Essai Clinique

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Titre	Étude randomisée de phase III comparant un traitement adjuvant de doxorubicin et cyclophosphamide suivi de paclitaxel hebdomadaire avec ou sans ajout de carboplatine chez les patientes atteintes d'un cancer du sein triple négatif soit avec ganglions atteints ou ganglions négatif à haut risque
Protocole ID	NRG-BR003
ClinicalTrials.gov ID	NCT02488967
Type(s) de cancer	Sein
Phase	Phase III
Type étude	Traitement
Institution	CENTRE HOSPITALIER DE L'UNIVERSITE DE MONTREAL
Ville	Montréal
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Statut	Fermé
Date d'activation	22-03-2016
But étude	This randomized phase III trial studies how well doxorubicin hydrochloride and cyclophosphamide followed by paclitaxel with or without carboplatin work in treating patients with triple-negative breast cancer. Drugs used in chemotherapy, such as doxorubicin hydrochloride, cyclophosphamide, paclitaxel, and carboplatin, work in different ways to stop the growth of tumor cells, either by killing the cells, by stopping them from dividing, or by stopping them from spreading. It is not yet known whether doxorubicin hydrochloride and cyclophosphamide is more effective when followed by paclitaxel alone or paclitaxel and carboplatin in treating triple-negative breast cancer.
Critères d'éligibilité	• The patient must have signed and dated an institutional review board (IRB)-approved consent form that conforms to federal and institutional guidelines • Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 • The tumor must be unilateral invasive adenocarcinoma of the breast on histologic examination • All of the following staging criteria (according to the 7th edition of the American Joint Committee on Cancer [AJCC] Cancer Staging Manual) must be met: • By pathologic evaluation, primary tumor must be pT1-3 • By pathologic evaluation, ipsilateral nodes must be pN0, pN1 (pN1mi, pN1a, pN1b, pN1c), pN2a, pN2b, pN3a, or pN3b • If pN0, tumor must be > 3.0 cm • The tumor must have been determined to be human epidermal growth factor receptor 2 (HER2)-negative as follows: • Immunohistochemistry (IHC) 0-1+; or • IHC 2+ and in situ hybridization (ISH) non-amplified with a ratio of HER2 to centromere enumerator probe 17 (CEP17) < 2.0, and if reported, average HER2 gene copy number < 4 signals/cells; or • ISH non-amplified with a ratio of HER2 to CEP17 < 2.0, and if reported, average HER2 gene copy number < 4 signals/cells • The tumor must have been determined to be estrogen receptor (ER)-and progesterone receptor (PgR)-negative assessed by current American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) guidelines; patients with < 1% ER and PgR staining by IHC are considered negative • The patient must have undergone either a mastectomy (total, skin-sparing, or nipple-sparing) or lumpectomy • For patients who undergo lumpectomy, the margins of the resected specimen must be

