TPS1127 Poster Session

ELCIN: Elacestrant in women and men with CDK4/6 inhibitor (CDK4/6i)-naïve estrogen receptor-positive (ER+), HER2-negative (HER2-) metastatic breast cancer (mBC)—An open-label multicenter phase 2 study.

Virginia G. Kaklamani, Giorgi Dzagnidze, Nicoleta Zenovia Antone, Anu Thummala, Mikheil Janjalia, Patricia Xavier Santi, Carlos H. Barrios, Mehmet Ali Nahit Sendur, Xiaoling Zhang, Angela Gambioli, Manuel Domínguez Lizarbe, Kathy Puyana Theall, Tomer Wasserman, William John Gradishar; University of Texas Health Science Center at San Antonio, San Antonio, TX; S. Khechinashvili University Hospital, Tbilisi, Georgia; Institutul Oncologic Prof Dr Ion Chiricuta, Cluj-Napoca, Romania; Comprehensive Cancer Centers of Nevada, Las Vegas, NV; Tbilisi Cancer Center, Tbilisi, Georgia; Centro de Oncologia do ABC, Santo André, São Paolo, Brazil; Latin American Cooperative Oncology Group (LACOG) - Porto Alegre, Brazil Oncoclinicas Group, Porto Alegre, Brazil; Ankara Yıldırım Beyazıt University and Ankara Bilkent City Hospital, Istanbul, Turkey; Menarini Group, Florence, Italy; Menarini Group, New York, NY; Department of Medicine, Division of Hematology and Oncology, CTC Core Facility, Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Chicago, IL

Background: Endocrine therapy (ET) plus a CDK4/6i is the mainstay treatment in first-line ER+/HER2- mBC; however, a subset of patients are unable to tolerate CDK4/6i, and resistance to ET emerges. Intrinsic resistance mechanisms include alterations in the PI3K/AKT/mTOR or cell cycle pathways; acquired resistance mechanisms include estrogen receptor gene 1 mutations (*ESR1*-mut), which emerge in up to 50% of patients during prolonged aromatase inhibitor therapy in mBC. In the phase 3 EMERALD trial, elacestrant significantly prolonged PFS vs standard-of-care (SOC) ET and was associated with a manageable safety profile in patients with ER+/HER2- mBC previously treated with ET+CDK4/6i, leading to its approval as the first clinically available oral SERD. Elacestrant significantly reduced the risk of progression or death vs SOC ET by 30% in the overall population (HR 0.70; 95% CI 0.55-0.88; P=0.002) and by 45% in patients with *ESR1*-mut tumors (HR 0.55; 95% CI 0.39-0.77; P=0.0005) [Bidard, 2022]. Preclinical studies demonstrated that elacestrant is equally active in both in vitro and in vivo models of ER+/HER2- breast cancer, regardless of prior exposure to CDK4/6i. Based on preclinical models and clinical efficacy data, elacestrant may improve clinical outcomes in CDK4/6i-naïve patients and provide a convenient all-oral treatment option if combined with CDK4/6i. The ELCIN trial will evaluate efficacy and safety of elacestrant in patients with ER+/HER2- mBC who received prior ET and no prior CDK4/6i in the metastatic setting. **Methods:** ELCIN (NCT05596409) is an open-label, multicenter, single-arm phase 2 trial. Eligible patients are women or men with ER+/HER2− mBC who received 1-2 lines of prior ET and no prior CDK4/6i or chemo in the metastatic setting. Patients must have measurable disease per RECIST v1.1 or a mainly lytic bone lesion (for bone disease only), ECOG PS ≤1, adequate bone marrow and organ function, and no active or newly diagnosed CNS metastases or visceral crisis. Patients will receive elacestrant 345 mg once daily. The primary objective is investigator-assessed PFS. Secondary objectives are ORR, DoR, CBR, OS, PROs-QoL, and safety. Exploratory objectives include elacestrant efficacy according to *ESR1*-mut status, changes in biomarkers, including allele mutation frequencies (cfNAs), and relationship between efficacy endpoints. Status: ELCIN has a planned sample size of 60 patients; recruitment is ongoing worldwide. Clinical trial information: NCT05596409. Research Sponsor: Menarini Group.