

Testing the Use of Ado-Trastuzumab Emtansine Compared to the Usual Treatment (Chemotherapy With Docetaxel Plus Trastuzumab) or Trastuzumab Deruxtecan for Recurrent, Metastatic, or Unresectable HER2-Expressing Salivary Gland Cancers

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* Pathologically (histologically or cytologically) proven diagnosis of HER2-positive OR HER2-low expressing recurrent/metastatic salivary gland cancer (SGC) * HER2-positive cohort: * Note: The majority of HER2-positive SGCs are salivary duct carcinoma (SDCs), but to a lesser extent, other SGC subtypes can be HER2-positive (e.g., adenocarcinomas, mucoepidermoid carcinomas, etc.) and are eligible to be included on the study. Additionally, pathologists may sign out SDCs under other descriptors (e.g., ex-pleomorphic adenoma, adenocarcinoma), and these would be eligible if they are HER2-positive. * Note: HER2 evaluation based on local site immunohistochemistry (IHC), fluorescent in-situ hybridization (FISH), or local/commercial next-generation sequencing (NGS) is required. Any one of the following criteria observed in a primary tumor or metastasis would meet the study definition for "HER2-positive": * Immunohistochemistry (IHC) (3+) per the College of American Pathologists (CAP) breast cancer guidelines * Gene amplification by FISH (HER2/CEP17 ratio ≥ 2.0) * Gene amplification by NGS (fold change ≥ 2) * HER2-low expressing cohort: * Note: Local HER2 evaluation by immunohistochemistry (IHC) or fluorescent in-situ hybridization (FISH) is required. Any one of the following criteria observed in a primary tumor or metastasis would meet the study definition for "HER2-low": * IHC 1+ per the College of American Pathologists (CAP) breast cancer guidelines * IHC 2+ without evidence of amplification by FISH * Patients with unresectable disease who are not candidates for curative surgery or radiation OR recurrent OR metastatic disease that is evident on radiologic imaging * Patients with treated brain metastases are eligible if follow-up brain imaging after central nervous system (CNS)-directed therapy shows no evidence of progression * Patients with new or progressive brain metastases (active brain metastases) or leptomeningeal disease are eligible if the treating physician determines that immediate CNS specific treatment is not required and is unlikely to be required during the first cycle of therapy * HER2-positive cohort: Measurable or non-measurable disease by the RECIST v1.1 criteria. HER2-low expressing cohort: Measurable disease by the RECIST v1.1 criteria * History/physical examination within 30 days prior to registration * The following imaging within 60 days prior to registration: * CT or MRI of the neck (diagnostic quality with contrast, unless contraindicated) AND * CT scan of the chest (diagnostic quality with contrast, unless contraindicated) AND * If clinically indicated, CT or MRI of the abdomen and pelvis (diagnostic quality with contrast, unless contraindicated) * Age ≥ 18 * Left ventricular ejection fraction (LVEF) $\geq 50\%$ assessed by echocardiogram or multigated acquisition (MUGA) scan within 30 days prior to registration * Zubrod (Eastern Cooperative Oncology Group [ECOG]) Performance Status of 0-2 within 14 days prior to registration * Absolute neutrophil count (ANC) $\geq 1,500$ cells/mm³ (within 14 days prior to registration) * Platelets $\geq 100,000$ cells/mm³ (within 14 days prior to registration) * Hemoglobin ≥ 9.0 g/dL (within 14 days prior to registration) * HER2-positive cohort: Note: The use of transfusion or other intervention to achieve hemoglobin [Hgb] ≥ 9.0 g/dL is acceptable * HER2-low expressing cohort: Note: Transfusion (red blood cell or platelet) or granulocyte-colony stimulating factor (granulocyte colony-stimulating factor [G-CSF]) is not allowed * Serum creatinine ≤ 1.5 x upper limit of normal (ULN) OR calculated creatinine clearance (CrCl) ≥ 30 mL/min by the Cockcroft-Gault formula (within 14 days prior to registration) * HER2-positive cohort: Total bilirubin ≤ 1.5 x ULN (within 14 days prior to registration) (Not applicable to patients with known Gilbert's syndrome) (within 14 days prior to registration) * HER2-positive cohort: Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤ 1.5 x ULN (within 14 days prior to registration) * HER2-low expressing cohort: Total bilirubin ≤ 1.5 x ULN if no liver metastases; or ≤ 3 x ULN in the presence of documented Gilbert's Syndrome or liver metastases (within 14 days prior to registration) (within 14 days prior to registration) * HER2-low expressing cohort: AST and ALT ≤ 3 x ULN if no liver metastases; or ≤ 5 x ULN with liver metastases (within 14 days prior to registration) * HER2-low expressing cohort: Serum albumin ≥ 2.5 g/dL (within 14 days prior to registration) * Known human immunodeficiency virus (HIV) infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months prior to registration are eligible for this trial. Testing is not required for entry into protocol * For patients with known evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated * Note: Known positive test for hepatitis B virus surface antigen (HBV sAg) indicating acute or chronic infection would make the patient ineligible unless the viral load becomes undetectable on suppressive therapy. Patients who are immune to hepatitis B (anti-hepatitis B surface antibody positive) are eligible (e.g., patients immunized against hepatitis B) * For patients with a known history of hepatitis C virus (HCV) infection, they must have been treated and cured. For patients with HCV infection who are currently on treatment, they are eligible if they have an undetectable HCV viral load * Note: Known positive test for hepatitis C virus ribonucleic acid (HCV RNA) indicating acute or chronic infection would make the patient ineligible unless the viral load becomes undetectable on suppressive therapy * Negative urine or serum pregnancy test (in persons of childbearing potential) within 14 days prior to registration. Childbearing potential is defined as any person who has experienced menarche and who has not undergone surgical sterilization (hysterectomy or bilateral oophorectomy) or who is not postmenopausal * Willing to use highly effective contraceptives for participants of childbearing potential (participants who may become pregnant or who may impregnate a partner) during therapy and for 7 months following last dose of study drug; this inclusion is necessary because the treatment in this study may be significantly teratogenic. Women must refrain from donating eggs during this same period * Men with partners of childbearing potential must be willing to use a highly effective form of non-hormonal contraception or two effective forms of non-hormonal contraception by the patient and/or partner, and to continue the use of contraception for the duration of study treatment and for at least 7 months after the last dose of study treatment. Male patients whose partners are pregnant should use condoms for the duration of the pregnancy. Men must refrain from donating sperm during this same period * Prior to registration, patients who have had chemotherapy or palliative-intent radiotherapy must have all toxicities related to prior treatment recovered to \leq grade 1 * Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial * The patient or a legally authorized representative must provide study-specific informed consent prior to study entry and, for patients treated in the United States (U.S.), authorization permitting release of personal health information

