Trial in progress: Phase 1/2a trial of LAVA-1207, a novel bispecific gamma-delta T-cell engager alone, or with low dose IL-2 or pembrolizumab, in metastatic castration resistant prostate cancer (mCRPC). Abstract TPS2672.

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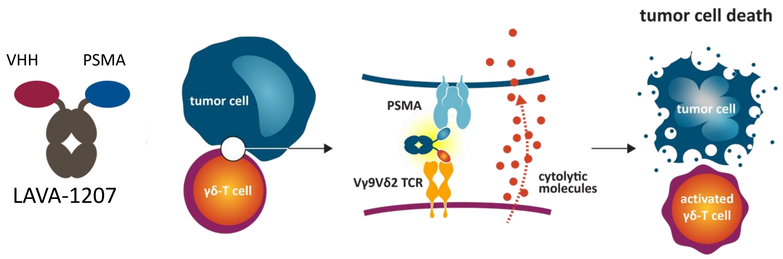
Background:

- LAVA-1207 is a humanized bispecific antibody that binds with high affinity to the Vδ2 chain of Vγ9Vδ2-T cells and to prostate-specific membrane antigen (PSMA).
- It comprises a heterodimer of two fusion proteins, each consisting of a VHH linked to a (silenced) human IgG1 Fc domain. Preclinical evidence demonstrates that, upon binding both targets, LAVA-1207 leads to potent Vγ9Vδ2-T cell degranulation and cytolytic activity against PSMA-expressing prostate cancer cells.
- IL-2 is an immune modulator which has been shown to support expansion of activated Vγ9Vδ2-T cells.
- PD-1 is an inhibitory immune checkpoint receptor that can dampen Vγ9Vδ2-T cell reactivity, suggesting that pembrolizumab, an anti-PD1 antibody, could potentiate the effect of LAVA-1207.

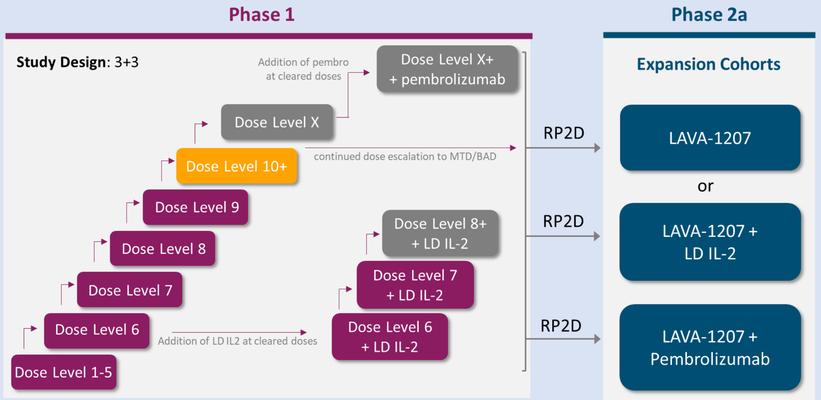


Study objectives:

- Primary objective: to assess the safety of LAVA-1207 alone or with low dose IL-2 or with pembrolizumab, and to determine the recommended Phase 2a dose (RP2D).
- Secondary objectives: To determine the pharmacokinetics, pharmacodynamics, immunogenicity, and preliminary antitumor activity of LAVA-1207.
- Exploratory objectives: To determine the effect of LAVA-1207 on circulating tumor cells (CTCs) and circulating tumor DNA (ctDNA).

Study design:

This trial is a phase 1/2a open label study with a 3+3 design in patients with refractory mCRPC.



- LAVA-1207 is administered Q2W, with two priming doses.
- Two parallel cohorts assessing LAVA-1207 with low dose subcutaneous IL-2 have been implemented: (1) single IL-2 administration and (2) three IL-2 administrations on consecutive days per cycle for up to four cycles.
  - **An additional dose escalation arm evaluates LAVA-1207 in combination with pembrolizumab, 400mg Q6W, IV.**
- This study is in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Further information:
This poster was presented at ASCO 2024 annual meeting
Protocol number: LAVA-1207-001/LAVA-1207-002
Status: recruiting
Clinical trials.gov identifier: NCT05369000
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Key Eligibility Criteria:

- Patients with mCRPC that have failed at least one prior AR therapy and taxane-based chemotherapy (unless deemed medically unsuitable to receive a taxane) will be enrolled.
- Patients should have progressive disease either by a) PSA, b) RECIST 1.1 or, c) appearance of 2 or more bone metastases.
- Patients must have ECOG performance status of 0-1.
- PSMA-PET is performed at baseline. Paired biopsies are requested to further assess LAVA-1207 activity.

Current status (as of 10th April 2024):

- Study began enrolling patients in Feb 2022 and is ongoing in Europe and USA, with 71 enrolled patients to date.
- Dose escalation cohorts 9 and 7A1 have been completed and enrollment to cohort 10 started in April 2024.
- Dose escalation is ongoing. Expansion arm(s) will be included based on available data from Phase 1 of the study and may include one or more of: LAVA-1207, LAVA-1207 with low dose IL-2, or LAVA-1207 in combination with pembrolizumab.