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Press Release for Study OOTR-N016/ KBCRN-B-003/ HT-PAB

A Phase III Randomized, Double-Blind, Neoadjuvant Study of Hormonal Therapy plus Palbociclib versus Hormonal Therapy plus Placebo in Women with Operable, Hormone Sensitive and HER2-Negative Primary Breast Cancer

Kyoto Breast Cancer Research Network (KBCRN) today announced that the Phase 3 study did not meet the primary objective of improved efficacy as measured by Pre-operative Endocrine Prognostic Index (PEPI) Score in patients with operable, HR-positive, HER2-negative primary breast cancer.

OOTR-N016/KBCRN-B-003/HT-PAB is a randomized, double-blind, placebo-controlled Phase 3 study evaluating the superiority of 16 weeks of palbociclib plus hormone therapy compared with hormone therapy alone in untreated pre/peri- and post-menopausal women with HR-positive, HER2-negative early invasive (Stage 1 and Stage 2) breast cancer with Ki67 index ≥14% by central assessment in neoadjuvant setting (NCT03969121). Palbociclib is an oral inhibitor of CDK 4 and 6, which are key regulators of the cell cycle. It is currently approved for the treatment of patients with advanced or metastatic HR-positive, HER2-negative breast cancer. The trial was sponsored by KBCRN as part of a clinical research collaboration with Pfizer.

For both control and test arms, 100 eligible patients were to be enrolled in this study. Given the unprecedented challenges caused by COVID-19 pandemics since 2020, between 16 July 2019 till 7 July 2021, 141 eligible patients were randomized from 25 participating institutes in Japan, Korea, Taiwan, Hong Kong and Australia in a 1:1 fashion to receive 16 weeks of palbociclib plus hormonal therapy or placebo plus hormonal therapy. Randomization was stratified by menopausal status (pre/peri vs. post), Ki67 labelling index (<20% vs. ≥20%) and nodal status (positive vs. negative). Primary Objective was to evaluate the efficacy of the pre-operative use of palbociclib plus hormonal therapy vs. placebo plus hormonal therapy as measured by PEPI and EPclin Risk Score using tumor samples at the surgery. Palbociclib/placebo 125 mg/day was administered orally once a day (QD) for 21 days of every 28-day cycle followed by 7 days off treatment. Pre- and peri-menopausal women received

Ovarian Function Suppression (OFS) by either leuprorelin or goserelin plus tamoxifen 20 mg QD in 28-day cycle. Post-menopausal women received letrozole 2.5 mg QD in 28-day cycle. Surgery was planned after treatment completion. Palbociclib or placebo was stopped 2 to 3 weeks before the surgery and hormonal therapy could be continued until one day before the surgery. Surgical post-treatment samples were analyzed for Ki67 index and EndoPredict® at central pathology laboratory. ER assessment was conducted at local pathology. PEPI Scores were calculated using T, N and ER by local pathology and Ki67 by central pathology. EPclin Risk Score was calculated using EndoPredict® Report Generator at central pathology laboratory.

One hundred twenty-six patients completed the treatment duration and their surgical samples were collected for evaluating endpoints, i.e., PEPI Score and EPclin Risk Score. Because statistical significance was not detected on the PEPI Score, hypothesis testing was not performed on EPclin Risk Score according to the gatekeeping procedure.

Demographic and baseline characteristics including age, menopausal status and breast cancer stage ensured that randomization was well balanced. The observed Treatment Emergent Adverse Events were generally consistent with the known safety profile of palbociclib plus hormone therapy. There were no unexpected safety findings in this study population.

Further analyses (including biomarker assessment) will be conducted to determine if there are HR-positive, HER2-negative early breast cancer patients who might benefit from addition of palbociclib to neoadjuvant hormone treatment.

The detailed findings from the study will be shared with the scientific community at an upcoming medical congress.