A PHASE II STUDY OF PEMBROLIZUMAB AND ERIBULIN IN PATIENTS WITH HR-POSITIVE/HER2-NEGATIVE METASTATIC BREAST CANCER (MBC) PREVIOUSLY TREATED WITH ANTHRACYLINES 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 activity11.
- However, no data are available with anti-PD-L1 agents in combination with chemotherapy in this tumor subtype in the metastatic setting12.
- 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

1. Patients have received prior to first dose:
   - Eribulin and/or anti-PD1 or anti-PD-L1 agents.
   - Chemotherapy, targeted therapy or radiotherapy within ≤2 weeks.
   - Monoclonal antibody or investigational agent/device within ≤4 weeks.
   - Live vaccines within ≤30 days.
   - Systemic steroid or immunosuppressive agent ≥7 days.
2. HR-positive/HER2-negative inoperable locally recurrent or MBC.
3. Prior anthracycline and taxane.
4. One or two previous chemotherapy regimens for locally recurrent or MBC.
5. Measurable disease based on RECIST v.1.1.
7. Eastern Cooperative Oncology Group (ECOG) performance status ≤1.
8. Adequate bone marrow and organ function.

EXCLUSION CRITERIA

1. Female age ≥ 18 years.
2. Prior brain metastases.
3. Prior chemotherapy and taxane.
4. Two or more previous chemotherapeutic regimens for locally recurrent or MBC.
5. Clinically significant cardiovascular disease.
6. Autoimmune disease or active uncontrolled infection that contraindicate her participation.
   - Active tuberculosis
   - Current known infection with HIV or Hepatitis C (HCV)
7. Severe and/or uncontrolled medical condition that contraindicate her participation.

EXPECTED ACCRUAL

- Expected accrual will be 44 patients:
  - Single stage design with binary outcomes.
  - Clinical benefit rate (CBR) ≤ 30% with CB*.

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 from 20% 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.

EXPECTED 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.

TRIAL REGISTRATION:

NCT03222856. Date of registration: July 19th, 2017

First patient included: February 19th, 2018

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REFERENCES