A Phase 1 and 2a open-label trial to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, immunogenicity, and antitumor activity of LAVA-1207, a PSMA-targeting bispecific γδ-T cell engager, alone or with low dose interleukin-2 or Pembrolizumab, in patients with therapy refractory metastatic castration resistant prostate cancer

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This study has been transitioned to CTIS with ID 2024-515821-27-00 check the CTIS register for the current data. Primary objectivesPart 1 Dose Escalation for LAVA-1207 alone, LAVA-1207 plus LDSC IL-2, and LAVA-1207 plus pembrolizumab• To investigate...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Reproductive neoplasms male malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON56169

Source
ToetsingOnline

Brief title
LAVA1207-001

Condition

- Reproductive neoplasms male malignant and unspecified

Synonym
mCRPC, Prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: LAVA Therapeutics NV
Source(s) of monetary or material Support: LAVA Therapeutics NV

Intervention

Keyword: LAVA-1207, mCRPC, Phase 1/2a open label trial

Outcome measures

Primary outcome

Primary endpoints

Part 1 Dose Escalation for LAVA-1207 alone, LAVA-1207 plus LDSC IL-2, and

LAVA-1207 plus pembrolizumab

Frequency and severity of AEs using the Common Terminology Criteria for Adverse

Events (CTCAE) version 5.0 and ASTCT grading for CRS.

Frequency and type of DLT.

Part 2 Expansion Cohort for LAVA-1207 alone and/or LAVA-1207 plus LDSC IL-2,

and/or LAVA-1207 plus pembrolizumab

Frequency and severity of AEs using the CTCAE version 5.0 and ASTCT grading of

CRS at the RP2D.

Secondary outcome

Secondary endpoints

Part 1 Dose Escalation and Part 2 Expansion Cohort (for LAVA-1207 alone and/or LAVA-1207 plus LDSC IL-2 and/or LAVA-1207 plus pembrolizumab)

Number of participants with an antitumor response according to immune response evaluation criteria in solid tumors (RECIST and iRECIST) in patients with measurable disease.

Duration of response.

Disease control rate (DCR) for patients with measurable disease at 8, 16 and 24 weeks.

Number of participants who experience any PSA decrease, and number of participants who experience a PSA decrease of >= 50% from baseline.

Progression free survival (using Prostate Cancer Working Group 3 [PCWG3] for bone lesions and/or iRECIST criteria for soft-tissue lesions).

Pharmacokinetic parameters.

Pharmacodynamic markers.

Incidence and prevalence of anti-LAVA-1207 antibodies.

Study description

Background summary

LAVA-1207 is an experimental treatment. LAVA-1207 is a bispecific humanized antibody, developed in a laboratory and designed to help the immune system fight cancer cells. LAVA-1207 binds to a particular protein called "PSMA", which is found on the surface of tumor cells. By binding to it, LAVA-1207 activates the immune system to kill the tumor cells.

In this study, LAVA-1207 is administered to humans for the first time. It has previously been tested in the lab, as well as on animals.

Study objective

This study has been transitioned to CTIS with ID 2024-515821-27-00 check the CTIS register for the current data.

Primary objectives
Part 1 Dose Escalation for LAVA-1207 alone, LAVA-1207 plus LDSC IL-2, and LAVA-1207 plus pembrolizumab
• To investigate the safety and tolerability of treatment in patients with therapy refractory mCRPC.
• To determine the preliminary RP2D in patients with therapy refractory mCRPC for LAVA-1207 monotherapy, LAVA-1207 + LDSC IL-2, and LAVA-1207 + pembrolizumab.

Part 2 Expansion Cohort for LAVA-1207 alone, LAVA-1207 plus LDSC IL-2, and LAVA-1207 plus pembrolizumab
• To investigate the safety and tolerability at the RP2D in therapy refractory mCRPC patients with measurable and non-measurable disease.

Secondary objectives
Part 1 Dose Escalation and Part 2 Expansion Cohort for LAVA-1207 alone, LAVA-1207 plus LDSC IL-2, and LAVA-1207 plus pembrolizumab
• To explore the preliminary antitumor activity.
• To evaluate the pharmacokinetics of LAVA-1207.
• To evaluate the pharmacodynamics of LAVA-1207.
• To evaluate the immunogenicity of LAVA-1207.

Study design

This trial is an open-label, multi-center, Phase 1 and 2a dose escalation trial with an expansion cohort to investigate the safety, tolerability, pharmacokinetics, pharmacodynamics, immunogenicity and preliminary antitumor activity of LAVA-1207 in patients with therapy refractory mCRPC.

The trial will start with an open-label, dose-escalation part (Part 1) which will include dose optimization to determine the preliminary RP2D with or without LDSC IL-2.
Alternative dose schedules may be implemented, based on preliminary data

review, e.g., weekly administrations for LAVA-1207. An additional dose escalation/expansion will be conducted with LAVA-1207 plus pembrolizumab assuming safety data and preliminary antitumor activity data support expansion. The second part of the trial (Part 2) will be an open-label expansion cohort at the RP2D and schedule, in which the number of patients will be expanded to confirm safety in a patient population with therapy refractory mCRPC with measurable disease.

Intervention

LAVA-1207 is a concentrate for solution for infusion and will be administered as IV infusion with a 14-day dosing interval. The infusion duration will be 2 hours in the first cycle, 1 hour in the 2nd cycle and 30 minutes in subsequent cycles.
LDSC IL-2 will be administered as a single dose or as 3 daily doses starting at 24 hours (-1 hr- and +2 hrs) after the start of LAVA-1207 infusion for a total duration of 4 cycles.
The study group receiving infusions of pembrolizumab will begin infusions every 6 weeks, starting with the second target dose of LAVA-1207.

In Part 2, patients will receive IV infusions of LAVA-1207 at the RP2D (dose and schedule) as established in the dose escalation part of the trial (with- or without LDSC IL-2).

Study burden and risks

Discomfort and Risks:
- Possible side effects of the treatment (possible) side effects are described in the patient information
- Discomfort, pain, bruising: in rare cases infection, light-headedness / fainting due to blood sampling
- Rash or irritation from ECG stickers.
- Following instructions related to study treatment and the visit schedule

Benefit:
It is possible that the study patient will benefit from the treatment but this is not guaranteed.

Contacts

Public
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Scientific
LAVA Therapeutics NV

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NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Patient must be 18 years of age inclusive or above, at the time of signing the informed
consent.
2. Male patient with mCRPC as defined by PCWG3 criteria (histologically confirmed
adenocarcinoma; adenocarcinoma with <=10% small-cell or neuroendocrine features is
allowed). Brain metastases are allowed as long as the patient*s symptoms are well controlled.
Patients is unlikely to tolerate or derive clinically meaningful benefit from other
available therapy.
3. Patient should have failed at least 1 line of taxane-based chemotherapy or is deemed
medically unsuitable to be treated with a taxane regimen.

Exclusion criteria

1. Other malignancies within the last 2 years except adequately treated

carcinoma in situ, basal
or squamous cell skin carcinoma.
2. Uncontrolled or severe intercurrent medical condition.
3. Positive serological testing for human immunodeficiency virus (HIV)
antibody.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-01-2022
Enrollment:	42
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	LAVA-1207
Generic name:	-

Ethics review

Approved WMO

Date:	15-06-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	13-07-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-02-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-10-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-10-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-12-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-02-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-06-2023
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-07-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-08-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-10-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-11-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-03-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-05-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-05-2024
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
EU-CTR	CTIS2024-515821-27-00
EudraCT	EUCTR2021-001789-39-NL
CCMO	NL77530.056.21