Exclusion Criteria:

* HER2-positive cohort: Prior systemic therapy for the study cancer in the unresectable or recurrent and/or metastatic disease setting * Note: Prior chemotherapy for a different cancer is allowed; prior androgen receptor targeted therapy in any setting is allowed; prior systemic therapy, including HER2-directed therapies given as neoadjuvant therapy, adjuvant therapy, and/or concurrently with radiation is allowed * HER2-low expressing cohort: HER2 directed therapy for unresectable or recurrent or metastatic disease is not allowed * Severe, active co-morbidity defined as follows: * Unstable angina requiring hospitalization in the last 6 months * Myocardial infarction within the last 6 months * New York Heart Association Functional Classification III/IV (Note: Patients with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, should have a clinical risk assessment of cardiac function using the New York Heart Association Functional Classification.) * Persistent grade 3-4 (CTCAE version 5.0) electrolyte abnormalities that cannot be reversed despite replacement as indicated by repeat testing * Patient must not have an active infection requiring IV antibiotics, antivirals, or antifungals * HER2-positive cohort only: \geq grade 3 peripheral neuropathy * Interstitial lung disease or pulmonary fibrosis, organizing pneumonia (e.g., bronchiolitis obliterans), drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on chest CT scan * Any hemorrhage or bleeding event grade ≥ 3 within 28 days prior to registration * History of allergic reactions to compounds of similar chemical or biologic composition to: HER2-positive cohort: ado-trastuzumab emtansine, trastuzumab, and/or docetaxel (or any of their excipients). HER2-low expressing

cohort: DS-8201a (trastuzumab deruxtecan), trastuzumab * History of exposure to the following cumulative doses of anthracyclines: * Doxorubicin or liposomal doxorubicin ≤ 500 mg/m² * Epirubicin ≤ 900 mg/m² * Mitoxantrone ≤ 120 mg/m² * Note: If another anthracycline, or more than one anthracycline has been used, the cumulative dose must not exceed the equivalent of doxorubicin 500 mg/m² * HER2-low expressing cohort only: Receipt of live, attenuated vaccine (messenger ribonucleic acid [mRNA and replication deficient adenoviral vaccines are not considered attenuated live vaccines) within 30 days prior to the first dose of DS-8201a (trastuzumab deruxtecan) * Pregnancy and individuals unwilling to discontinue nursing

Conditions & Interventions

Interventions:

PROCEDURE: Biopsy Procedure, PROCEDURE: Biospecimen Collection, PROCEDURE: Computed Tomography, DRUG: Docetaxel, PROCEDURE: Echocardiography Test, PROCEDURE: Magnetic Resonance Imaging, PROCEDURE: Multigated Acquisition Scan, OTHER: Questionnaire Administration, BIOLOGICAL: Trastuzumab, BIOLOGICAL: Trastuzumab Deruxtecan, BIOLOGICAL: Trastuzumab Emtansine

Conditions:

Metastatic Salivary Gland Carcinoma, Recurrent Salivary Gland Carcinoma, Stage III Major Salivary Gland Cancer AJCC v8, Stage IV Major Salivary Gland Cancer AJCC v8, Unresectable Salivary Gland Carcinoma

More Information

Contact(s): ctrrecruit@vcu.edu

Principal Investigator:

Phase: PHASE2

IRB

Number:

System ID: NCT05408845

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