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)

Published: 15-08-2019
Last updated: 10-04-2024

Part A:* To obtain evidence of antitumor effect of CX-072 in combination with ipilimumab in subjects withsolid tumors based on the objective response rate (ORR) as defined by the Response EvaluationCriteria in Solid Tumours (RECIST) v1.1Part B:* To...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metastases
Study type	Interventional

Summary

ID

NL-OMON49159

Source
ToetsingOnline

Brief title
PROCLAIM -CX-072-002

Condition

- Metastases

Synonym
cancer, tumor

Research involving

Human

Sponsors and support

Primary sponsor: CytomX Therapeutics, Inc.,
Source(s) of monetary or material Support: industry

Intervention

Keyword: Cancer, CX-072, Open-label, Probody

Outcome measures

Primary outcome

Part A: The primary criterion for defining evidence of anticancer activity is

RECIST v1.1. The criterion

for management of subject care and treatment discontinuation is irRECIST.

Part B: The primary criterion for defining evidence of anticancer activity is

pathologic response based

on central review of tumor sample from surgical resection. The criteria for

management of subject care

and treatment discontinuation are radiographic response assessment (prior to

surgery), local pathologic

assessment of surgical sample after surgery, or disease relapse. Tumor response

as defined by RECIST

v1.1 will be assessed prior to surgical resection; however, responses will not

be confirmed, because the

tumor assessment will be followed by surgical resection.

Secondary outcome

Pharmacokinetics: Concentration versus time data will be tabulated and plotted

for the individual and
mean serum total and Intact CX-072 moieties. Maximum observed plasma concentration (Cmax) and
minimum observed plasma concentration (Cmin) will be tabulated individually and summarized using
descriptive statistics (eg, mean, standard deviation, and coefficient of variation). Ipilimumab Cmax and
Cmin will be summarized using descriptive statistics. Population PK (POPPK) analysis of the data may be
performed as warranted by the data, and results of the analysis will be reported separately.
Immunogenicity: Serum samples will be collected to assess the immunogenicity of CX-072 and
ipilimumab. All samples will be initially screened for ADAs. If the sample is found to be ADA positive
in the screening assay, a confirmatory assay will be performed. Confirmed positive samples will be
evaluated with a titer assay and may be further characterized for the presence of neutralizing or domainspecific
ADA.
Exploratory Biomarkers: Exploratory studies will include the evaluation of the presence of PD-L1,
tumor mutation burden (TMB), T cell receptor (TCR) repertoire, and circulating exploratory biomarkers

including, but not limited to PD-L1.

Study description

Background summary

CX-072 is a Probody* therapeutic directed against a protein in the body called PD-L1
(programmed cell death ligand 1). PD-L1 is present on cells of the immune system, on
healthy cells of the body and can also be present on cell walls of tumor cells. With this protein the tumor cell can protect itself from being attacked by the immune system.
CX-072 is developed in such a way that it blocks PD-L1, after it has been activated by an enzyme. It is thought that this enzyme is only present in tumor cells. The goal is to prevent activation of Probody in healthy tissues this way.
CX-072 is not yet registered and not approved by the EMA (European Medicine Agency) nor by the Dutch regulatory authorities. The possibility exists that the study drug will never be approved. So CX-072 is a study drug that can (not) yet be prescribed by doctors outside studies.

Study objective

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 Tumours (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 pathologic response following neoadjuvant administration of combination
treatment

Study design

STUDY DESIGN AND DURATION
This is a Phase 2, multicenter, global, open-label, multi-cohort and parallel-cohort study of PD-L1
Probody therapeutic CX-072 in combination with ipilimumab designed to assess the antitumor effect of
combination treatment and to characterize the safety, tolerability, PK,

immunogenicity, and biomarkers
of combination treatment in subjects with solid tumors.
This Module is comprised of 2 parts and 4 cohorts:
* Part A:
o Cohort A1: Subjects with histologically or cytologically confirmed Stage III (unresectable) or Stage
IV melanoma who have received no prior treatment for unresectable or metastatic melanoma
o Cohort A2: Subjects with histologically or cytologically confirmed Stage III (unresectable) or Stage
IV melanoma who have experienced progressive disease or relapse following monotherapy with
a PD-1/PD-L1 immune checkpoint inhibitor
o Cohort A3: Subjects with histologically or cytologically confirmed, advanced/unresectable or
metastatic, transitional cell carcinoma of the urothelium who have experienced disease
progression during or following treatment with platinum-based therapy
* Part B:
o Cohort B1: Subjects with histologically confirmed resectable Stage III melanoma with palpable
disease suitable for curative surgery

