1 (current)
This version publication date	06 August 2021
First version publication date	06 August 2021

Trial information

Trial identification

Sponsor protocol code	CTMX-M-072-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03993379
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 142922

Notes:

Sponsors

Sponsor organisation name	CytomX Therapeutics, Inc.
Sponsor organisation address	151 Oyster Point Boulevard Suite 400, South San Francisco, United States, CA 94080-1913
Public contact	Clinical Trial Team, CytomX Therapeutics, Inc. , +1 (650) 515-3185, Clinicaltrials@cytomx.com
Scientific contact	Clinical Trial Team, CytomX Therapeutics, Inc. , +1 (650) 515-3185, Clinicaltrials@cytomx.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	27 July 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 May 2020
Global end of trial reached?	Yes
Global end of trial date	21 May 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Part A:
• To obtain evidence of antitumor effect of CX-072 in combination with ipilimumab in subjects with solid tumors based on the objective response rate (ORR) as defined by the Response Evaluation Criteria in Solid Tumors (RECIST) v1.1

Part B:
• To obtain evidence of antitumor effect of CX-072 in combination with ipilimumab in subjects with solid tumors based on the pathologic response following neoadjuvant administration of combination treatment

Protection of trial subjects:

This study was conducted in accordance with the clinical protocol as approved by the applicable Institutional Review Board/Independent Ethics Committee, International Council for Harmonisation Good Clinical Practice Guidelines, and other applicable regulatory requirements.

The informed consent form (ICF) was explained to the subjects for the risks and benefits of study participation in simple terms before they entered into the study. Each subject signed an ICF containing appropriate study and study drug information and was provided a copy of the ICF.

Appropriate study restrictions based on the mechanism of action of CX-072 (i.e., targeting the programmed death 1 [PD-1]/programmed death-ligand 1 [PD-L1] pathway) were implemented including screening procedures and exclusion criteria to ensure the safety of subjects.

Proper instruction regarding adverse events (AEs) of special interest was provided to each site to ensure prompt reporting and communication between the Sponsor, Investigators, and the applicable regulatory agencies or health authorities. Individual subject safety was assessed by the Investigator on an ongoing basis during the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 November 2019
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 States: 3
Worldwide total number of subjects	3
EEA total number of subjects	0

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	1

Subject disposition

Recruitment

Recruitment details:

This is a Phase 2, multicenter, global, open-label, multi-cohort, and parallel-cohort study. This study was composed of 2 parts (Part A and Part B) and 4 cohorts (Cohorts A1, A2, A3, and B1). Enrollment into each cohort was to occur in parallel and in 2 stages for all cohorts of Part A and Part B.

Pre-assignment

Screening details:

A total of 3 subjects were enrolled into Cohort A2 of the study. The study was terminated early after these 3 subjects were enrolled. Only Cohort A2 is represented in this summary because all other study cohorts (A1, A3, and B1) did not enroll any subjects.

Period 1

Period 1 title	Overall study (Part A [Cohort A2]) (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Cohort A2

Arm description:

Subjects with histologically or cytologically confirmed Stage III (unresectable) or Stage IV melanoma who had experienced progressive disease or relapse following treatment with a PD-1/PD-L1 immune checkpoint inhibitor received CX-072 in combination with ipilimumab in Cohort A2.

Subjects were to be treated with 4 doses of combination therapy (intravenous infusion of 800 mg CX-072 plus 3 mg/kg ipilimumab) once every 3 weeks and then with 800 mg CX-072 intravenous monotherapy once every 2 weeks after the 3 weeks of the fourth dose of combination therapy until the occurrence of progressive disease by immune-related RECIST (irRECIST), unacceptable toxicity, or the subjects met any other criterion for treatment discontinuation.

Arm type	Experimental
Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

CX-072 was supplied as a sterile solution for intravenous administration in a 10 mL volume, and each vial contained 100 mg of CX-072 formulated with suitable compendial excipients.

