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THE POWER OF SHARED PURPOSE: Transforming Gynecologic Cancer Care

Phase 2 Basket Study of Disitamab Vedotin in Patients With Previously Treated, Locally Advanced Unresectable or Metastatic Solid Tumors That Express HER2: Ovarian and Endometrial Cancer Cohorts (DV-005; Trial in Progress)

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Summary

DV monotherapy has shown promising clinical activity across several HER2-expressing advanced solid tumors. Available data suggest that DV may be a potential treatment option in previously treated advanced ovarian and endometrial cancer with HER2 expression

DV-005 is a phase 2, multicohort, multicenter, open-label, basket trial evaluating DV monotherapy in patients with previously treated advanced solid tumors that express HER2 defned by IHC level 1+-3+

Enrollment is ongoing in the US and Canada

Abbreviations

ADC, antibody–drug conjugate; AE, adverse event; AESI, adverse event of special interest; *BRCA*, Breast Cancer gene; CNS, central nervous system; DCR, disease control rate; DOR, duration of response; DV, disitamab vedotin; ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; mc-vc, maleimidocaproyl-valine-citrulline; MMAE, monomethyl auristatin E; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PARP, poly (ADP-ribose) polymerase; PD(L)1, programmed cell death (ligand) 1; PFS, progression-free survival; PK, pharmacokinetics; Q2W, every 2 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

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XL: Employment: Pfizer Inc. MY: Employment: Pfizer Inc.

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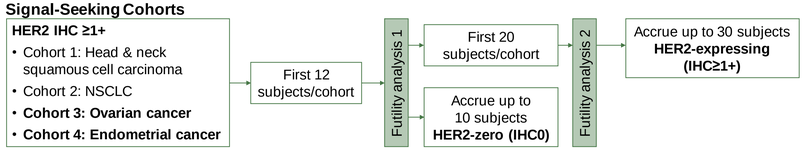
Background

- Chemotherapy-based treatment is the standard of care first-line systemic treatment for advanced endometrial and ovarian cancers, with platinum-based regimens and taxanes being used the most commonly, alone or in combination.[1-3]
- The majority of patients will eventually relapse with platinum-based chemotherapy and have poor responses to limited subsequent treatment options.[4]
- Given the unmet clinical need in patients who have relapsed following prior treatments, effective novel therapies in the late-line setting are needed.
- HER2 expression detected by IHC (defined as IHC 1+-3+) has been reported in approximately 50% of ovarian and endometrial cancers.[5]
- Patients with tumors that express HER2, including HER2-low (IHC 1+ or IHC 2+/ISH–) tumors, may be targeted with HER2-directed ADCs.
- DV (RC48-ADC) is an investigational ADC comprising a fully humanized HER2-directed monoclonal antibody, disitamab, conjugated to MMAE via a protease-cleavable mc-vc linker.[6-8]
- DV is proposed to elicit antitumor activity through multimodal mechanisms of action, including MMAE-mediated direct cytotoxicity, bystander effect, and immunogenic cell death.[6-8]
- DV has shown clinical activity with a manageable safety profile across several solid tumors, including gastric, urothelial, and breast cancers.[9-12]
- Available data suggest that DV may be a potential treatment option in previously treated advanced ovarian and endometrial cancer with HER2 expression.

Study Schema

- DV-005 (NCT06003231) is a phase 2, multicohort, multicenter, open-label, basket trial assessing the clinical activity, safety, and tolerability of DV monotherapy for the treatment of patients with previously treated advanced solid tumors with HER2 expression defined by IHC level 1+-3+.
- Cohorts 3 and 4 will enroll patients with ovarian and endometrial cancer, respectively.

