A Phase 2 Study of ACR-368 in Endometrial Adenocarcinoma

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

General 1. Participant must be able to give signed, written informed consent. 2. Participant must have histologically documented, high-grade endometrial cancer. 3. Treatment History Requirements: 1. Subject must have received prior platinum-based chemotherapy 2. Subject must have received prior anti-PD-(L)1 therapy 4. Participant must have histologically confirmed metastatic cancer that has progressed during or after at least 1 prior therapeutic regimen. 5. Participant must have at least 1 measurable lesion per RECIST v1.1 criteria (by local Investigator) in a baseline tumor imaging that has been obtained within 28 days of the treatment start. Participant must have radiographic evidence of disease progression based on RECIST v1.1 criteria following the most recent line of treatment. 6. Arm 1 and 2 only: Participant must be willing to provide tissue from a newly obtained tumor biopsy from an accessible tumor lesion not previously irradiated after written informed consent. Newly obtained is defined as a specimen taken after written informed consent is obtained, during the 28-day Screening period. 7. Participant must be willing to provide an archival tumor tissue block or at least 20 unstained slides, if available. 8. Participant must have stabilized or recovered (Grade 1 or baseline) from all prior therapy related toxicities, except as follows: 1. Alopecia is accepted. 2. Endocrine events from prior immunotherapy stabilized at ≤ Grade 2 due to need for replacement therapy are accepted (including hypothyroidism, diabetes mellitus, or adrenal insufficiency). 3. Neuropathy events from prior cytotoxic therapies stabilized at ≤ Grade 2 are accepted. 9. Participant must have an Eastern Cooperative Oncology Group Performance Status 0 or 1. 10. Participant must have an estimated life expectancy of longer than 3 months. 11. Participant must have adequate organ function at Screening, defined as: 1. Absolute neutrophil count \> 1500 cells/µL without growth factor support within 1 week prior to obtaining the hematology values at Screening. 2. Hemoglobin ≥ 9.0 g/dL. 3. Platelets ≥ 150,000 cells/µL without transfusion within 1 week prior to obtaining the hematology values at Screening. 4. Calculated creatinine clearance (CrCl) ≥ 50 mL/min as calculated by the Cockcroft-Gault formula. 5. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤ 3 × upper limit of normal (ULN); ≤ 5 × ULN if liver metastases are present. 6. Total bilirubin ≤ 1.5 × ULN not associated with Gilbert's syndrome. If associated with Gilbert's syndrome ≤ 3 x ULN is acceptable. 7. Serum albumin ≥ 3 g/dL. 12. Participant must have adequate coagulation profile as defined below if not on anticoagulation. If subject is receiving anticoagulation therapy, then subject must be on a stable dose of anticoagulation for ≥ 1 month: 1. Prothrombin time within 1.5 x ULN. 2. Activated partial thromboplastin time within 1.5 x ULN.

Exclusion Criteria:

General 1. Participant with known symptomatic brain metastases requiring \> 10 mg/day of prednisolone (or its equivalent). Participants with previously diagnosed brain metastases are eligible if they have completed their treatment, have recovered from the acute effects of radiation therapy or surgery prior to the start of ACR-368 treatment, fulfill the steroid requirement for these metastases, and are neurologically stable based on central nervous system imaging ≥ 4 weeks after treatment. 2. Participant has mesenchymal tumors of the uterus. 3. Participant has a history of clinically meaningful ascites, defined as history of paracentesis or thoracentesis with therapeutic intent, within 4 weeks of Screening. Subjects with planned therapeutic paracentesis or thoracentesis between Screening and Cycle 1 Day 1 dosing are excluded. 4. Participant had systemic therapy or radiation therapy within 3 weeks prior to the first dose of study drug. 5. Participants has known human immunodeficiency virus (HIV), hepatitis B, or hepatitis C infection that is considered uncontrolled based on the criteria included in Appendix 2. 6. Participant has a history of clinically meaningful coagulopathy, bleeding diathesis. 7. Participant has cardiovascular disease, defined as: 1. Uncontrolled hypertension defined as blood pressure \> 160/90 mmHg at Screening confirmed by repeat (medication permitted). 2. History of torsades de pointes, significant Screening electrocardiogram (ECG) abnormalities, including ventricular rhythm disturbances, unstable cardiac arrhythmia requiring medication, pathologic symptomatic bradycardia, left bundle branch block, second degree atrioventricular (AV) block type II, third degree AV block, Grade ≥ 2 bradycardia, uncorrected hypokalemia not amenable to correction, congenital long QT syndrome, prolonged QT interval due to medications, corrected QT based on Fridericia's formula (QTcF) \> 450 msec (for men) or \> 470 msec (for women). 3. Symptomatic heart failure (per New York Heart Association guidelines; (Caraballo, 2019), unstable angina, myocardial infarction, severe cardiovascular disease (ejection fraction \< 20%, transient ischemic attack, or cerebrovascular accident within 6 months of Day 1). 8. Participant has a history of major surgery within 4 weeks of Screening. 9. Participant has experienced bowel obstruction related to the current cancer within the last 6 months or signs or symptoms of intestinal obstruction, which include nausea, vomiting, or objective radiologic finding of bowel obstruction in the last 4 weeks before the start of the treatment. 10. Participant has taken a prior cell cycle CHK1 inhibitor, including ACR-368

Conditions & Interventions

Interventions:
DRUG: ACR-368, DRUG: Gemcitabine, DIAGNOSTIC_TEST: OncoSignature
Conditions:
Endometrial Adenocarcinoma
Keywords:
Endometrial Cancer, Endometrial Neoplasm, Ultralow dose gemcitabine, ACR-368

More Information

Contact(s): Mansoor Raza Mirza, MD - ACR-368-201ClinicalTrial@acrivon.com
Principal Investigator:
Phase: PHASE2
IRB
Number:
System ID: NCT05548296
