NRG-GY033

SCHEMA

Patients with recurrent adult-type Ovarian Granulosa Cell Tumor (AGCT)

- **Histologically confirmed AGCT**
- **≥1 Prior treatment regimen**
- **Progression on a prior aromatase inhibitor**

<u>Treatment</u>

Darolutamide 600 mg PO twice daily, exemestane 25 mg PO once daily, and leuprolide acetate 7.5 mg IM every four weeks

3. ELIGIBILITY AND INELIGIBILITY CRITERIA

3.1 On Study Guidelines

This clinical trial can fulfill its objectives only if patients appropriate for this trial are enrolled. Investigators should consider all relevant factors (medical and non-medical), as well as the risks and benefits of the study therapy, when deciding if a patient is an appropriate candidate for this trial.

Physicians should consider the following when evaluating if the patient is appropriate for this protocol:

- Patients must have adequate health that permits completion of the study requirements and required follow up.
- For patients with known HIV, HBV, and/or HCV infection:
    - HIV-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial.
    - For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated.
    - Patients with a history of hepatitis C virus (HCV) infection must have been treated and cured. For patients with HCV infection who are currently on treatment, they are eligible if they have an undetectable HCV viral load.
- Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial.

In addition:

- The effects of the combination of darolutamide, leuprolide acetate, and exemestane on the developing human fetus are unknown. For this reason, and because androgen receptor inhibitor agents as well as other therapeutic agents used in this trial are known to be teratogenic, participants of child-bearing potential must agree to use adequate contraception (hormonal or barrier method of birth control; abstinence) during study therapy and for 1 month following the completion of study therapy. Should a participant become pregnant or suspect pregnancy while participating in this study, they should inform their treating physician immediately.

Notes: Per NCI guidelines, exceptions to eligibility criteria are not permitted. For questions concerning eligibility see protocol cover page.

NIH Participant Population Inclusion Policy
NIH policy requires that participants regardless of gender identity and members of minority groups and their subpopulations be included in all NIH-supported biomedical and behavioral research projects involving NIH-defined clinical research unless a clear and compelling rationale and justification establishes to the satisfaction of the funding Institute & Center (IC) Director that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. Exclusion under other circumstances must be designated by the Director, NIH, upon the recommendation of an IC Director based on a compelling rationale and justification. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. Participants of childbearing potential should not be routinely excluded from participation in clinical research. Please see http://grants.nih.gov/grants/funding/phs398/phs398.pdf

3.2 Eligibility Criteria

A patient cannot be considered eligible for this study unless ALL of the following conditions are met.

Submission of tissue is required. Investigators should check with their pathology department regarding release of tissue before approaching patients about participation in the trial (see Section 10 for details).

3.2.1 Histologically confirmed diagnosis of recurrent adult-type granulosa cell tumor.

3.2.2 Patient must have measurable disease. Measurable disease is defined in the protocol per RECIST 1.1 criteria. Measurable disease is defined as at least one lesion that can be accurately measured in at least one dimension (longest diameter to be recorded). Each lesion must be ≥ 10 mm when measured by CT or MRI. Lymph nodes must be ≥ 15 mm in short axis when measured by CT or MRI.

3.2.3 Patient must have had ≥1 treatment regimen.

3.2.4 Subject must have progressed on an aromatase inhibitor (letrozole, exemestane, anastrozole) in a prior treatment line.

3.2.5 Age ≥ 18 years

3.2.6 ECOG Performance Status of ≤ 2 (see Appendix I).

3.2.7 Not Pregnant and Not Nursing

3.2.8 Adequate hematologic function defined as follows:

- Absolute neutrophil count (ANC) ≥ 1,500 cells/mm^3
- Platelets ≥ 100,000 cells/mm^3
- Hemoglobin ≥ 8 g/dl **(08-DEC-2023)**

3.2.9 Adequate renal function defined as follows:

- Creatinine clearance (CrCL) of ≥30 mL/min by the Cockcroft-Gault formula

$$\text{CrCl (mL/min)} = \frac{[140 - \text{age (years)}] \times \text{weight (kg)}}{72 \times \text{creatinine (mg/dL)}} \quad \{\times 0.85 \text{ for female patients}\}$$

3.2.10 Adequate hepatic function defined as follows:

- Total bilirubin ≤ 1.5 x institutional upper limit of normal (ULN) (patients with known Gilbert's disease who have bilirubin level ≤ 3 x ULN may be enrolled)
- AST and ALT ≤ 1.5 x institutional ULN

3.2.11 Adequate cardiac function defined as follows:

- Patients with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, should have a clinical risk assessment of cardiac function using the New York Heart Association Functional Classification. To be eligible for this trial, patients should be class 2B or better (See Appendix II)

3.2.12 Comorbid conditions

- No active infection requiring parenteral antibiotics;
- No current evidence of intra-abdominal abscess, abdominal/pelvic fistula (not diverted), gastrointestinal perforation, GI obstruction, and/or need for drainage nasogastric or gastrostomy tube

3.2.13 The patient or a legally authorized representative must provide study-specific informed consent prior to study entry and, for patients treated in the U.S., authorization permitting release of personal health information.

3.3 Ineligibility Criteria

Patients with any of the following conditions are NOT eligible for this study.

3.3.1 Prior treatment with AR inhibitors

3.3.2 Known hypersensitivity to the study drugs or their ingredients.