	histologically free of invasive tumor and ductal carcinoma in situ (DCIS) as determined by the local pathologist; if pathologic examination demonstrates tumor at the line of resection, additional excisions may be performed to obtain clear margins; if tumor is still present at the resected margin after re-excision(s), the patient must undergo mastectomy to be eligible; (patients with margins positive for lobular carcinoma in situ [LCIS] are eligible without additional resection) • For patients who undergo mastectomy, the margins must be free of residual gross tumor; (patients with microscopic positive margins are eligible as long as post-mastectomy radiation therapy [RT] of the chest wall will be administered) • The patient must have completed one of the procedures for evaluation of pathologic nodal status listed below. • Sentinel lymphadenectomy alone: • If pathologic nodal staging based on sentinel lymphadenectomy is pN0 or pN1b; • If pathologic nodal staging based on sentinel lymphadenectomy is pN1mi or pN1a and the patient has undergone breast conserving surgery (with planned breast radiotherapy), the primary tumor must be T1 or T2 by pathologic evaluation and the nodal involvement must be limited to 1 or 2 positive nodes • Sentinel lymphadenectomy followed by removal of additional non-sentinel lymph nodes if the sentinel node (SN) is positive; or • Axillary lymphadenectomy with or without SN isolation procedure • The interval between the last surgery for breast cancer (including re-excision of margins) and randomization must be no more than 60 days • Absolute neutrophil count (ANC) must be >= 1200/mm^3 • Platelet count must be >= 100,000/mm^3 • Hemoglobin must be >= 10 g/dL • Total bilirubin must be =< upper limit of normal (ULN) for the laboratory (lab) unless the patient has a bilirubin elevation > ULN to 1.5 x ULN due to Gilbert's disease or similar syndrome involving slow conjugation of bilirubin • Alkaline phosphatase must be =< 2.5 x ULN for the lab • Aspartate aminotransferase (AST) must be =< 1.5 x ULN for the lab • Note: If alanine aminotransferase (ALT) is performed instead of AST (per institution's standard practice), the ALT value must be =< 1.5 x ULN; if both were performed, the AST must be =< 1.5 x ULN • Patients with AST or alkaline phosphatase > ULN are eligible for inclusion in the study if liver imaging (computed tomography [CT], magnetic resonance imaging [MRI], positron emission tomography [PET]-CT, or PET scan) performed within 90 days prior to randomization does not demonstrate metastatic disease and the requirements above are met • Patients with alkaline phosphatase that is > ULN but =< 2.5 x ULN or unexplained bone pain are eligible for inclusion in the study if a bone scan, PET-CT scan, or PET scan performed within 90 days prior to randomization does not demonstrate metastatic disease • Adequate renal function determined within 6 weeks prior to randomization defined as the most recent serum creatinine =< ULN or measured or calculated creatinine clearance > 60 mL/min • Left ventricular ejection fraction (LVEF) assessment must be performed within 90 days prior to randomization; (LVEF assessment performed by 2-dimensional [D] echocardiogram is preferred; however, multi gated acquisition [MUGA] scan may be substituted based on institutional preferences;) the LVEF must be >= 50% regardless of the cardiac imaging facility's lower limit of normal
Critères d'exclusion	• T4 tumors including inflammatory breast cancer • Definitive clinical or radiologic evidence of metastatic disease; required imaging studies must have been performed within 90 days prior to randomization • Synchronous or previous contralateral invasive breast cancer; (patients with synchronous and/or previous contralateral DCIS or LCIS are eligible) • Any previous history of ipsilateral invasive breast cancer or ipsilateral DCIS; (patients with synchronous or previous ipsilateral LCIS are eligible) • History of non-breast malignancies (except for in situ cancers treated only by local excision and basal cell and squamous cell carcinomas of the skin) within 5 years prior to randomization • Previous therapy with anthracyclines or taxanes for any malignancy • Chemotherapy administered for the currently diagnosed breast cancer prior to randomization • Any continued use of sex hormonal therapy, e.g., birth control pills, ovarian hormone replacement therapy; patients are eligible if these medications are discontinued prior to randomization • Cardiac disease (history of and/or active disease) that would preclude the use of the drugs included in the treatment regimens; this includes but is not confined to: • Active cardiac disease • Angina pectoris that requires the current use of anti-anginal medication; • Ventricular arrhythmias except for benign premature ventricular contractions; • Supraventricular and nodal arrhythmias requiring a pacemaker or not controlled with medication; • Conduction abnormality requiring a pacemaker; • Valvular disease with documented compromise in cardiac function; or • Symptomatic pericarditis • History of cardiac disease • Myocardial infarction documented by elevated cardiac enzymes or persistent regional wall abnormalities on assessment of left ventricle (LV) function; • History of documented congestive heart failure (CHF); or

- Documented cardiomyopathy
- Uncontrolled hypertension defined as sustained systolic blood pressure (BP) > 150 mmHg or diastolic BP > 90 mmHg; (patients with initial BP elevations are eligible if initiation or adjustment of BP medication lowers pressure to meet entry criteria)
- Active hepatitis B or hepatitis C with abnormal liver function tests
- Patients known to be human immunodeficiency virus (HIV) positive with a baseline cluster of differentiation (CD)4 count of < 250 cells/mm^3 or have a history of acquired immune deficiency syndrome (AIDS) indicator conditions
- Intrinsic lung disease resulting in dyspnea
- History of hospitalization in past 12 months for diabetic ketoacidosis (DKA) or hyperosmolar hyperglycemic nonketotic syndrome (HHNS)
- Active infection or chronic infection requiring chronic suppressive antibiotics
- Nervous system disorder (paresthesia, peripheral motor neuropathy, or peripheral sensory neuropathy) >= grade 2, per the Common Terminology Criteria for Adverse Events (CTCAE) version (v)4.0
- Conditions that would prohibit administration of corticosteroids
- Chronic daily treatment with corticosteroids with a dose of >= 10 mg/day methylprednisolone equivalent (excluding inhaled steroids)
- Known hypersensitivity to any of the study drugs or excipients, e.g., polysorbate 80 and Cremophor® EL
- Other non-malignant systemic disease that would preclude the patient from receiving study treatment or would prevent required follow-up
- Psychiatric or addictive disorders or other conditions that, in the opinion of the investigator, would preclude the patient from meeting the study requirements
- Pregnancy or lactation at the time of study entry; (note: pregnancy testing according to institutional standards for women of childbearing potential must be performed within 2 weeks prior to randomization)
- Use of any investigational product within 4 weeks prior to randomization