## Essai Clinique

**Titre**  
Phase II Randomized Study of Whole Brain Radiotherapy in Combination With Concurrent Lapatinib in Patients With Brain Metastasis From HER2-Positive Breast Cancer: A Collaborative Study of NRG Oncology and KROG

**Protocole ID**  
RTOG 1119

**ClinicalTrials.gov ID**  
NCT01622868

**Site Anatomique**  
Sein

**Phase**  
Phase II

**Type étude**  
Traitement

**Institution**  
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**Statut**  
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## But étude
This randomized phase II trial studies how well whole-brain radiation therapy (WBRT) with or without lapatinib ditosylate works in treating patients with breast cancer that has too many of a protein called human epidermal growth factor receptor 2 (HER2) on its cells and has spread to the brain. Radiation therapy uses high energy x rays to kill tumor cells. Lapatinib ditosylate may stop the growth of tumor cells by blocking some of the enzymes needed for cell growth. It is not yet known whether radiation therapy together with lapatinib ditosylate is an effective treatment for brain metastasis from breast cancer.

## Critères d'éligibilité
- Pathologically (histologically or cytologically) proven diagnosis of invasive breast cancer
- HER2-overexpressing breast cancer (3+ staining by immunohistochemistry or HER2 gene amplification by fluorescent in situ hybridization [FISH] or silver in situ hybridization [SISH] >= 2.0)
- At least 1 measurable, unirradiated parenchymal brain metastasis within 21 days prior to study entry; the minimum size as measured on T1-weighted gadolinium-enhanced MRI must be as follows according to the number of brain metastases:
  - For a single solitary lesion the size must be >= 10 mm
  - For 2 or more lesions, the size of at least 2 of the lesions must be >= 5 mm
- Patients may also have the following provided the size requirements above are met:
  - Progressive parenchymal brain metastasis following stereotactic radiosurgery for 1-3 brain metastases, with at least 1 new measurable lesion
  - Progressive parenchymal brain metastasis following surgical resection of 1-3 brain metastases, with at least 1 measurable brain lesion
  - History/physical examination within 21 days prior to study entry
  - Karnofsky performance status >= 60% within 21 days prior to study entry
  - Able to swallow and retain oral medication (note: for patients unable to swallow tablets, an oral suspension preparation is acceptable)
  - Absolute neutrophil count (ANC) >= 1,200 cells/mm³
  - Platelets >= 70,000 cells/mm³
  - Hemoglobin >= 8.0 g/dL (note: the use of transfusion or other intervention to achieve hemoglobin [Hgb] >= 8.0 g/dL is acceptable)
  - Creatinine < 1.5 times institutional upper limit of normal
  - Bilirubin < 1.5 times institutional upper limit of normal
  - Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) <= 3.0 times institutional upper limit of normal with or without liver metastasis
  - Patient must provide study specific informed consent prior to study entry
  - Women of childbearing potential must have a negative serum pregnancy test within 21 days
prior to study entry
- Sexually active women of childbearing potential and sexually active men must practice adequate contraception during therapy and for 12 months after protocol treatment completion
- Prior lapatinib is allowed as long as the last dose received was > 21 days prior to study entry and provided the patient has not received it at any time after the diagnosis of brain metastasis

Critères d'exclusion
- Prior WBRT
- Prior radiation therapy (RT) (any site) with concurrent lapatinib defined as 1 or more days on which the patient received both radiation therapy and lapatinib on the same day
- Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements
- Prior invasive malignancy (except non-melanomatous skin cancer, curatively resected thyroid papillary carcinoma, and invasive and non-invasive cancers related to the breast cancer) unless disease free for a minimum of 3 years
- Leptomeningeal disease
- Prior radiotherapy to the region of the study cancer that would result in overlap of radiation therapy fields except patients who have progressed following stereotactic radiosurgery for 1-3 brain metastases, with at least one new lesion
- Severe, active co-morbidity, defined as follows:
  - Unstable angina and/or congestive heart failure requiring hospitalization within the last 6 months
  - Transmural myocardial infarction within the last 6 months
  - Acute bacterial or fungal infection requiring intravenous antibiotics at the time of study entry
  - Chronic obstructive pulmonary disease exacerbation or other respiratory illness requiring hospitalization or precluding study therapy at the time of study entry
  - Hepatic insufficiency resulting in clinical jaundice and/or coagulation defects; hepatic or biliary disease that is acute or currently active or that requires antiviral therapy (with the exception of patients with Gilbert's syndrome, asymptomatic gallstones, liver metastases, or stable chronic liver disease per investigator assessment)
- History of left ventricular ejection fraction (LVEF) below institutional normal unless repeated and within institutional normal range within 90 days of study entry
- Grade 2 or greater rash of any cause at time of study entry
- Grade 2 or greater diarrhea of any cause at time of study entry