In combination therapy, CX-072 was administered first, followed by a saline flush, and then followed by the ipilimumab infusion. During monotherapy, 800 mg CX-072 was infused over 60 minutes.

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

Ipilimumab was supplied as a sterile, preservative-free solution in 10 mL (50 mg) and 40 mL (200 mg) vials at a concentration of 5 mg/mL. Ipilimumab dosing was based on the subject’s weight and dose level assignment. Ipilimumab could be diluted with 0.9% sodium chloride injection, United States Pharmacopoeia (USP) or 5% Dextrose Injection, USP to a final concentration ranging from 1 to 2 mg/mL.

Ipilimumab (3 mg/kg) was administered as a 90-minute intravenous infusion and was infused no sooner than 30 minutes after completion of the CX-072 infusion.

Number of subjects in period 1	Cohort A2
Started	3
Completed	0
Not completed	3
Consent withdrawn by subject	1
Termination of study by sponsor	2

Baseline characteristics

Reporting groups	
Reporting group title	Cohort A2

Reporting group description:

Subjects with histologically or cytologically confirmed Stage III (unresectable) or Stage IV melanoma who had experienced progressive disease or relapse following treatment with a PD-1/PD-L1 immune checkpoint inhibitor received CX-072 in combination with ipilimumab in Cohort A2.

Subjects were to be treated with 4 doses of combination therapy (intravenous infusion of 800 mg CX-072 plus 3 mg/kg ipilimumab) once every 3 weeks and then with 800 mg CX-072 intravenous monotherapy once every 2 weeks after the 3 weeks of the fourth dose of combination therapy until the occurrence of progressive disease by immune-related RECIST (irRECIST), unacceptable toxicity, or the subjects met any other criterion for treatment discontinuation.

Reporting group values	Cohort A2	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)	1	1	
From 65-84 years	1	1	
85 years and over	1	1	
Gender categorical Units: Subjects			
Female	1	1	
Male	2	2	

End points

End points reporting groups

Reporting group title	Cohort A2

Reporting group description:

Subjects with histologically or cytologically confirmed Stage III (unresectable) or Stage IV melanoma who had experienced progressive disease or relapse following treatment with a PD-1/PD-L1 immune checkpoint inhibitor received CX-072 in combination with ipilimumab in Cohort A2.

Subjects were to be treated with 4 doses of combination therapy (intravenous infusion of 800 mg CX-072 plus 3 mg/kg ipilimumab) once every 3 weeks and then with 800 mg CX-072 intravenous monotherapy once every 2 weeks after the 3 weeks of the fourth dose of combination therapy until the occurrence of progressive disease by immune-related RECIST (irRECIST), unacceptable toxicity, or the subjects met any other criterion for treatment discontinuation.

Primary: Number of subjects with ORR by the RECIST v1.1

End point title	Number of subjects with ORR by the RECIST v1.1[1]

End point description:

For solid tumors, response evaluation is based upon RECIST criteria (v1.1) and ORR was defined as the proportion of subjects with complete response (CR) or partial response (PR) on 2 consecutive tumor assessments at least 4 weeks apart according to RECIST (RECIST v1.1). However, after enrollment of 3 subjects, the study was terminated at the Sponsor's discretion. Descriptive statistical summaries were produced.

End point type	Primary

End point timeframe:

Not applicable

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: Data tabulations and summaries were performed, but no formal statistical analyses were undertaken due to early study termination. With 3 subjects enrolled, there was insufficient subject data to determine stable estimates for any of the proposed efficacy study endpoints. Additionally, pharmacokinetic analyses were not performed.

End point values	Cohort A2			
Subject group type	Reporting group			
Number of subjects analysed	3[2]			
Units: Not analysed	0			

Notes:

[2] - Due to early termination, efficacy analyses were not performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Numbers of subjects experiencing antitumor activity by irRECIST

End point title	Numbers of subjects experiencing antitumor activity by irRECIST

End point description:

Antitumor activity was to be evaluated in the subjects with solid tumors treated with CX-072 in combination with ipilimumab based on ORR by irRECIST. However, after enrollment of 3 subjects, the study was terminated at the Sponsor's discretion. Descriptive statistical summaries were produced.

