CT122. A Phase 1/2 Open-Label, Multicenter, Dose Escalation and Expansion Study of AVB-001, an Intraperitoneally Administered, Cell-Generated, Human IL-2 Immunotherapy in Patients with Platinum-Resistant, High-Grade, Serous Adenocarcinoma of the Ovary, Primary Peritoneum, or Fallopian Tube

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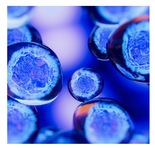
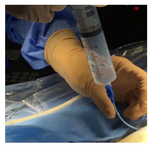
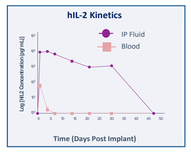
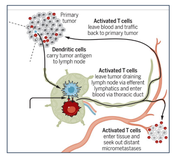
LOCOcyte™ Platform: Localized Delivery with Systemic Efficacy

- Allogeneic human cell line is **engineered** and selected to express **native** human immunomodulators with sustained/high productivity
- Engineered cells are **encapsulated** with biomaterials and administered in proximity to the tumor/tumor draining lymph nodes
- High sustained **localized concentrations** of immunomodulators with **low systemic exposure** and **biologic "off-switch" mechanism**
- Tumor adjacent delivery initiates robust **local and systemic innate and adaptive** immune response
- Immunomodulators targeting tumor draining lymph nodes **precipitate systemic immune activation**





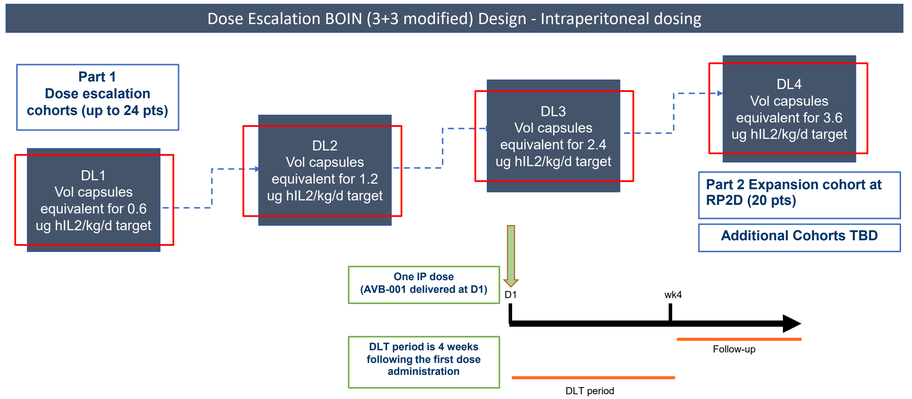




Background

- The potential of cytokines as cancer therapeutics has been limited by short half-life and severe adverse effects associated with high systemic exposure when delivered intravenously. Many strategies are being explored to overcome these limitations. A locoregional delivery to achieve high sustained concentrations in the tumor microenvironment with minimal systemic exposure could widen the therapeutic window.
- Early experience with free recombinant human IL-2 given intraperitoneally showed meaningful clinical activity in relapsed ovarian cancer[1]. Still, the cumbersome delivery procedure requiring indwelling catheters and need for high volume IP infusions leading to frequent complications and poor patient compliance limited the utility of this approach.
- Avenge Bio developed a localized delivery LOCOcyteTM platform comprised of polymer encapsulated allogeneic epithelial cells engineered to produce immune effector molecules for local delivery with temporal regulation. The first product, AVB-001, produces native human IL-2, for the treatment of ovarian cancer and other peritoneal malignancies.
- Murine data show strong dose-dependent antitumor effect with complete tumor eradication by day 21 post IP treatment and improved survival in an ID8 ovarian cancer murine model[2] and other tumor types.
- Sustained IL-2 production with well tolerated high IP concentrations were achieved, with >100x differential concentration vs. systemic blood levels in both mice and non-human primates.
- Strong local and systemic immune activating effects, optimized T cell profile and immune memory were observed without concomitant increase of T regs.
- High-grade serous adenocarcinoma accounts for 70% of all ovarian cancers. After recurrence, most patients will die of their disease despite additional lines of therapy. Progression is mainly confined to the peritoneal cavity within an immunosuppressive TME. Immune checkpoint inhibitors do not provide meaningful benefit.
- The first in human study of AVB-001 in patients with advanced ovarian cancer (NCT05538624) is described. This multicenter study is currently open at three sites. The first patient was dosed in December 2022.

