Background

Unmet Medical Need in Gynecologic and Breast Cancers

- Patients with advanced/recurrent endometrial cancer (EC) have a poor prognosis and limited therapeutic options.
- Subset of patients may be eligible for treatment with PD-1 inhibitors and/or targeted therapies, but reported OS remains low (17–18 months) and positive treatment duration (33%) are high.
- Ovarian cancer (OC) is the second most common gynecologic malignancy, and the majority of patients are diagnosed at an advanced stage. I1 The standard of care (SOC) is platinum-based therapy, and nearly all patients will progress; less than 15% will survive for 5 years from diagnosis.
- Breast cancer (BC) is the most common cancer diagnosed in women. I1–7 Of patients are diagnosed with HR+/HER2- disease, and 10–15% of patients are diagnosed with triple-negative disease (TNBC). I1–7
- Among BC subtypes, patients with TNBC have the poorest prognosis and survival.
- Despite some recent therapeutic advances, there is still a large unmet medical need for patients with advanced endometrial, ovarian, and breast cancers, as there is no clear treatment algorithm for the majority of patients who progress on the current SOC.

XMT-1660: An Investigational B7-H4-targeting Dolastatin ADC

- B7-H4 is part of the CD28/B7 family of immune co-stimulatory and co-inhibitory molecules, and it promotes tumorigenesis by suppressing anti-tumor immunity. I1
- B7-H4 is broadly expressed in endometrial, ovarian, and breast cancers (Fig 1);B protein expression is limited in normal endometrium.
- XMT-1660 is a B7-H4-directed Dolastatin ADC with a precise, target-optimized drug-to-antibody-ratio (DAR) and clinically validated Dolastatin microbicide inhibitor payload with controlled bystander effect.

Antibody: Monoclonal anti-B7-H4 (linker: Polymer scaffold, degradable ester linker)

Payload: AF-HPA (Dolastatin controlled bystander with DAR = 6 (Dolastatin platform))

Methods

Study Design and Eligibility

- This Phase 1, first-in-human trial will examine XMT-1660 safety and efficacy in both dose escalation (DES) and expansion (EXP) phases in patients with endometrial, ovarian, and breast cancers following progression on SOC therapies.
- Patients are not selected by B7-H4 status, but baseline tumor samples are collected for retrospective analysis.

Key Enrollment Criteria for Both DES and EXP Phases Include:

- Recurrent or advanced/metastatic disease
- Measurable disease as defined by RECIST v1.1
- Received to Grade ≤1 toxicity from previous therapies, with exception of Grade 2 peripheral neuropathy, alopecia

Key Escalation Criteria

- PD: advanced/metastatic setting
- OC: ≥2 LoT in endometrial/stromal setting
- TNBC: ≥2 LoT in endometrial/stromal setting
- HR+ BC: ≥2 LoT in advanced/metastatic setting, after at least 2 lines of treatment that included CDK4/6 plus ET

Primary Endpoints

- RP2D
- Safety and tolerability
- Secondary Endpoints

- ORR
- DOR

Dose Expansion – Patients will be divided into 3 cohorts

- EC/OC (N=38): DC-007
- BC (N=35): DC-008

Primary Endpoints

- Safety and tolerability
- ORR
- DOR

Secondary Endpoints

- PK
- AD
- B7-H4 expression
- PD-L1 expression
- Additional biomarkers

Statistical Considerations

- BON design will be used in the design to determine the RP2D
- Additional patients may be enrolled in both the DES and EXP based on emerging data

Conclusions

- XMT-1660 is a novel, investigational ADC targeting B7-H4, an immune co-inhibitory molecule
- DES and EXP phases of this first-in-human, Phase 1 study will evaluate the preliminary safety and efficacy of XMT-1660 monotherapy in EC, OC, TNBC, and HR+/HER2- BC
- Primary endpoint of DES is to establish the RP2D and safety
- Primary endpoint of EXP is to assess preliminary efficacy and safety at the RP2D
- Additional therapeutic options for patients with endometrial, ovarian, and breast cancers that progress on the SOC therapies are needed, as current options are limited for this patient population

ClinicalTrials.gov registries: NCT03577996

Acknowledgments

We would like to thank the patients, their families, and the site staff for making this study possible.

This study is sponsored by Mersana Therapeutics, Inc.

Support for this poster was provided by Blueprint Oncology.

References


Additional Information

For more information on this study, visit ClinicalTrials.gov page NCT03577996

viq code provided or contact

For more information on this study, visit ClinicalTrials.gov page NCT03577996

viq code provided or contact

clinicalinformation@mersana.com