ForPatients
by Roche

Breast Cancer

A Study to Evaluate the Safety and Efficacy of Ipatasertib in Combination With Atezolizumab and Paclitaxel or Nab-Paclitaxel in Participants With Locally Advanced or Metastatic Triple-Negative Breast Cancer

Trial Status	Trial Runs In	Trial Identifier
Completed	5 Countries	NCT03800836 CO40151

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

A Phase Ib, Open-Label, Multicenter Study Evaluating the Safety and Efficacy of Ipatasertib in Combination With Atezolizumab and Paclitaxel or Nab-Paclitaxel in Patients With Locally Advanced or Metastatic Triple-Negative Breast Cancer

Trial Summary:

This is a study consisting of four cohorts in this setting. In Cohort 1, the safety and efficacy of ipatasertib (ipat) in combination with atezolizumab (atezo) and paclitaxel (pac) or nab-paclitaxel will be evaluated for participants with locally advanced or metastatic triple-negative breast cancer (TNBC) who have not previously received chemotherapy. In Cohort 2, ipatasertib and atezolizumab (with no chemotherapy), will be administered to participants with locally advanced or metastatic TNBC. In Cohort 3, the safety and efficacy of neoadjuvant ipatasertib, atezolizumab, doxorubicin and cyclophosphamide (AC) (Ipat + Atezo + AC) followed by Ipat + Atezo + Pac will be evaluated in participants with locally advanced Type 2-4 (T2-4) TNBC. In Cohort 4, the safety and efficacy of Ipat + Atezo + Pac will be evaluated in participants with PD-L1 (Programmed Death-Ligand-1) positive locally advanced or metastatic TNBC that is not amenable to resection and who have not previously received chemotherapy in the advanced setting.

Hoffmann-La Roche
Sponsor

Phase 1
Phase

NCT03800836 CO40151
Trial Identifiers

Eligibility Criteria:

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Gender	Age	Healthy Volunteers
All	**#18 Years**	**No**

Inclusion Criteria:

General:

- Eastern Cooperative Oncology Group Performance Status of 0 or 1.
- Adequate hematologic and organ function.
- For Cohorts 1, 2 and 4: Life expectancy of at least 6 months.
- 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, 6 months after the last dose of paclitaxel, nab-paclitaxel, or doxorubicin, and 12 months after the last dose of cyclophosphamide, and 5 months after the last dose of atezolizumab, whichever occurs later along with refraining from donating sperm or eggs during this same period.

Disease-specific:

- For Cohorts 1, 2 and 4: histologically documented TNBC that is locally advanced or metastatic and is not amenable to resection with curative intent.
- For Cohort 2: disease progression following one or two lines of systemic therapy for inoperable locally advanced or metastatic TNBC.
- For Cohorts 1, 2 and 4: measurable disease according to RECIST v1.1 criteria.
- For Cohort 2: Treated brain or spinal cord metastases are allowed if participants have stable disease and are not on steroid treatment.
- For Cohort 3: histologically documented TNBC with a primary breast tumour size of > 2 cm by at least one radiographic or clinical measurement and disease stage at presentation of cT2-4 cN0-3 cM0.
- For Cohort 3: participant agreement to undergo appropriate surgical management, including axillary lymph node surgery and partial or total mastectomy, after completion of neoadjuvant treatment.
- For Cohort 4: participants must have centrally confirmed PD-L1-positive tumour.

Exclusion Criteria:

General:

- History of malabsorption syndrome or other condition that would interfere with enteral absorption or results in the inability or unwillingness to swallow pills.
- Active infection requiring antibiotics.
- History of or current evidence of HIV infection.
- Known clinically significant history of liver disease.
- Major surgical procedure, open biopsy, or significant traumatic injury within 28 days prior to Day 1 of Cycle 1 or anticipation of need for a major surgical procedure (other than anticipated breast surgery for Cohort 3) during the course of the study.
- Pregnant or breastfeeding.
- New York Heart Association (NYHA) Class II, III, or IV heart failure; left ventricular ejection fraction < 50%; or active ventricular arrhythmia requiring medication.
- Treatment with approved or investigational cancer therapy within 14 days prior to Day 1 of Cycle 1.
- Prior treatment with an Akt inhibitor.

Disease-specific:

- For Cohorts 1 and 4: history of or known presence of brain or spinal cord metastases.
- For Cohorts 1 and 4: participants who have received previous systemic therapy for inoperable locally advanced or metastatic TNBC, including chemotherapy, immune checkpoint inhibitors, or targeted agents.
- Unresolved, clinically significant toxicity from prior therapy, except for alopecia and Grade 1 peripheral neuropathy.
- Participants who have received palliative radiation treatment to peripheral sites (e.g., bone metastases) for pain control and whose last treatment was completed 14 days prior to Day 1 of Cycle 1 and have recovered from all acute, reversible effects.
- Uncontrolled pleural effusion, pericardial effusion, or ascites.
- Uncontrolled tumor related complications.
- Uncontrolled hypercalcaemia or symptomatic hypercalcaemia requiring continued use of bisphosphonate therapy.
- Malignancies other than breast cancer within 5 years prior to Day 1 of Cycle 1.
- For Cohort 3, participants with the following are excluded: [1] prior history of invasive breast cancer; [2] prior systemic therapy for treatment and/or prevention of invasive breast cancer; [3] previous therapy with anthracyclines or taxanes for any malignancy; [4] bilateral breast cancer; [5] undergone incisional and/or excisional biopsy of primary tumor and/or axillary lymph nodes; [6] undergone axillary lymph node dissection (ALND) prior to initiation of neoadjuvant therapy; [6] history of other malignancy within 5 years prior to screening; [7] history of cerebrovascular accident within 12 months prior to initiation of study treatment; [8] cardiopulmonary dysfunction; [9] known allergy or hypersensitivity to the components of cyclophosphamide/doxorubicin formulations and filgrastim or pegfilgrastim formulations; [10] severe infection within 4 weeks prior to initiation of study treatment; [11] treatment with therapeutic oral or IV (Intravenous) antibiotics within 2 weeks prior to initiation of study treatment and [12] prior treatment with CD137 agonists or immune checkpoint - blockade therapies.

Ipatasertib-specific:

- History of Type I or Type II diabetes mellitus requiring insulin.
- Grade >= 2 uncontrolled or untreated hypercholesterolemia or hypertriglyceridemia.
- History of or active inflammatory bowel disease or active bowel inflammation.
- Clinically significant lung disease.
- Treatment with strong CYP3A inhibitors or strong CYP3A inducers.

Atezolizumab-specific:

- Active or history of autoimmune disease or immune deficiency.
- History of idiopathic pulmonary fibrosis, organizing pneumonia (e.g., bronchiolitis obliterans), drug-induced pneumonitis, idiopathic pneumonitis, or evidence of active pneumonitis on screening chest computed tomography (CT) scan.
- Prior allogeneic stem cell or solid organ transplantation.
- Treatment with a live, attenuated vaccine within 4 weeks prior to initiation of study treatment, or anticipation of need for such a vaccine during treatment with atezolizumab or within 5 months after the last dose of atezolizumab.
- History of hypersensitivity reactions to study drug or any component of the study drug formulation.
- Treatment with systemic immunostimulatory agents and immunosuppressive medication treatment, or anticipation of need for systemic immunosuppressive medication during the course of the study.

Paclitaxel-specific:

- Grade >= 2 peripheral neuropathy.