Essai Clinique

Généré le 01 mai 2024 à partir de

Titre	A Phase-3, Open-Label, Randomized Study of Dato-DXd Versus Investigator's Choice of Chemotherapy (ICC) in Participants With Inoperable or Metastatic HR-Positive, HER2-Negative Breast Cancer Who Have Been Treated With One or Two Prior Lines of Systemic Chemotherapy
Protocole ID	TROPION-Breast01
ClinicalTrials.gov ID	NCT05104866
Type(s) de cancer	Sein
Phase	Phase III
Type étude	Clinique
Médicament	Dato-DXd versus une chimiothérapie au choix de l'investigateur
Institution	CHU DE QUEBEC – UNIVERSITE LAVAL HOPITAL DU SAINT-SACREMENT 1050 Ch Ste-Foy, Québec, QC, G1S 4L8
Ville	
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But étude	The study will evaluate the safety and efficacy of datopotamab deruxtecan (also known as Dato-DXd, DS-1062a), when compared with Investigator's choice of standard of care single-agent chemotherapy (eribulin, capecitabine, vinorelbine, or gemcitabine) in participants with inoperable or metastatic HR-positive, HER2- negative breast cancer who have been treated with one or two prior lines of systemic chemotherapyThe primary objective of this study will assess the safety and efficacy of datopotamab deruxtecan (Dato-DXd) in participants with inoperable or metastatic HR-positive, HER2-negative breast cancer who have been treated with one or two prior lines of systemic chemotherapyThe study will be stratified based on number of previous lines of chemotherapy (1 vs. 2), prior use of CDK4/6 inhibitors (Yes vs. no) and geographic region of participant (US/Canada/Europe vs. rest of world).This study aims to see if datopotamab deruxtecan allows patients to live longer without their breast cancer getting worse, or simply to live longer, compared to patients receiving standard of care chemotherapy. This study is also looking to see how the treatment and the breast cancer affects patients' quality of life.
Critères d'éligibilité	**Age** • Participant must be ≥ 18 years at the time of screening. **Type of Participant and Disease Characteristics** • Inoperable or metastatic HR+, HER2-negative breast cancer • Progressed on and not suitable for endocrine therapy per investigator assessment and treated with 1 to 2 lines of prior chemotherapy in the inoperable/metastatic setting. Participant must have documented progression on their most recent line of chemotherapy. • Eligible for one of the chemotherapy options listed as ICC (eribulin, capecitabine, vinorelbine, gemcitabine), per investigator assessment. • ECOG PS of 0 or 1, with no deterioration over the previous 2 weeks prior to day of first dosing. • At least 1 measurable lesion not previously irradiated that qualifies as a RECIST 1.1. Note: Participants with bone-only metastases are not permitted. • Participants with a history of previously treated neoplastic spinal cord compression, or clinically inactive brain metastases, who require no treatment with corticosteroids or anticonvulsants, may be included in the study, if they have recovered from the acute toxic effect of radiotherapy.

A minimum of 2 weeks must have elapsed between the end of radiotherapy and study enrolment.

- Adequate organ and bone marrow function within 7 days before day of first dosing as follows:
  - Hemoglobin: ≥ 9.0 g/L.
  - Absolute neutrophil count: 1500/mm3.
  - Platelet count: 100000/mm3. • Total bilirubin: ≤ 1.5 × ULN if no liver metastases; or ≤ 3 × ULN in the presence of documented Gilbert's syndrome (unconjugated hyperbilirubinemia) or liver metastases at baseline.
  - ALT and AST: ≤ 3 × ULN for AST/ALT; however, if elevation is due to liver metastases, ≤ 5.0 × ULN is allowed.
  - Calculated creatinine clearance: ≥ 30 mL/min as calculated using the Cockcroft-Gault equation (using actual body weight).
- LVEF ≥ 50% by either an echocardiogram or MUGA within 28 days of first dosing.
- Has had an adequate treatment washout period before Cycle 1 Day 1, defined as:
  - Major surgery: ≥ 3 weeks.
  - Radiation therapy including palliative radiation to chest: ≥ 4 weeks (palliative radiation therapy to other areas ≥ 2 weeks).
  - Anticancer therapy including hormonal therapy: ≥ 3 weeks (for small molecule targeted agents: ≥ 2 weeks or 5 half-lives, whichever is longer).
  - Antibody-based anticancer therapy: ≥ 4 weeks with the exception of receptor activator of nuclear factor kappa-B ligand (RANKL) inhibitors (eg, denosumab for the treatment of bone metastases).
  - Immunotherapy (non-antibody-based therapy): ≥ 2 weeks or 5 times the terminal elimination T½ of the agent, whichever is longer.
  - Chloroquine/hydroxychloroquine: > 14 days.
- Have available a FFPE tumor sample (block preferred, or a minimum of 20 freshly cut slides), at the time of screening. Note: Sample collection in China will comply with local regulatory approval.
- Minimum life expectancy of 12 weeks at screening.