Intervention

DOSAGE FORMS AND ROUTE OF ADMINISTRATION
Part A:
o Combination treatment (intravenous [IV]): 800 mg CX-072 + 3 mg/kg ipilimumab, once every
3 weeks (q3w)
o Monotherapy treatment (IV): 800 mg CX-072, q2w
Part B:
o Combination treatment (IV): 800 mg CX-072 + 1 mg/kg ipilimumab, q3w
o Monotherapy treatment (IV): 800 mg CX-072, q2w

Study burden and risks

Usually the patient may only visit the doctor for follow-up of the disease once every two months. The study-related visits will replace and will be additional to these regular visits.

Disadvantages of participation in the study may be
- possible side effects/complications of the study drug;
- possible side effects/discomforts of the evaluations in the study.

Participation in the study also means:

- additional time;
- additional or longer hospital stays;
- additional tests;
- instructions you need to follow.

More blood will be taken, you will experience more radiation.
You will also be tested for HIV and hepatitis B/C.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. At least 18 years of age
2. Measurable disease as defined by RECIST v1.1
3. Eastern Cooperative Oncology Group (ECOG) performance status of *1

4. Agree to provide tumor tissue and blood samples for biomarker assessment
* Part A: Must agree to provide mandatory archival tumor tissue (formalin-fixed paraffin embedded tumor block or unstained slides) or undergo a new tumor biopsy
* Part B: Must agree to provide tumor tissue from the initial diagnostic biopsy and prospectively agree to provide tumor tissue obtained from surgery on study for pathologic analysis and for biomarker assessment
5. Subjects with treated brain metastases are eligible if the brain metastases are stable (no magnetic resonance imaging [MRI] evidence of progression for at least 8 weeks after treatment is complete and within 28 days prior to first dose of study treatment) and the subject does not require radiation therapy or steroids. Active screening for brain metastases (eg, brain computed tomography [CT] or MRI) is not required
6. Screening laboratory values must meet all of the following criteria:
* White blood cells >2000/µL or 2.0 × 10 to the power of 9/L
* Neutrophils *1500/µL or 1.5 × 10 to the power of 9/L
* Platelets *100 × 10 to the power of 3/µL or 100 × 10 to the power of 9/L
* Hemoglobin *9.0 g/dL (may have been transfused) or 90.0 g/L
* Creatinine *2 mg/dL or 176.8 µmol/L OR measured or calculated creatinine clearance (glomerular filtration rate can also be used in place of creatinine or creatinine clearance) >50 mL/min
* AST and ALT *2.5 × upper limit of normal (ULN)
* Total bilirubin within ULN (unless diagnosed with Gilbert*s syndrome, those subjects must have a total bilirubin <3.0 mg/dL or 51.3 µmol/L)
* Amylase and lipase *1.5 × ULN
* International normalized ratio (INR) and activated partial thromboplastin time (aPTT) *1.5 × ULN (unless subject is on therapeutic anticoagulation, at which time the INR and aPTT must be in the target therapeutic anticoagulation range)
* Serum albumin *2.5 g/dL
7. Females of childbearing potential and nonsterile males must agree to practice highly effective methods of birth control (as described in Appendix C) for the duration of the study and for 6 months after the last dose of study treatment
8. The ability to understand and the willingness to sign a written ICF and adhere to study schedule and prohibitions
See additional cohort-specific inclusion criteria in Sections 4.2, 4.3, 4.4, and 4.5 of the Protocol.

