# A PHASE II STUDY OF PEMBROLIZUMAB AND ERIBULIN IN PATIENTS WITH HR-POSITIVE/HER2-NEGATIVE METASTATIC BREAST CANCER (MBC) PREVIOUSLY TREATED WITH ANTHRACYCLINES AND TAXANES (KELLY STUDY)

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## BACKGROUND

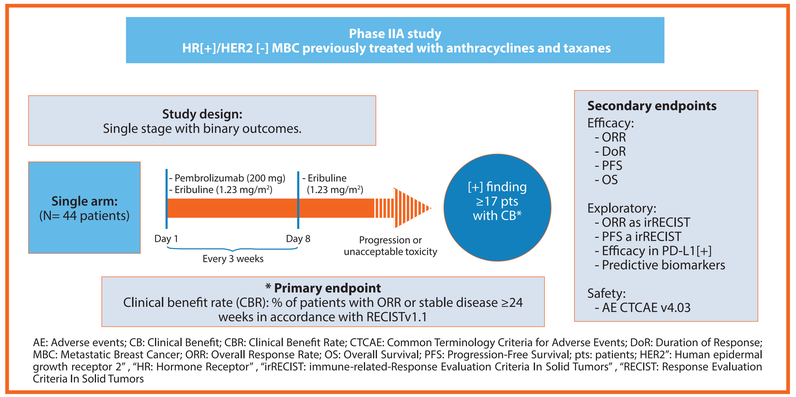
- Preliminary results with MK3475 (pembrolizumab) in heavily pretreated ER-positive/HER2-negative MBC patients have shown promising antitumor activity [(1)].
- However, no data are available with anti-PD-L1 agents in combination with chemotherapy in this tumor subtype in the metastatic setting [(2)].
- The aim of this trial is to evaluate the efficacy of pembrolizumab in combination with eribulin in patients with HR-positive/HER2-negative MBC who have been previously treated with an anthracycline and a taxane.

## TRIAL DESIGN

- This is an open label, non-randomized, multicenter phase IIA clinical trial (**Figure 1**).
- Patients will receive intravenously pembrolizumab (200 mg) on day 1, followed by eribuline (1.23 mg/m2) on days 1 and 8 (every three weeks) until progression or unacceptable toxicity.
- The end of study will be 12 months after last study dose or progressive disease experienced in all patients.
- Main eligibility criteria are reported in **Table 1**.

| INCLUSION CRITERIA | EXCLUSION CRITERIA |
|---|---|
| 1. Female age ≥ 18 years. | 1. Patients have received prior to first dose:<br>- Eribulin and/or anti-PD1 or anti-PD-L1 agents.<br>- Chemotherapy, targeted therapy or radiotherapy within ≤2 weeks.<br>- Monoclonal antibody or investigational agent/device within ≤4 weeks.<br>- Live vaccines within ≤30 days.<br>- Systemic steroid or immunosuppressive agent ≤7 days. |
| 2. HR-positive/HER2-negative inoperable locally recurrent or MBC. | 2. Symptomatic or uncontrolled brain metastases. |
| 3. Prior anthracycline and taxane. | 3. Grade ≥ 2 peripheral neuropathy or clinically relevant toxic effects of any prior therapy at baseline. |
| 4. One or two previous chemotherapeutic regimens for locally recurrent or MBC. | 4. Other malignancy ≤ 5 years. |
| 5. Measurable disease based on RECIST v.1.1. | 5. Clinically significant cardiovascular disease. |
| 6. Available tumor tissue for PD-L1 biomarker analysis. | 6. Autoimmune disease or active uncontrolled infection that contraindicate her participation:<br>- Active tuberculosis<br>- Current known infection with HIV<br>- Active hepatitis B (HBV) or Hepatitis C (HCV) |
| 7. Eastern Cooperative Oncology Group (ECOG) performance status ≤ 1. | 7. Severe and/or uncontrolled medical condition that contraindicate her participation. |
| 8. Adequate bone marrow and organ function. | |

**Figure 1. KELLY study design**




AE: Adverse events; CB: Clinical Benefit; CBR: Clinical Benefit Rate; CTCAE: Common Terminology Criteria for Adverse Events; DoR: Duration of Response; MBC: Metastatic Breast Cancer; ORR: Overall Response Rate; OS: Overall Survival; PFS: Progression-Free Survival; pts: patients; HER2": Human epidermal growth receptor 2" , "HR: Hormone Receptor" , "irRECIST: immune-related-Response Evaluation Criteria In Solid Tumors" , "RECIST: Response Evaluation Criteria In Solid Tumors

## PRIMARY OBJECTIVE

- The primary objective of the study is to assess the efficacy of this combination as determined by the clinical benefit rate (CBR).

**PRIMARY ENDPOINT:**

CBR is defined as the percentage of patients who achieve best response:

- Complete response (disappearance of all target lesions),
- Partial response (≥30% decrease in the sum of the longest diameter of target lesions)
- Or stable disease ≥24 weeks based on RECIST v.1.1.

## SAMPLE SIZE

- Expected accrual will be 44 patients:
  - Single stage design with binary outcomes based on excluding a CBR ≤30% while targeting an improvement of the CBR to ≥50%.
  - Final analysis: 39 evaluable patients (positive finding ≥17 patients with clinical benefit).
  - Total accrual 44 patients with 10% drop-out rate correction.
  - Primary analysis will report percentage of pts with clinical benefit and the p-value based exact binomial test.
  - Expected sample size to attain 80% power at nominal level of one-sided alpha of 0.05.

## SECONDARY OBJECTIVES

- The secondary objectives include efficacy endpoints:
  - ORR: percentage of pts with complete or partial response as best response, in accordance with RECISTv1.1.
  - DoR: is defined as the time from documentation of tumor response until disease progression or death from any cause.
  - PFS: time from the first dose of treatment until objective tumor progression or death by any cause.
  - OS: time from the first dose of treatment until death by any cause.

## EXPLORATORY OBJECTIVES

- PFS based on immune-related Response Evaluation Criteria In Solid Tumors (irRECIST).
- ORR based on irRECIST
- Efficacy in pts with PD-L1 positive tumors.
- The identification of new predictive factors of response to the combination of pembrolizumab and eribulin based on:
  - gene signatures
  - mutational load
  - circulating tumor cells
- Safety-related endpoints:
  - Adverse events assessed using the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.

## BIBLIOGRAPHY

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**Trial registration: NCT03222856.** **Date of registration: July 19th, 2017** **First patient included: February 19th, 2018**