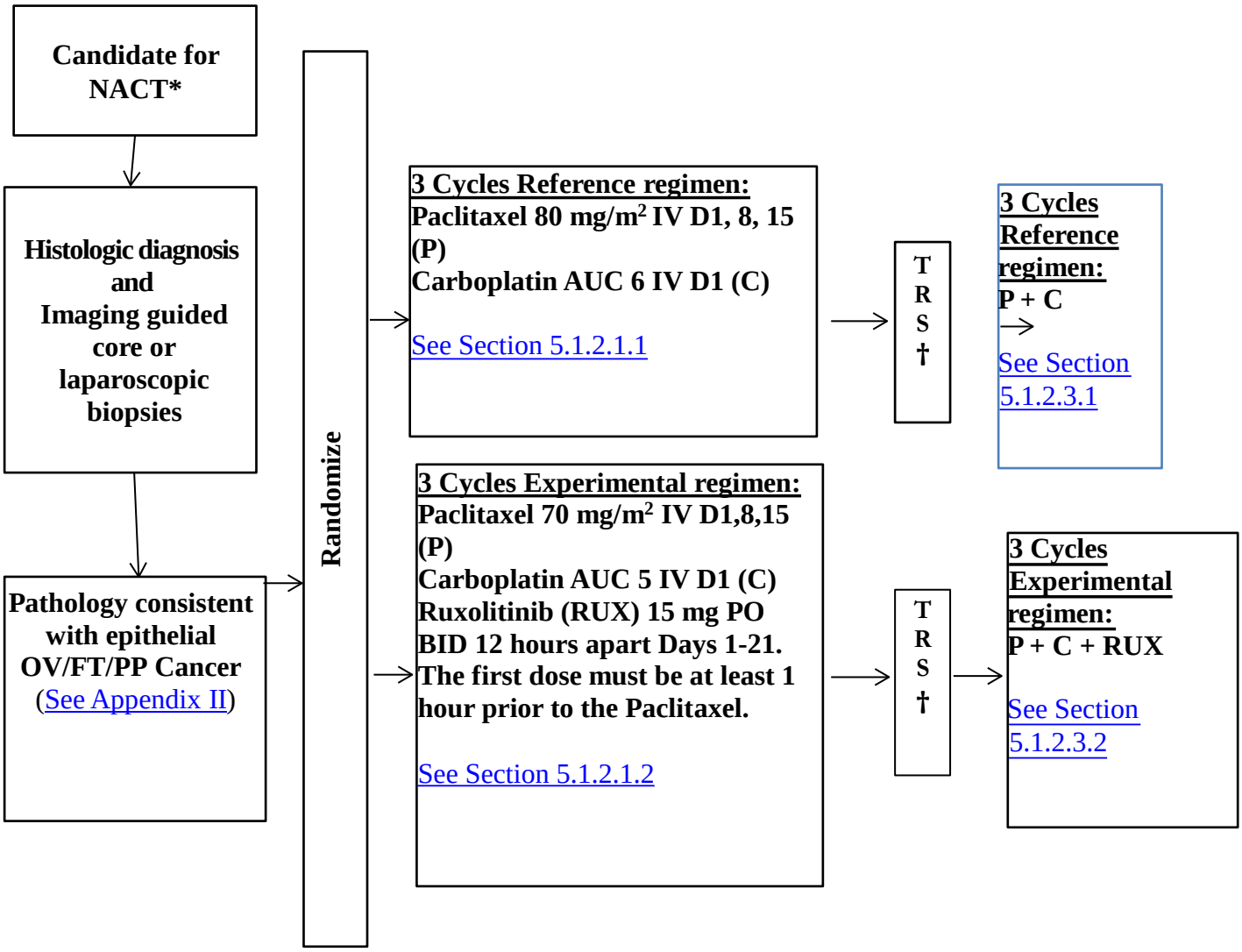
NRG-GY007 Phase II Component



A Cycle is 21 days in length

*NACT = Neoadjuvant chemotherapy
† TRS = Tumor Reductive Surgery

Primary Endpoint: Progression-Free Survival
N = Maximum 87 patients enrolled to experimental regimen, 43 enrolled to reference regimen **(10/10/2016)**
† Interval tumor reductive surgery; or core biopsies in case of progression, failure to respond to first 3 cycles or tumor reductive surgery medically contraindicated (See Section 5.1.2.2)

3.1 Patient Selection Guidelines

Although the guidelines provided below are not inclusion/exclusion criteria, investigators should consider these factors when selecting patients for this trial. Investigators also should consider all other 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.

3.1.1 Patients must have the psychological ability and general health that permits completion of the study requirements and required follow up.

3.1.2 Women of childbearing potential should be willing and able to use medically acceptable forms of contraception during the trial.

3.2 Eligibility Criteria (10/10/2016)

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

3.2.1 Patients must have clinically and radiographically suspected and previously untreated FIGO stage (Appendix I) III or IV epithelial ovarian, primary peritoneal or fallopian tube cancer, high grade, for whom the plan of management will include neoadjuvant chemotherapy (NACT) with interval tumor reductive surgery (TRS) who have undergone biopsies for histologic confirmation. See Appendix II for Guidelines to Aid in Classification of Tumor Cell Type.

3.2.2 Institutional confirmation of Müllerian epithelial adenocarcinoma on core biopsy (not cytology or fine needle aspiration) or laparoscopic biopsy. (For Phase II of the study FFPE tissue should be available for laboratory analysis.) Patients with the following histologic epithelial cell types are eligible: high grade serous carcinoma, high grade endometrioid carcinoma, clear cell carcinoma, or a combination of these.

3.2.3 All patients must have measurable disease as defined by RECIST 1.1. 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, MRI or caliper measurement by clinical exam; or ≥ 20 mm when measured by chest x-ray. Lymph nodes must be ≥ 15 mm in short axis when measured by CT or MRI.

3.2.4 Appropriate stage for study entry based on the following diagnostic workup:

- History/physical examination within 28 days prior to registration;
- Radiographic imaging of the chest, abdomen and pelvis within 28 days prior to registration documenting disease consistent with FIGO stage III or IV disease;
- Further protocol-specific assessments as detailed in section 4.1.

3.2.5 Age ≥ 18

3.2.6 The trial is open to females only.

3.2.7 ECOG/Karnofsky Performance Status of 0, 1, or 2 (see Appendix III) within 28 days prior to registration.

3.2.8 Adequate hematologic function within 14 days prior to registration defined as follows:

- ANC greater than or equal to 1,500/mcl. This ANC cannot have been induced by granulocyte colony stimulating factors.
- Platelets greater than or equal to 100,000/mcl
- Hemoglobin greater than 9.0 mg/dl (transfusions are permitted to achieve baseline hemoglobin level)

3.2.9 Adequate renal function within 14 days prior to registration defined as follows:

- Estimated CrCl $\geq$ 50 mL/min/1.73 m^2 according to the Cockcroft-Gault formula.

3.2.10 Adequate hepatic function within 14 days prior to registration defined as follows:

- Bilirubin $\leq$ 1.5 x ULN
- ALT and AST $\leq$ 3 x ULN
- Alkaline phosphatase $\leq$ 2.5 x ULN

3.2.11 Neurologic function: Neuropathy (sensory and motor) less than or equal to CTCAE Grade 1.

3.2.12 Ability to swallow and retain oral medication.

3.2.13 The patient must provide study-specific informed consent prior to study entry.

3.3 Ineligibility Criteria (10/10/2016)

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

3.3.1 Patients with suspected non-gynecologic malignancy, such as gastrointestinal.

3.3.2 Patients with a history of other invasive malignancies, with the exception of non-melanoma skin cancer and other specific malignancies as noted in Section 3.33 and Section 3.3.7 are excluded if there is any evidence of other malignancy being present within the last three years (2 years for breast cancer, see Section 3.33). Patients are also excluded if their previous cancer treatment contraindicates this protocol therapy.