End point type	Secondary

End point timeframe:
Not applicable

End point values	Cohort A2			
Subject group type	Reporting group			
Number of subjects analysed	3[3]			
Units: Not analysed	0			

Notes:
[3] - Due to early termination, efficacy analyses were not performed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs occurring after the ICF was signed and up to 30 days after the last dose of the study drug were reported.

Adverse event reporting additional description:

Subjects were continued to be monitored for immune-related AEs, AEs ≥ Grade 3, and serious AEs (SAEs) up to 90 days following their last dose of the study drug. All the treatment-emergent adverse events reported during the study are provided here for the enrolled subjects.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Cohort A2

Reporting group description:

Safety assessments included all 3 subjects who were enrolled in Cohort A2 and received at least one dose of the study drug.

Serious adverse events	Cohort A2		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Hepatobiliary disorders			
Immune-mediated hepatitis			
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: 0 %

Non-serious adverse events	Cohort A2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)		
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Neoplasms benign, malignant and			

unspecified (incl cysts and polyps) Cancer pain subjects affected / exposed occurrences (all)	 1 / 3 (33.33%) 1		
Injury, poisoning and procedural complications Infusion related reaction subjects affected / exposed occurrences (all)	 1 / 3 (33.33%) 2		
General disorders and administration site conditions Generalised oedema subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all)	 1 / 3 (33.33%) 1 1 / 3 (33.33%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 1 / 3 (33.33%) 1 1 / 3 (33.33%) 1 1 / 3 (33.33%) 1		
Hepatobiliary disorders Immune-mediated hepatitis subjects affected / exposed occurrences (all)	 2 / 3 (66.67%) 2		
Skin and subcutaneous tissue disorders Rash generalised subjects affected / exposed occurrences (all)	 1 / 3 (33.33%) 1		
Infections and infestations Cellulitis subjects affected / exposed occurrences (all)	 1 / 3 (33.33%) 1		

Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Hypokalaemia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Hypophosphataemia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 May 2019	No subject enrolled in the study under Amendment 1 (24 May 2019) of the protocol. Major changes to the conduct of the study implemented with Amendment 1 were as follows: • Further defined the patient population in Cohort A2 who experienced disease progression during treatment with an anti-PD-1/PD-L1 antibody to include the time since last progression, progression criteria, and minimum number of cycles • Revised to routinely collect SAEs and Grade 3 and 4 AEs up to 90 days after the last dose of study treatment • Instructed investigators to follow the CX-072 Module if/when there were overlapping directives between the Module and Common Core
21 August 2019	All 3 subjects were enrolled in the study under Amendment 2 (21 August 2019) of the protocol. Major changes to the conduct of the study implemented with Amendment 2 were as follows: • Specified the terms and planned number of enrollment into study Part A, Cohort A2, under a Simon's 2-Stage design, so that for Amendment 2, only Stage 1 of Cohort A2 was included with an accompanying rationale for change in statistical assumptions for that cohort • Revised the eligibility criteria for the study and updated dose modification details for select adverse events (such as myasthenia gravis or Guillain-Barré syndrome and hypothyroidism or hyperthyroidism) • Revised the biomarker/antidrug antibody serum sample time for predose, study treatment days, and at the end of treatment visit • Updated reference safety information based on local ipilimumab package insert.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
30 March 2020	Due to developmental strategic reasons and slow enrollment because of the COVID-19 pandemic, the study was terminated early. Three subjects were enrolled, all in Cohort A2. The last subject observation for this study was on 21 May 2020.	-

Notes:

Limitations and caveats

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

No formal statistical analyses were undertaken due to early study termination. There was insufficient subject data (3 subjects enrolled) to determine stable estimates for any of the proposed study endpoints. Pharmacokinetic analyses were not done.

Notes: