Refractory Hormone Receptor–Positive Breast Cancer: A Role for Estrogen Receptor β

Principal Investigator: Matthew Cherian, MBBS

Condition: Breast cancer – preclinical

Institution: The Ohio State University Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute

In the development of resistance to first-line endocrine and CDK4/6 inhibitors, the greatest challenge in the management of estrogen receptor α –positive breast cancer is maintained by diverse and intersecting signaling pathways, precluding the development of therapies that target a single resistance factor. Dr. Cherian's data demonstrate that activation of a second estrogen receptor, estrogen receptor β (ER β), leads to transcriptional upregulation of key tumor suppressors known as the FOXO transcription factors. Dr. Cherian proposes a novel therapeutic strategy that will reactivate FOXO transcription factors using combinations of a highly specific, ER β agonist, LY500307, and abemaciclib to concurrently counter the multiple mechanisms of endocrine and CDK4/6 resistance in breast cancer. This is an in vivo, retrospective study.

Primary Objectives/Aims:

- Aim 1: to counter endocrine resistance in preclinical models of breast cancer with ER β agonist–CDK4/6 inhibitor combinations
- Aim 2: to override CDK4/6 inhibitor resistance in preclinical models of breast cancer with ER β agonist–CDK4/6 inhibitor combinations

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NCCN ORP studies typically explore new avenues of clinical investigation and seek answers to important cancer-related questions. All studies are approved and funded through a scientific peer-review process and are overseen by the ORP.

This feature highlights an NCCN study funded through the grant mechanism.

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For more information on specific trials, including patient selection criteria, use the contact information listed with each study.

For more information on the NCCN ORP, including a complete detailing of the clinical studies currently underway at NCCN Member Institutions, go to www.nccn.org/education-research/nccn-oncology-research-program/clinical-trials.