3.3.3 Patients who have received prior chemotherapy for any abdominal or pelvic tumor within the last three years are excluded. Patients may have received prior adjuvant chemotherapy and radiotherapy for localized breast cancer, provided that it was completed more than 2 years prior to registration, the patient remains free of recurrent or metastatic disease and hormonal therapy has been discontinued.

3.3.4 Patients who have received prior radiotherapy to any portion of the abdominal cavity or pelvis or thoracic cavity within the last three years are excluded. Prior radiation for localized cancer of the head and neck or skin is permitted, provided that it was completed more than three years prior to registration, and the patient remains free of recurrent or metastatic disease.

3.3.5 Patients who have received any targeted therapy (including but not limited to vaccines, antibodies, tyrosine kinase inhibitors) or hormonal therapy for management of their epithelial ovarian, fallopian tube or peritoneal primary cancer.

3.3.6 Patients with mucinous carcinoma, low grade endometrioid carcinoma, low grade serous carcinoma or carcinosarcoma.

3.3.7 Patients with synchronous primary endometrial cancer, or a past history of primary endometrial cancer, unless all of the following conditions are met: Stage not greater than I-A, grade 1 or 2, no more than superficial myometrial invasion, without vascular or lymphatic invasion; no poorly differentiated subtypes, including serous, clear cell or other FIGO grade 3 lesions.

3.3.8 Severe, active co-morbidity defined as follows:

- Chronic or current active infectious disease requiring systemic antibiotics, antifungal or antiviral treatment
- Known brain or central nervous system metastases or history of uncontrolled seizures
- Clinically significant cardiac disease including unstable angina, acute myocardial infarction within 6 months from enrollment, New York Heart Association Class III or IV congestive heart failure, and serious arrhythmia requiring medication (this does not include asymptomatic atrial fibrillation with controlled ventricular rate).
- Partial or complete gastrointestinal obstruction

3.3.9 Patients who are not candidates for major abdominal surgery due to known medical comorbidities.

3.3.10 Patients with any condition that in the judgment of the investigator would jeopardize safety or patient compliance with the protocol.

3.3.11 Patients who are unwilling to be transfused with blood components.

3.3.12 Concurrent anticancer therapy (e.g. chemotherapy, radiation therapy, biologic therapy, immunotherapy, hormonal therapy, investigational therapy).

3.3.13 Receipt of an investigational study drug for any indication within 30 days or 5 half-lives (whichever is longer) prior to Day 1 of protocol therapy.

3.3.14 Patients who, in the opinion of the investigator, are unable or unlikely to comply with the dosing schedule and study evaluations.

3.3.15 Patients who are pregnant or nursing. The effects of ruxolitinib on the developing human fetus are unknown. For this reason, women of child-bearing potential (WOCBP) must agree to use adequate contraception (hormonal or barrier method of birth control; abstinence) prior to study entry and for the duration of study participation. WOCBP must have a screening negative serum or urine pregnancy test within 14 days of registration. A second pregnancy test must be done within 24 hours prior to the start of the first cycle of study treatment. Women must not be breastfeeding. (01/09/2017)

Women who are not of childbearing potential (i.e., who are postmenopausal or surgically sterile) do not require contraception.

Women of childbearing potential (WOCBP) is defined as any female who has experienced menarche and who has not undergone surgical sterilization (hysterectomy and/or bilateral oophorectomy) or who is not postmenopausal. Menopause is defined clinically as 12 month amenorrhea in a woman over 45 in the absence of other biological or physiological causes. In addition, women under the age of 55 must have a documented serum follicle stimulating hormone (FSH) level greater than 40mIU/mL.

3.3.16 Known history of human immunodeficiency virus (HIV), hepatitis B, or hepatitis C infection or known history of tuberculosis. (This exclusion criterion is necessary because the treatments involved in this protocol may be immunosuppressive.)