The NCCN Oncology Research Program (ORP) strives to improve the quality of life for patients and reduce cancer-related deaths by advancing cancer therapies through research. Since the program's establishment in 1999, the NCCN ORP has brought millions of dollars in research grants to investigators at NCCN Member Institutions. Research grants are provided to NCCN through collaborations with pharmaceutical and biotechnology companies; these grants are in turn used to support scientifically meritorious cancer research efforts.

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.

Inhibition of Aurora A Kinase Restores Sensitivity to CDK 4/6 Blockade of ER-Positive Breast Cancers

Principal Investigator: Mateusz Opyrchal, MD, PhD

Condition: Breast cancer – preclinical

Institution: Washington University in St. Louis

Introduction of CDK 4/6 inhibitors has greatly improved response and duration of endocrine therapies in patients with estrogen receptor (ER)-positive metastatic breast cancer. Despite the clinical benefit, resistance to combination therapy with CDK 4/6 inhibition continues to be a major clinical problem. Multiple mechanisms for breast cancer resistance have been proposed, but most tumors present with decreased expression of ER/progesterone receptor (PR) and increased expression of mesenchymal genes. Aurora A kinase (AURKA) has been shown to lead to loss of ER expression and increase in stem cell-like properties, resulting in decreased sensitivity to endocrine targeting of breast cancer cell. This study will address the question of resistance to CDK 4/6 combination treatment by interrogating the hypothesis that inhibiting AURKA by LY3295668 in combination with abemaciclib will lead restoration of endocrine sensitivity.

Primary Objective:

- To evaluate the efficacy of abemaciclib and LY3295668 combination treatment in palbociclib-resistant patient-derived xenograft (PDX) models

Secondary Objective:

- To evaluate changes in gene expression 1 week after initiation of therapy and correlate with response of the specific PDX models to the expression data

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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/orp-main-page.