Highlights of the NCCN Oncology Research Program

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.

An NCCN study funded through the grant mechanism is highlighted below.

Women's Triple-Negative First-Line Study: A Phase II Trial of Mirvetuximab Soravtansine in Patients With Localized Triple-Negative Breast Cancer With Tumors Predicted Insensitive to Standard Neoadjuvant Chemotherapy, Including a Lead-in Cohort to Establish Activity in Patients With Metastatic TNBC

Principal Investigator: Stacy Moulder, MD

Co-Investigators: Senthil Damodaran, MD; Elizabeth Mittendorf, MD, PhD; and W. Fraser Symmans, MD

Condition: Triple-negative breast cancer

Institution: The University of Texas MD Anderson Cancer Center

Patients with triple-negative breast cancer (TNBC) who have residual disease after neoadjuvant chemotherapy (chemo-insensitive disease) have a dismal prognosis, with a 40% to 80% recurrence risk within 3 years. Thus, exploring novel agents to treat disease that has been identified as chemo-insensitive in the neoadjuvant setting is a viable strategy, because potentially curative chemotherapy is not compromised in this high-risk population. Ideally, agents should have demonstrated activity in metastatic disease before use in the neoadjuvant setting. Taken together, the activity of mirvetuximab soravtansine in advanced, heavily pretreated ovarian cancer and the common expression of high levels of FR α in TNBCs support the rationale to determine the activity of mirvetuximab soravtansine in metastatic breast cancer and, if response is confirmed, evaluating the drug for the neoadjuvant treatment of high-risk, chemo-insensitive TNBC.

Patients with metastatic or localized, chemo-insensitive TNBC that expresses moderate to high levels of FR α will be enrolled onto this study. This study will accrue 2 cohorts of patients: those with advanced/metastatic TNBC (cohort A) and those with localized, chemo-insensitive TNBC (cohort B). Several biomarkers, including FR α , will be evaluated as potential biomarkers of clinical response to IMGN853 (cohort B only). For purposes of study entry, moderate FR α expression will be defined as 25% to 74% of cells with $\geq 2+$ expression, and high FR α expression will be defined as $\geq 75\%$ of cells having $\geq 2+$ expression. TNBC will be defined as estrogen receptor (ER) $< 10\%$, progesterone receptor (PR) $< 10\%$, and HER2 0–2+ using standard immunohistochemistry (IHC). Tumors that are HER2 2+ by IHC must demonstrate nonamplification (ratio < 2) by standard in situ hybridization techniques (chromogenic or fluorescence).

Primary Objectives:

- Determine if single-agent mirvetuximab induces response with at least a 20% response rate per RECIST criteria in metastatic TNBC

The goal of the Highlights of the NCCN Oncology Research Program (ORP) is to provide readers with more information on the ORP, including studies currently accruing patients.

For more information on specific trials, including patient selection criteria, please 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, please access the NCCN ORP pages at NCCN.org/clinical_trials/clinicians.asp.

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- Determine if single-agent mirvetuximab in the neoadjuvant setting improves rate of excellent pathologic response (complete pathologic response or minimal residual disease) in patients identified as having chemo-insensitive TNBC

Secondary Objectives:

- Determine radiographic response
- Determine toxicity of mirvetuximab in cohorts A and B
- Determine disease-free survival at 3 years in the neoadjuvant setting, and progressive-free survival, duration of response, and overall survival at 3 years in metastatic TNBC
- In the neoadjuvant setting, compare disease response to mirvetuximab versus patients with similar molecular features receiving standard taxane-based chemotherapy

Exploratory Objectives:

- Correlate response to mirvetuximab with expression of FR α /FOLR1 in primary tumors
- Determine if treatment with mirvetuximab alters the tumor microenvironment, making the tumors more susceptible to treatment with immune-regulators

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