ForPatients
by Roche

Breast CancerProstate CancerOvarian Cancer

A Study Evaluating the Safety, Pharmacokinetics and Efficacy of Ipatasertib Administered in Combination With Rucaparib in Participants With Advanced Breast, Ovarian Cancer, and Prostate Cancer.

Trial Status	Trial Runs In	Trial Identifier
Completed	5 Countries	NCT03840200 BO40933

The clinical trial information herein is sourced from public registries such as ClinicalTrials.gov, EuClinicalTrials.eu, and ISRCTN.com. Additional patient-friendly (lay) content has been prepared by Roche to support understanding.

Official Title:

A Phase Ib, Open-Label, Multicenter Study Evaluating the Safety and Efficacy of Ipatasertib in Combination With Rucaparib in Patients With Advanced Breast, Ovarian, or Prostate Cancer

Trial Summary:

This is a study in participants with advanced breast, ovarian, or prostate cancer to investigate the dose, safety, pharmacokinetics, and preliminary efficacy of ipatasertib in combination with rucaparib. The study consists of two parts: a Dose-Escalation Phase (Part 1) in participants with previously treated advanced breast cancer, ovarian cancer, or prostate cancer and a Dose-Expansion Phase (Part 2) in participants with advanced prostate cancer who have had at least one line of prior therapy with second-generation androgen-receptor (AR)-targeted agents (e.g., abiraterone, enzalutamide, apalutamide).

Hoffmann-La Roche
Sponsor

Phase 1
Phase

NCT03840200 BO40933
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

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Inclusion Criteria:

- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1
- A life expectancy of at least 3 months
- Ability to swallow oral study drug
- Have adequate organ and marrow function as confirmed by the laboratory values listed below, obtained within 28 days prior to the first dose of study treatment:
- Bone marrow function assessments (without transfusion within 28 days prior to receipt of study treatment):
- ANC >= 1500 cells/uL (1.5 x 10^9/L) without granulocyte-colony stimulating factor support
- Platelet count >= 100.0 x 10^9/L
- Hemoglobin >= 9 g/dL (or 5.6 mmol/L)
- Chemistry panel assessments:
- AST and ALT <= 1.5 x upper limit of normal (ULN); if liver metastases, <= 2.5 x ULN
- Bilirubin <= 1.5 x ULN (<= 3 x ULN if hyperbilirubinemia is due to Gilbert's syndrome)
- Serum albumin >= 3.0 g/dL
- Serum creatinine <= 1.5 x ULN or creatinine clearance >= 50 mL/min
- Fasting glucose <= 150 mg/dL and hemoglobin A1c <= 7.5%
- Resolved or stabilized toxicities resulting from previous therapy to Grade 1 (except for alopecia and neuropathy).

Cancer-Related Inclusion Criteria

- Have a histologically confirmed diagnosis of ovarian (Part 1 only), breast (Part 1 only) or prostate cancer (Part 1 and Part 2)
- Disease must be either metastatic or locally advanced disease that cannot be treated with curative intent
- For patients with ovarian cancer (Part 1 only):
- High-grade (2 or 3) serous or endometrioid or clear cell epithelial ovarian, fallopian tube, or primary peritoneal cancer (PPC)
- Must have received at least one prior platinum-based therapy and may have platinumsensitive disease (i.e., documented radiologic disease progression >= 6 months following the last dose of the platinum treatment administered) or platinum-resistant disease
- Have a CA-125 level that is > 2 x ULN
- Must have measurable disease by RECIST v1.1
- For patients with breast cancer (Part 1 only): must be human epidermal growth factor receptor 2 negative (HER2-) (estrogen receptor [ER]/progesterone positive or negative):
- ER/progesterone-positive patients must have received and progressed on at least one endocrine therapy (adjuvant or metastatic)
- ER/progesterone-negative/HER2- (triple-negative breast cancer [TNBC]) patients must have received at least one prior line of chemotherapy for metastatic breast cancer
- Must not have received more than two prior lines of chemotherapy for metastatic breast cancer
- Must have measurable disease by RECIST v1.1