Sex • Contraceptive use by men or women should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies; (oral estrogens are not permitted).
Reproduction

- Negative pregnancy test (serum) for women of childbearing potential
- Female participants must be post-menopausal for at least 1 year, surgically sterile, or using one highly effective form of birth control. Female participants must refrain from egg cell donation and breastfeeding while on study and for at least 7 months after the last dose of study intervention. Non-sterilized male partners of a woman of childbearing potential must use a male condom plus spermicide throughout this period.
- Male participants who intend to be sexually active with a female partner of childbearing potential must be surgically sterile or using a highly effective method of contraception from the time of screening throughout the total duration of the study and the drug washout period (at least 4 months after the last dose of study intervention) to prevent pregnancy in a partner. Male participants must not donate or bank sperm during this same time period. Not engaging in heterosexual activity (sexual abstinence) for the duration of the study and drug washout period is an acceptable practice if this is the preferred usual lifestyle of the participant; however, periodic or occasional abstinence, the rhythm method, and the withdrawal method are not acceptable methods of contraception. Female partners of male participants are allowed to use HRT for contraception.

Informed Consent

- Capable of giving signed informed consent.
- Provision of signed and dated written Optional Genetic Research Information informed consent prior to collection of sample for optional genetic research that supports Genomic Initiative.

Critères d'exclusion

Medical Conditions

- Any evidence of diseases which, in the investigator's opinion, makes it undesirable for the participant to participate in the study or that would jeopardize compliance with the protocol.
- History of another primary malignancy except for malignancy treated with curative intent with no known active disease within 3 years before the first dose of study intervention and of low potential risk for recurrence. Exceptions include basal cell carcinoma of the skin and squamous cell carcinoma of the skin that has undergone potentially curative therapy, adequately resected non-melanoma skin cancer, curatively treated in situ disease, or other solid tumors curatively treated.
- Persistent toxicities caused by previous anticancer therapy (excluding alopecia), not yet improved to CTCAE Version 5.0 Grade ≤ 1 or baseline. Note: participants may be enrolled with some chronic, stable Grade 2 toxicities (defined as no worsening to > Grade 2 for at least 3 months prior to first dosing and managed with SoC treatment) which the investigator deems related to previous anticancer therapy.
- Uncontrolled infection requiring IV antibiotics, antivirals, or antifungals; suspected infections (eg, prodromal symptoms); or inability to rule out infections.
- Known active or uncontrolled hepatitis B or C infection; or positive for hepatitis B or C virus based on the evaluation of results of tests for hepatitis B (HBsAg, anti-HBs, anti-HBc, or HBV DNA) or hepatitis C (HCV antibody or HCV RNA) infection at screening.
- Known HIV infection that is not well controlled.

- Uncontrolled or significant cardiac disease, including myocardial infarction or uncontrolled/unstable angina within 6 months prior to C1D1, CHF (New York Heart Association Class II to IV), uncontrolled or significant cardiac arrhythmia, or uncontrolled hypertension (resting systolic blood pressure > 180 mmHg or diastolic blood pressure > 110 mmHg).
- Investigator judgment of 1 or more of the following:
    - Mean resting corrected QTcF interval > 470 ms , obtained from triplicate ECGs performed at screening.
    - History of QT prolongation associated with other medications that required discontinuation of that medication, or any current concomitant medication known to prolong the QT interval and cause Torsades de Pointes.
    - Congenital long QT syndrome, family history of long QT syndrome, or unexplained sudden death under 40 years of age in first-degree relatives.
- History of (non-infectious) ILD/pneumonitis that required steroids, has current ILD/pneumonitis, or where suspected ILD/pneumonitis cannot be ruled out by imaging at screening.
- Clinically severe pulmonary compromise resulting from intercurrent pulmonary illnesses including, but not limited to, any underlying pulmonary disorder, or any autoimmune, connective tissue or inflammatory disorders with pulmonary involvement, or prior pneumonectomy.
- Leptomeningeal carcinomatosis.
- Clinically significant corneal disease.
- Known active tuberculosis infection

Prior/Concomitant Therapy

- Any of the following prior anticancer therapies:
    - Any treatment (including ADC) containing a chemotherapeutic agent targeting topoisomerase I
    - TROP2-targeted therapy
    - Prior treatment with same ICC agent
- Any concurrent anticancer treatment, with the exception of bisphosphonates, denosumab, for the treatment of bone metastases.
- Concurrent use of systemic hormonal replacement therapy (eg, estrogen). However, concurrent use of hormones for non-cancer related conditions (eg, insulin for diabetes) is acceptable.
- Major surgical procedure (excluding placement of vascular access) or significant traumatic injury within 3 weeks of the first dose of study intervention or an anticipated need for major surgery during the study.
- Receipt of live, attenuated vaccine within 30 days prior to the first dose of study treatment.

Prior/Concurrent Clinical Study Experience

- Previous treatment in the present study.
- Participation in another clinical study with a study intervention or investigational medicinal device administered in the last 4 weeks prior to first dosing, randomization into a prior Dato-DXd or T-DXd (trastuzumab deruxtecan) study regardless of treatment assignment, or concurrent enrolment in another clinical study, unless it is an observational (noninterventional) clinical study or during the follow-up period of an interventional study.
- Participants with a known hypersensitivity to Dato-DXd, or any of the excipients of the product (including, but not limited to, polysorbate 80).
- Known history of severe hypersensitivity reactions to other monoclonal antibodies.

Other Exclusions

- Involvement in the planning and/or conduct of the study (applies to both AstraZeneca staff and/or staff at the study site).
- Judgment by the investigator that the participant should not participate in the study if the participant is unlikely to comply with study procedures, restrictions and requirements.
- For women only, currently pregnant (confirmed with positive pregnancy test) or breastfeeding, or who are planning to become pregnant.