Signal-Seeking Cohorts

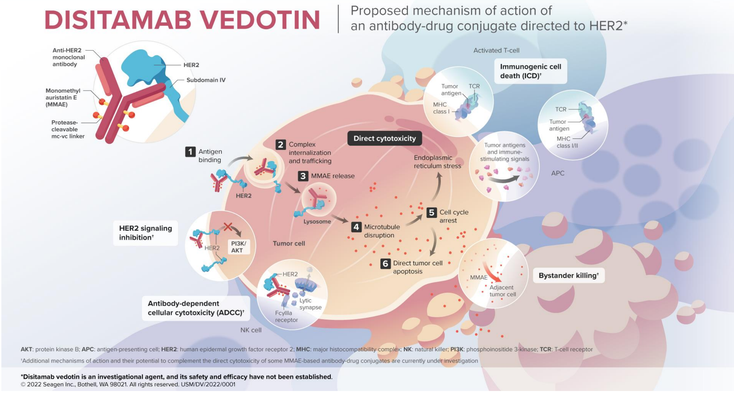


- Study treatment involves intravenous DV Q2W until disease progression, unacceptable toxicity, death, or withdrawal of consent.
- Two interim analyses for futility will be performed separately for each cohort. The first and second assessments will be performed when 12 and 20 evaluable patients have had at least 2 post-baseline tumor assessments or terminated from the study treatment, respectively.

Objectives and Endpoints

Primary Objective	Corresponding Endpoints
Evaluate the antitumor activity of DV in patients with previously treated advanced HER2-expressing solid tumors	• ORR per RECIST v.1.1 by investigator assessment
Secondary Objectives	**Corresponding Endpoints**
Evaluate the safety and tolerability of DV	• Type, incidence, severity, seriousness, and relatedness of AEs including AESIs • Type, incidence, and severity of laboratory abnormalities as well as significant changes from baseline • Frequency of treatment interruptions, dose reductions, and treatment discontinuations due to AEs
Assess other measures of antitumor activity of DV per investigator assessment by other clinically relevant measures	• DCR, DOR, PFS per RECIST v.1.1 by investigator assessment • OS
Evaluate the PK of DV	• Select PK parameters, total antibody, and unconjugated MMAE
Evaluate the immunogenicity of DV	• Incidence of antidrug antibodies against DV

DV Proposed Mechanism of Action



Eligibility Criteria

Key Inclusion Criteria

All patients:
- Must have unresectable locally advanced or metastatic disease
- Must have measurable disease per RECIST v.1.1
- Must have an ECOG performance status score of 0 or 1
- May have received prior anti-PD(L)1 therapy
- Must have HER2 expression 1+, 2+, or 3+ as determined by local IHC testing on a fresh or archival tumor tissue

Cohort 3 – ovarian cancer:
- Must have pathologically documented epithelial cancers of ovarian, fallopian tube, or peritoneal origin
- Must have platinum-resistant disease (≤6 months between the completion of platinum-based treatment and identification of recurrence)
- Must not have received >4 lines of prior chemotherapy for advanced disease
- Patients with *BRCA* mutations must have had prior treatment with a PARP inhibitor

Cohort 4 – endometrial cancer:
- Must have pathologically documented adenocarcinoma of the endometrium
- Must have relapsed/progressed after ≥1 prior platinum-based chemotherapy for recurrent, metastatic, or primary unresectable disease
- Must not have received >3 lines of chemotherapy for advanced disease

Key Exclusion Criteria

All patients:
- Prior MMAE-based treatment
- Have known hypersensitivity to any excipient contained in DV formulation
- Have history of another invasive malignancy within 2 years before the first dose of study intervention, or any evidence of residual disease from a previously diagnosed malignancy
- Have peripheral neuropathy grade ≥2
- Have active CNS or leptomeningeal metastasis. Subjects with treated brain metastasis (surgery and/or radiotherapy) are eligible if:
  - All known CNS lesions have been treated
  - No evidence of clinical or radiographic disease progression in the CNS for ≥4 weeks after definitive treatment
  - Neurological symptoms attributed to brain metastases have returned to baseline
  - No steroids to manage symptoms related to CNS disease or its treatment within 28 days. Anti-convulsant treatment is allowed if the dose has been stable for 2 weeks

Enrollment Sites

United States
- Ironwood Cancer & Research Centers - Chandler, AZ
- Valkyrie Clinical Trials, CA
- Providence Medical Foundation, CA
- Eastern CT Hematology and Oncology Associates, CT
- Karmanos Cancer Institute / Wayne State University, MI
- HealthPartners Institute, MN
- St. Vincent Frontier Cancer Center, MT
- Optimum Clinical Research Group, LLC (Southwest Women's Oncology), NM
- NYU Langone Hospital, NY
- Gabrail Cancer Center Research, LLC, OH
- Providence Portland Medical Center, OR
- Renovatio Clinical, TX
- MD Anderson Cancer Center, University of Texas, TX
- Renovatio Clinical, TX

Canada
- CHU de Quebec-Universite Laval, QC