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BARBICAN: A randomized, phase II study to determine the contribution of ipatasertib to neoadjuvant chemotherapy plus atezolizumab in women with triple-negative breast cancer

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Background

Pathological complete response (pCR) to neoadjuvant treatment in TNBC is strongly correlated with improved EFS and OS. Randomised trials have demonstrated increased pCR rates with the addition of checkpoint inhibitors to NACT in TNBC. Preclinical evidence suggests that AKT inhibition can enhance checkpoint inhibitor efficacy. The AKT inhibitor ipatasertib (IPAT) has shown promising activity in combination with paclitaxel as 1L therapy for metastatic TNBC. BARBICAN was designed to evaluate the clinical and biological effects of adding IPAT to NACT plus atezolizumab (atezo).

Methods

International phase II, randomised trial in 146 patients (pts) with newly diagnosed, non-metastatic, high risk (node+ and/or tumour size ≥2 cm) TNBC. Patients were randomised (1:1) to receive one cycle of atezo (1200mg Q3W) ± IPAT (400mg D1-14), followed by 3 cycles of atezo (840mg Q2W) + weekly paclitaxel (80mg/m^2) ± IPAT (400mg D1-21), followed by 4 cycles of atezo (840mg Q2W) + dose-dense doxorubicin (60mg/m^2)/cyclophosphamide (600 mg/m^2). Tumour biopsies were obtained at baseline, after each treatment phase and surgery. The primary clinical endpoint was pCR rate (ypT0/is ypN0). PD-L1 expression was assessed using the SP142 assay (1% cut-off).

Results

144 pts received treatment, IPAT (n = 72) vs no ipatasertib (no-IPAT) (n = 72). There was no difference in pCR rates between treatment groups (chemo/atezo + IPAT, 49.3%, 95%CI, 36.8%-61.8%; chemo/atezo alone, 48.5%, 95%CI, 36.2%-61.0%). For IPAT vs no-IPAT, pCR was 66.7% vs 75.0% in the PD-L1-positive population (65 pts) and 32.4% vs 25.0% in the PD-L1-negative population (70 pts). pCR in node-positive pts was 55.6% (IPAT, 51.6%, no-IPAT 59.4%) compared to 43.1% (IPAT, 47.2%, no-IPAT 38.9%) in node-negative pts. Grade 3 or higher AE rates were 73.6% in the chemo/atezo + IPAT group and 40.3% in the chemo/atezo alone group, with rash, neutropenia, ALT increase, diarrhoea and mucosits being the most common. The majority of patients required IPAT dose modifications and the dose intensity was low.

Conclusions

Addition of IPAT to neoadjuvant atezo plus chemotherapy did not improve pCR rates. IPAT dose intensity was low due to increased toxicity.

Clinical trial identification

NCT03800836.

Legal entity responsible for the study

Queen Mary University London.

Funding

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Disclosure

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