Study Design



THE UNIVERSITY OF TEXAS MD Anderson Cancer Center Making Cancer History® · MASSACHUSETTS GENERAL HOSPITAL CANCER CENTER HARVARD MEDICAL SCHOOL · WOMEN & INFANTS

The first patient was dosed in December 2022. Recruitment is ongoing

Key Eligibility Criteria

- Histologically confirmed, metastatic or unresectable, high-grade serous adenocarcinoma of the ovary, primary peritoneum, or fallopian tube
- Have intraperitoneal disease and measurable disease (RECIST v1.1). Disease in the pleural cavity or distant metastases eligible if measurable or evaluable disease in the IP cavity
- Should have either progressed during initial platinum-based chemotherapy or have resistant disease (relapsed ≤ 6 mos of prior platinum containing chemotherapy). If platinum sensitive disease, have received ≥2 lines of platinum-containing chemotherapy and progressed. No more than 5 lines of prior therapy overall
- May have received PARP inhibitors (patients with germline or somatic *BRCA* mutations must have progressed or been intolerant to PARP inhibitors), bevacizumab (or any other antiangiogenic agent), immunotherapy, or cell therapies
- ECOG Performance Status 0-1
- Not eligible if symptomatic or uncontrolled brain metastases (including leptomeningeal involvement); patients with an abnormal clinical examination or history will require imaging to rule out brain metastases
- Should have recovered from prior clinically significant AEs to G≤1 per CTCAE v5.0 due to prior therapy
- Not eligible if persistent irAEs from prior immune therapies. Prior history of severe side effects such as carditis, pneumonitis, encephalitis, hepatitis, or colitis with prior immune therapies will be excluded
- Other novel forms of IL-2 or IL-2-like molecules at any time point not allowed

Study Endpoints (Parts 1 & 2)

Primary endpoints in Part 1

- Safety (incidence and severity of adverse events per NCI CTCAE v5.0), tolerability, and feasibility of intraperitoneal delivery of AVB-001
- Determine the MTD and the RP2D of AVB-001

Primary endpoint in Part 2

- Efficacy based on Objective Response Rate per RECIST v1.1

Secondary endpoints (Parts 1 and 2)

- Efficacy based on Objective Response Rate per RECIST v1.1 (Part 2),
- Efficacy per iRECIST (Parts 1 & 2)
- TTR, DOR, mPFS, mOS
- Incidence of AEs and SAEs according to the NCI CTCAE v5.0 (Part 2)
- IL-2 pharmacokinetics in serum and peritoneal fluid and anti-drug antibodies
- CA125
- Pharmacodynamic immune correlates (FACS immune phenotype, serum cytokines & chemokines)

Definition of Dose-Limiting Toxicities

For hematologic events:

- Grade 4 neutropenia (if lasting more than 7 days)
- Febrile neutropenia, defined per NCI CTCAE v5.0
- Grade 4 anemia that does not resolve in 7 days; or
- Grade 4 thrombocytopenia or Grade 3 thrombocytopenia lasting >7 days or associated with clinically significant bleeding

For non-hematologic events:

- Grade ≥3 toxicities possibly or probably related to the study procedures
- Grade ≥3 toxicities involving major organ systems (e.g., cardiac, dermatologic, gastrointestinal, hepatic, pulmonary, renal), not pre-existing, and not related to the underlying malignancy
- Grade ≥3 cytokine release syndrome, capillary leak syndrome, hypotension event, or allergic reaction at least possibly related to study drug that does not resolve to ≤Grade 1 within 72 hours
- Grade ≥2 neurotoxicity that does not resolve to ≤Grade 1 within 72 hours
- AST or ALT ≥3 × ULN with concurrent increase in total bilirubin ≥2 × ULN without evidence of cholestasis or alternative explanations (e.g., viral hepatitis, disease progression in the liver); or ALT or AST >8 × ULN or total bilirubin >5 × ULN

References

1. Vlad *et al.*, Cancer Immunol Immunother (2010) 59:293–301
2. Nash *et al.*, *Sci. Adv.* **8**, eabm1032 (2022) 2 March 2022

Abbreviations

IL-2: Interleukin-2
IP: Intraperitoneal
TME: Tumor microenvironment
DLT: Dose Limiting Toxicity
DL: Dose Level
BOIN: Bayesian Optimal Interval design
RPD: Recommended Phase 2 Dose
CTCAE: Common Terminology Criteria for Adverse Events
RECIST: Response Evaluation Criteria in Solid Tumors
iRECIST: modified RECIST for immune-based therapeutics
FACS: Fluorescence-activated cell sorting

NOW ENROLLING – FOR MORE INFORMATION

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ClinicalTrials.gov: NCT05538624

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