For patients with prostate cancer:

- Adenocarcinoma of the prostate without small cell or neuroendocrine features
- Surgical or medical castration with testosterone < 50 ng/dL (1.7 nM)
- Patients treated with luteinizing hormone-releasing hormone analogs must have initiated therapy at least 4 weeks prior to the first dose of study treatment and continue throughout the study treatment
- Progression of prostate cancer either via PSA progression (two rising PSA levels measured >= 1 week apart, with second result >= 1 ng/mL) or radiographic progression with or without PSA progression

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- Must have received at least one prior line of second-generation androgen receptor targeted therapy (e.g., abiraterone, enzalutamide, apalutamide)
- Patients with prostate cancer must have either measurable disease by RECIST v1.1 or bone lesions by bone scan, or both.
- Submission of a formalin-fixed, paraffin-embedded (FFPE) tumor tissue block or a minimum of 12 freshly cut, unstained, serial tumor slides from the most recently collected tumor tissue for central molecular analysis (retrospective NGS testing for HR and PI3K-AKT pathway status and for other protocol-mandated secondary and exploratory assessments). Cytologic or fine needle aspirate samples are not acceptable. Tumor tissue from bone metastases is not acceptable.
- For men and women of child bearing potential: agreement to remain abstinent or use protocol defined contraceptive measures during the treatment period and for at least 28 days after the last dose of ipatasertib,or 6 months after the last dose of rucaparib, whichever occurs later

Exclusion Criteria:

- Pregnant or breastfeeding, or intending to become pregnant during the study or within 28 days after the final dose of ipatasertib or 6 months after the final dose of rucaparib
- Prior treatment with a PARP inhibitor, AKT inhibitor, or PI3K inhibitor
- Treatment with investigational therapy within 14 days prior to initiation of study drug
- Symptomatic and/or untreated CNS metastases
- Uncontrolled tumor-related pain
- Non-study-related minor surgical procedures <= 5 days or major (invasive) surgical procedure <=14 days prior to first dose of study treatment
- Patients with active hepatitis C virus (HCV)
- Hepatitis B virus (HBV) infection (chronic or acute), defined as having a positive hepatitis B surface antigen (HBsAg) test or a positive quantitative HBV DNA test
- Known HIV infection
- Illicit drug or alcohol abuse within 12 months prior to screening, in the investigator's judgment
- Malabsorption syndrome or other condition that would interfere with enteral absorption
- Serious infection requiring antibiotics within 14 days of first dose of study treatment
- Any serious medical condition or abnormality in clinical laboratory tests that, in the investigator's judgment, precludes the patient's safe participation in and completion of the study
- Need for chronic corticosteroid therapy of >= 10 mg of prednisone per day or an equivalent dose of other anti-inflammatory corticosteroids or immunosuppressants for a chronic disease
- History of another malignancy within 5 years prior to randomization, except for either adequately treated non-melanomatous carcinoma of the skin, adequately treated melanoma in situ, adequately treated non-muscle-invasive urothelial carcinoma of the bladder (Tis, Ta, and low-grade T1 tumors), or other malignancies where the patient has undergone potentially curative therapy with no evidence of disease and are deemed by the treating physician to have a recurrence rate of < 5% at 5 years.
- History of clinically significant cardiovascular dysfunction
- Presence of any other condition that may have increased the risk associated with study participation or may have interfered with the interpretation of study results, and, in the opinion of the investigator, would have made the patient inappropriate for entry into the study

Ipatasertib-Specific Exclusion Criteria:

- Type 1 or Type 2 diabetes mellitus requiring insulin at study entry
- History of inflammatory bowel disease (e.g., Crohn disease and ulcerative colitis), active bowel inflammation (e.g., diverticulitis)
- Treatment with strong CYP3A inhibitors or strong CYP3A inducers within 4 weeks or five elimination half-live of the inhibitors, whichever is longer, prior to initiation of study drug

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