Opti-HER HEART: A prospective, multicenter, single-arm, phase II study to evaluate the safety of neoadjuvant liposomal doxorubicin plus paclitaxel, trastuzumab, and pertuzumab in patients with HER2-positive breast cancer

SOLTI
INNOVATIVE BREAST CANCER RESEARCH

OPTI HER HEART

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BACKGROUND

- In recent years, the concomitant use of two anti-HER2 therapies has generated great expectations[1-3]. Despite of the high activity reported by several studies, none has ever included a chemotherapeutic regimen with anthracyclines.
- The therapeutic value of anthracyclines in HER2-positive breast cancer has been well established. However, the feasibility of their combination with trastuzumab is still controversial[4].
- Liposomal anthracyclines may offer a safer alternative[5]. Of note, in our institutional experience using a regimen of liposomal doxorubicin plus weekly paclitaxel and trastuzumab as standard neoadjuvant therapy for stage II-III breast cancer, patients reached a pathological complete response (pCR) rate of 65%, without any grade 3/4 cardiac toxicity[6].
- In light of the recent data supporting the clinical benefit of the dual anti-HER2 blockade with trastuzumab and pertuzumab in combination with a taxane, we aim to investigate the feasibility of adding liposomal doxorubicin in order to optimize clinical response, while preserving cardiac safety.

KEY ELIGIBILITY CRITERIA

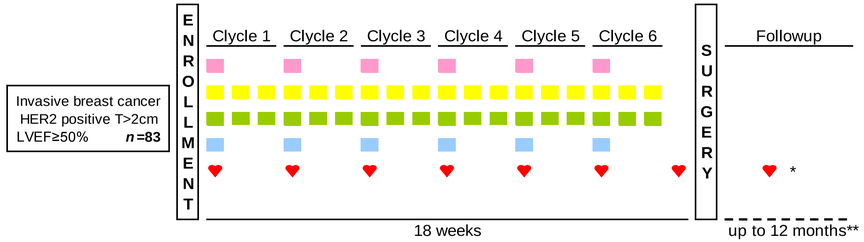
Inclusion

- Female, 18-74 years old
- Histologically confirmed, untreated, invasive HER2-positive breast carcinoma
- Baseline LVEF ≥ 55% measured by echocardiogram or MUGA scan
- ECOG Performance Status of 0 or 1

Exclusion

- Clinical or radiologic evidence of metastatic disease at the time of study entry
- Clinically significant (i.e. active) cardiovascular disease

STUDY DESIGN



Pertuzumab 840 mg loading dose on Day 1 of the first cycle, then 420 mg on Day 1, every 3 weeks
Trastuzumab 4 mg/kg loading dose on Day 1 of the first cycle, every 3 weeks, then 2 mg/kg on Days 8 and 15 of the first cycle and on Days 1, 8, and 15 of the subsequent cycles, every 3 weeks
Paclitaxel 80 mg/m2 on Days 1, 8, and 15, every 3 weeks
Myocet® (liposome-encapsulated doxorubicin) 50 mg/m2 on Day 1, every 3 weeks

♥Safety run-in analysis
* every 3 months
** from the first administration of the study treatment

OBJECTIVES

Primary

- To assess cardiac safety, measured by the incidence of symptomatic cardiac events and by asymptomatic left ventricular ejection fraction (LVEF) decline

Secondary

- To evaluate the efficacy of the study regimen assessed by pCR at the time of surgery
- To assess the breast conservation rate at surgery
- To determine the overall safety profile and tolerability of the regimen
- To evaluate predictive biomarkers of cardiotoxicity

STUDY STATUS

Enrollment will start in December 2012 for the safety run-in phase in three sites: FIVO, Vall d'Hebron, and 12 de Octubre. All other locations in Spain are expected to begin accrual in December 2013. Please check ClinicalTrials.gov for updates (NCTNCT01669239).

For additional information, contact the PI of the study, Dr. Joaquín Gavilá at jogagre@hotmail.com.

METHODS

- This is a multicenter, single-arm phase II clinical trial.
- Assuming that the incidences of cardiac events with regimens containing anti-HER2 agents are 3% for symptomatic and 15% for asymptomatic, 83 patients will be required to reject the null hypothesis with 80% confidence. Additionally, efficacy will be evaluated by pCR rates.

Cardiac Safety Assessment

- Cardiac safety will be monitored throughout the study treatment and follow-up periods. Cardiac AEs will be assessed by clinical evaluation, ECG, and LVEF measurement. Clinical evaluation and ECG will be performed at every planned visit. LVEF assessment will be performed at baseline, at 6 and 12 weeks, immediately before surgery, and then every 3 months until completion of 12 months from the first administration of the study treatment.
- The first 10 patients will be enrolled in a **safety run-in period** and subjected to intensified cardiac safety monitoring. These patients will have an LVEF assessment before each cycle of study medication and every 3 months during the follow-up period, until completion of 12 months from the first administration of the study treatment.

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AKNOWLEDGEMENTS

Trastuzumab and pertuzumab are kindly provided by Roche, and non-pegylated liposimal doxorubicin by Teva. The trial is supported by a grant from TEVA.

San Antonio Breast Cancer Symposium–December 6-10, 2012.
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