Background HR+ ESBC is associated with a suboptimal pathologic complete response rate (pCR, ~10%) following neoadjuvant cytotoxic chemotherapy. A genomic analysis among Ki67-high HR+ tumors identified 8-fold upregulation of BIRC5 (survivin), a gene commonly overexpressed in several cancers that regulates apoptosis and cell cycle progression and that is associated with poor clinical outcome. Maveropecipimut-S (MVP-S) is an immune-educating therapy including 5 HLA-restricted peptides from survivin leveraging the lipid-based DPX delivery platform. Treatment with MVP-S and intermittent, low-dose cyclophosphamide (CPA) has shown tumor infiltration of survivin-specific T cells in ovarian cancer. The goal of this study is to determine if MVP-S can be safely administered and whether MVP-S can instigate a survivin-specific immune response in this patient population.

Methods NCT04895761 is a phase I trial evaluating the safety and immunologic effects of neoadjuvant MVP-S plus letrozole. Three postmenopausal patients with T1c+ HR+HER2- breast cancer with Ki67>10% have been enrolled to arm A and received two doses of MVP-S and 7 weeks of neoadjuvant letrozole prior to surgery. The systemic type I survivin-specific immune response was measured by IFN-γ ELISPOT using the pooled peptides in MVP-S. Changes in tumor infiltrating lymphocytes (TILs) and Ki67 were determined. TILs were evaluated by hemoxylin and eosin staining (H&E) per Salgado et al.¹

Results Three patients have tolerated letrozole and MVP-S well without dose reductions or delays in surgery. All toxicities related to MVP-S were grade 1 injection site reactions including pruritis, induration, and erythema, occurring in all three patients. All toxicities related to letrozole are expected including hot flashes and joint pains. All three patients had at least a 50% decrease in Ki67 between biopsy and surgery, from median 24% (range 12% to 43%) before treatment to median 6% (range 5% to 10%) after treatment. All patients had pre-treatment TIL of 5-10%. One patient had patchy infiltrate of TIL up to 40% in the tumor after treatment but the other two had no increase in TIL by H&E. One patient had 8-fold increase of survivin-specific circulating IFN-γ T cells at surgery. One patient did not have a significant increase over baseline and the third patient was not evaluable.

Conclusions Combining MVP-S and letrozole is safe and well tolerated to date as neoadjuvant therapy in HR+ early-stage breast cancer. This neoadjuvant regimen decreased Ki67 in all patients. One patient had significantly increased survivin-specific IFN-γ T cells and one had increased TILs in the tumor.

Trial Registration Clinic trials. gov is NCT04895761

REFERENCE