Cancer Research Consortium of West Michigan
P: 616.391.1230 | 800.336.6299 | www.crcwm.org

FAST FACTS

A031902 - CASPAR - A PHASE III TRIAL OF ENZALUTAMIDE AND RUCAPARIB AS A NOVEL THERAPY IN FIRST-LINE METASTATIC CASTRATION-RESISTANT PROSTATE CANCER

Eligibility criteria

Pre-Registration Eligibility Criteria

1. Documentation of Disease
    a. Histologic/cytologic documentation of prostate adenocarcinoma
    b. **Adequate archival tumor specimen or archival slides must be available to be tested as part of the trial screening (most recent metastatic site biopsy preferred, but primary prostate biopsy allowed if metastatic biopsy is not available or inadequate. A new biopsy is not required for enrollment in the trial as long as sufficient archival tissue is available). Due to significant variability between tests, results from an existing targeted next-generation exome sequencing test may not be used for this trial. Progressive disease must be demonstrated at study entry while the patient is on continuous androgen deprivation therapy (ADT) or status post orchiectomy. Progressive disease is defined as one or more of the following criteria (choose all the apply):**
        i. **PSA progression, defined by at least 2 consecutive rising PSA values at a minimum of 1-week intervals with the most recent PSA value being 1.0 ng/mL or higher, if confirmed PSA rise is the only indication of progression. Patients who received an anti-androgen must have PSA progression after withdrawal of anti-androgen therapy.**
        j. **Radiographic progression per RECIST 1.1 criteria for soft tissue lesions**
        k. **Bone metastasis progression per Prostate Cancer Working Group 3 (PCWG3) criteria.**
2. **Measurable or non-measurable metastatic disease as defined in Section 11.0.**
3. Prior Treatment
    a. **No prior therapy for metastatic castration-resistant prostate cancer, defined as a treatment given for prostate cancer with radiographically-detectable metastasis and a serum testosterone level less than 50 ng/dl (1.73 nmol/L) at the time of pre-registration.**
    b. **≥2 weeks or 5 half-lives (whichever is longer) since prior therapy with flutamide, dutasteride, bicalutamide, niltamide, finasteride, aminoglutethimide, estrogens, cytoproterone, chemotherapy, abiraterone, apalutamide, or darolutamide**
    c. **≥4 weeks or 5 half-lives (whichever is longer) since any prior investigational therapy**
    d. **≥4 weeks since a major surgery or radiation**
    e. **No prior therapy with enzalutamide, rucaparib or any other PARP inhibitor, or platinum chemotherapy.**
    f. **Prior docetaxel and/or novel antiandrogen use is allowed only if given in the hormone-sensitive disease setting**
    g. **Patient must have discontinued all previous treatments for cancer (except ADT and bone anti-responsive therapies such as denosumab or zoledronic acid) and must have recovered from all acute side effects of prior therapy or surgical procedures to ≤ Grade**

1 or baseline prior to randomization, with the exception of fatigue, alopecia or peripheral neuropathy.

