University of Washington
Cancer Vaccine Institute

IRB Approved at the
Study Level
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DESTINY PAN-TUMOR	
Study Title	A Phase II, Multicenter, Open-label Study to Evaluate the Efficacy and Safety of Trastuzumab Deruxtecan (T-DXd, DS-8201a) for the Treatment of Selected HER2 Expressing Tumors (DESTINY-PanTumor02) – Part 2
Study Population	Patients with locally advanced, unresectable, or metastatic patients with HER2-overexpressed (IHC 3+ or IHC 2+) and HER2 low (IHC 1+) selected solid tumors detailed below: **Cohort A:** any tumor type that is HER2 IHC 3+ (excluding breast, gastric cancer, and colorectal cancer) **Cohort B:** any tumor type that is HER2 IHC 2+/ISH+ (excluding breast, gastric cancer, and colorectal cancer) **Cohort C:** HER2 IHC 2+ or 1+ endometrial Cancer **Cohort D:** HER2 IHC 2+ or 1+ ovarian cancer **Cohort E:** HER2 IHC 2+ or 1+ cervical cancer. 40 patients will be enrolled per cohort.
Study Design	This is an open-label, multi-center, multi-cohort, Phase II study to evaluate the efficacy and safety of T-DXd for the treatment in locally advanced, unresectable, or metastatic patients with HER2-overexpressed and HER2 low selected solid tumors not eligible for curative therapy. The initial study (Part I) has been completed. Data analysis of Part 1 found that specific tumor types, with HER2 expression, demonstrated efficacy. For this reason the study has been opened (Part 2) to treat more patients in the above specific tumor types.
Study Objective	**Primary:** To assess the efficacy of T-DXd in patients with metastatic or unresectable tumors in selected HER2-expressing tumor types **Secondary:** To further assess the efficacy, safety, tolerability, and immunogenicity of T-DXd **Exploratory:** Where applicable, to evaluate the efficacy of T-Dxd in patients with low HER2-expression (IHC 1+)
Key Eligibility Criteria	**Inclusion Criteria** • Locally advanced, unresectable, or metastatic select solid tumors who have progressed following at least one prior systemic treatment for metastatic or advanced disease • Diagnosis of metastatic or advanced solid tumors that are HER2 positive (IHC 3+) (excluding breast, gastric and colorectal cancer), patients with non-small cell lung cancer can be included, metastatic or advanced solid tumors that are HER2 IHC 2+/ISH+ (excluding breast, gastric and colorectal cancer), metastatic or advanced solid cervical cancer that is HER2 IHC 2+ or 1+, metastatic and advanced solid endometrial cancer that is HER2 IHC 2+ or 1+, metastatic or advanced ovarian cancer that is HER2 ICH 2+ or 1+ • Tissue sample available for HER2 testing that will be performed by AstraZeneca • Have measurable disease based on RECIST v1.1. • Have a MUGA or ECHO to evaluate LVEF is ≥ 50% • Adequate organ function as evidence by recent laboratory values

	Exclusion Criteria • Uncontrolled intercurrent illness • Lung-specific clinically significant severe illness • History of pneumonitis/ILD, or current ILD • Autoimmune, connective tissue or inflammatory disorders • Pleural effusion, ascites, or pericardial effusion that requires drainage. • Primary diagnosis of adenocarcinoma of the breast, adenocarcinoma of the colon or rectum, adenocarcinoma of the gastric body, or gastro-esophageal junction • History of myocardial infarction within 6 months before treatment assessment • Pregnant or breastfeeding female patients, or planning to become pregnant
Study Treatment	The enrolled patients will receive T-DXd intravenously every three weeks on Day 1 of each cycle. Patients will have weekly visits during the first cycle, then only on Day 1 during subsequent cycles. Patients may continue on study until PD or withdrawal of consent. - ECHO or MUGA will be done at baseline, prior to cycle 5, then every 4 cycles - Ophthalmologic exam may be performed at baseline and then as indicated - Tumor imaging done at baseline, then every 6 weeks for the first 48 weeks then every 12 weeks during the study - Clinical labs and research blood for immune analysis will be collected at baseline and prior to each T-DXd infusion. - We will collect archived tumor tissue. Optional fresh tumor tissue sample collection may be obtained pre-treatment or at disease progression
Contact	**Toll Free Number:** 1-866-932-8588 CVICoordinators@medicine.washington.edu