Exclusion criteria

1. Treatment with cytotoxic chemotherapy, biologic agents, radiation, immunotherapy, or any investigational agent within 28 days prior to the first dose of study treatment. This interval can be reduced to 2 weeks for subjects who received bone-only radiation therapy or for subjects whose most recent

prior therapy was a single-agent, small-molecule kinase inhibitor having a half-life of 3 days or less.
- For Cohort A2: Prior anti-PD-1/PD-L1 antibody given as a single agent is not excluded within the 28 days prior to the first dose of study treatment. Time from last dose of prior anti-PD-1/PD-L1 inhibitor to first dose of study treatment must be at least the same length as the time interval of the prior PD-1/PD-L1 dosing schedule (eg, if prior PD-1/PD-L1 dosing was once every 14 days, then the last dose must have been at least 14 days prior to first dose of study treatment)
2. Prior therapy with a chimeric antigen receptor T cell*containing regimen
3. History of active autoimmune disease(s) including but not limited to inflammatory bowel diseases, rheumatoid arthritis, autoimmune thyroiditis, autoimmune hepatitis, systemic sclerosis, systemic lupus erythematosus, autoimmune vasculitis, autoimmune neuropathies, type 1 insulin-dependent diabetes mellitus
4. History of myocarditis regardless of the cause
5. History of intolerance to prior checkpoint inhibitor therapy defined as the need to discontinue treatment due to an irAE
6. History of toxic epidermal necrolysis or Stevens-Johnson syndrome
7. History of any syndrome or medical condition that required treatment with systemic steroids (*10 mg daily prednisone equivalents) or immunosuppressive medications. However, subjects who required brief courses of steroids (eg, as prophylaxis for IV contrastor for treatment of an allergic reaction) may be eligible with Sponsor approval. Inhaled or topical steroids are permitted.
8. Baseline corrected QT interval (QTc) >470 ms. If a subject starts on a QTc prolonging drug(s), a series of electrocardiograms (ECGs) should be obtained to redefine the baseline QTc.
9. Unresolved acute toxicity CTCAE v5.0 Grade *1 (or baseline, whichever is greater) from prior anticancer therapy. Alopecia and other nonacute toxicities are acceptable. Hormone deficiency due to prior anticancer therapy that is deemed stable with supplementation or does not require supplementation is allowed.
10. History of severe allergic or anaphylactic reactions to human mAb therapy or known hypersensitivity to any Probody therapeutic
11. Subjects with known human immunodeficiency virus, acquired immune deficiency syndrome, or any related illness
12. Subjects with acute or chronic hepatitis B or C
13. History of allogeneic tissue/solid organ transplant, stem cell transplant, or bone marrow transplant
14. Major surgery (eg, that required general anesthesia) within 4 weeks prior to the first dose of study treatment (and must be confirmed to be completely healed), or minor surgery (eg, not
involving chest, abdomen, or intracranial structures) or gamma knife treatment (with adequate healing) within 14 days prior to first dose of study treatment (excluding biopsies conducted with local/topical anesthesia) if complete healing is confirmed
15. History of active malignancy not related to the cancer being treated within

the previous 2 years, with the exception of localized cancers that are considered cured and, in the opinion of the Investigator, present a low risk for recurrence. These exceptions include, but are not limited to, basal or squamous cell skin cancer, superficial bladder cancer, and carcinoma in situ of the prostate, cervix, or breast.
16. Received a live vaccine within 30 days prior to the first dose of study treatment. Examples of live vaccines include, but are not limited to, the following: measles, mumps, rubella, chicken pox/zoster, yellow fever, rabies, Bacillus Calmette-Guérin, and typhoid vaccine.
17. Intercurrent illness including, but not limited to:
* Ongoing severe aortic stenosis
* Myocardial infarction or stroke within 24 weeks prior to first dose of study treatment
* Any of the following within 12 weeks prior to first dose of study treatment: symptomatic congestive heart failure (ie, New York Heart Association Class III or IV), unstable angina pectoris, or clinically significant and uncontrolled cardiac arrhythmia
* Nonhealing wound or ulcer within 4 weeks prior to Cycle 1 Day 1
* Active infection requiring systemic antiviral, antibiotic, or antifungal therapy within 5 days prior to first dose of study treatment
18. Pleural or pericardial effusion or ascites requiring drainage *1 time(s) per month
19. History of multiple myeloma
20. Women who are pregnant or breastfeeding

See additional cohort-specific exclusion criteria in Sections 4.7 and 4.8 of the Protocol.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	25-09-2019
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	CX-072
Product type:	Medicine
Brand name:	Yervoy
Generic name:	ipilimumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	15-08-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-09-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-11-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-11-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-02-2020

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-03-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2019-000999-42-NL
Other	NA
CCMO	NL70737.056.19