4. Age ≥ 18 years
5. ECOG Performance Status 0-2
6. Required Initial Laboratory Values
    a. **Absolute Neutrophil Count (ANC) ≥ 1,500/mm3**
    b. **Platelet Count ≥ 100,000/mm3**
    c. **Hemoglobin ≥ 10 g/dL**
    d. **Serum testosterone ≤ 50 ng/dl (≤ 1.73 nmol/L)**
    e. **Serum Creatinine ≤ 1.5 x upper limit of normal (ULN)**
    f. **Total Bilirubin ≤ 1.5 x upper limit of normal (ULN)**
    g. **AST / ALT ≤ 2.5 x upper limit of normal (ULN)**
7. Comorbid conditions
    a. **No clinically suspected CNS (leptomeningeal or parenchymal) metastases. Patients with a history of CNS metastasis(s) will be allowed as long (1) as the metastatic site(s) were adequately treated as demonstrated by clinical and radiographic improvement, AND (2) the patient has recovered from the intervention (no residual adverse events > CTCAE grade 1), AND (3) the patient has remained without occurrence of new or worsening CNS symptoms for a period of 28 days prior to pre-registration.**
    b. **No known or suspected history of cytopenia (low WBC, hemoglobin or platelet count) of greater than 3 months duration with an unknown cause, myelodysplastic syndrome, or hematologic malignancies.**
    c. **No blood product transfusion, granulocyte/granulocyte-macrophage-colony stimulating factor (G-CSF/GM-CSF), or erythropoietin/thrombopoietin use within 14 days of pre-registration.**
    d. **No history of syncope of cardiovascular etiology, uncontrolled cardiac arrhythmia, History of Mobitz II second degree or third degree heart block without a permanent pacemaker in place, myocardial ischemia or infarction, severe or unstable angina, New York Heart Association (NYHA) class II to IV heart failure, or stroke/transient ischemic attack (TIA) within 3 months prior to pre-registration on A031902.**
    e. **No history of seizure or any condition that may increase the patient's seizure risk (e.g., prior cortical stroke, significant brain trauma) within 2 years prior to pre-registration on A031902.**
    f. **No clinically active or chronic liver disease resulting in moderate/severe hepatic impairment (Child-Pugh Class B or C), ascites, coagulopathy or bleeding due to liver dysfunction.**
    g. **No clinical, laboratory or radiographic evidence of an active bacterial, fungal, or viral infection requiring treatment at the time of pre-registration.**
    h. **No planned palliative procedures for alleviation of bone pain such as radiation therapy or surgery.**
    i. **No untreated spinal cord compression or evidence of spinal metastases with a risk of impending fracture or spinal cord compression.**
    j. **No known or suspected contraindications or hypersensitivity to enzalutamide, rucaparib, or to any of the excipients.**
    k. **No known or suspected gastrointestinal disorder affecting absorption of oral medications.**
    l. **No prior malignancy for which the last treatment was given within the past 2 years prior to pre-registration on A031902, or any active concurrent malignancy with the**

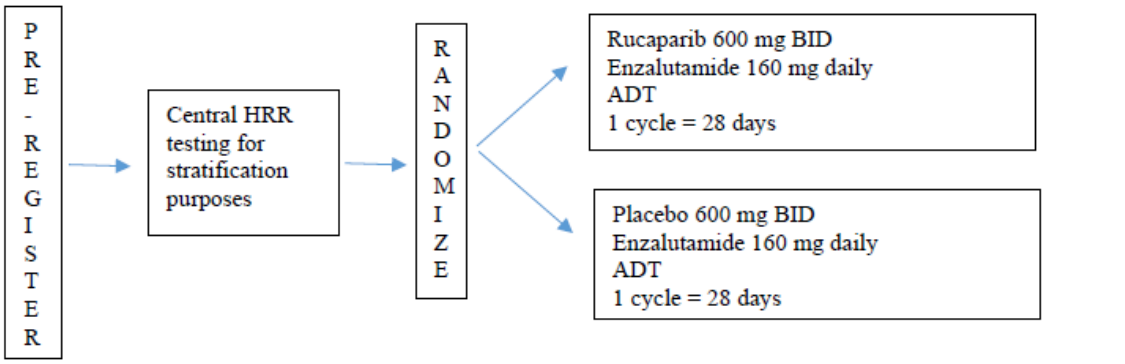
exception of non-melanomatous localized skin cancers (such as squamous or basal cell carcinoma of the skin).

8. Concomitant medications
    - **a.** Any concomitant medications that are strong inhibitors of CYP2C8 or inducers of CYP3A4 cytochrome enzymes must be discontinued prior to registration. Dose adjustments per FDA label or clinical judgement should be considered for any concomitant medications that are moderate inhibitors of CYP2C8 or inducers of CYP3A4 cytochrome enzymes.
    - **b.** **Any concomitant medications that are substrates of CYP3A4, CYP2C8 and CYP2C19 cytochrome enzymes should be monitored closely per clinical judgement of the treating physician.**
      An indicative list of medications with drug-drug interactions is provided in Appendix III.

Registration Eligibility Criteria

1. **Results of HRR testing available**
    - **a.** HRR testing results from the central laboratory (Tempus Labs) are required before registering. Tempus will forward the HRR results to the statistical center, and the statistical center will notify the site that the result is available. Since the results will be blinded to the site the notification from the Alliance registration/randomization office will serve as a confirmation of this eligibility criteria. After the site receives this confirmation e-mail from Alliance they can register the patient. **Patients with known HRR test results** may not use the known result for A031902, tissue must still be sent to Tempus Labs for testing.

Schema



For all patients, treatment is to continue until disease progression or unacceptable adverse event.
Patients will be followed for 5 years or until death, whichever comes first.