ForPatients
by Roche

Breast CancerSolid TumorsCancer

A study to evaluate the safety, tolerability, processing by the body, and antitumor activity of inavolisib and paclitaxel

A Phase Ib, open-label, dose-escalation and dose-expansion study evaluating the safety, tolerability, pharmacokinetics, and preliminary antitumor activity of inavolisib in combination with paclitaxel in patients with locally advanced or metastatic solid tumors

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	7 Countries	2023-506745-33-00 ISRCTN45319897 CO42800

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, dose-escalation and dose-expansion study evaluating the safety, tolerability, pharmacokinetics, and preliminary antitumor activity of inavolisib in combination with paclitaxel in patients with locally advanced or metastatic solid tumors

Trial Summary:

This study will evaluate the safety (side effects), how the body processes the treatment (pharmacokinetics), what the treatment does to the body (pharmacodynamic effects), and preliminary anti-cancer activity of the drug inavolisib given in combination with the drug paclitaxel in patients with locally advanced or metastatic solid tumors, and of inavolisib given in combination with paclitaxel, in patients with locally advanced or metastatic PIK3CA-mutated (altered gene), HER2-positive breast cancer. Locally advanced cancer is cancer that has spread only to nearby tissues or lymph nodes, while metastatic cancer is cancer that has spread to other parts of the body.

Genentech, Inc (USA)
Sponsor

Phase 1
Phase

2023-506745-33-00 ISRCTN45319897 CO42800
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
Male and Female	18 and up	no

1. Why is the CO42800 clinical trial needed?

Solid tumour cancers are cancers that grow in any of the body's organs or tissues. Standard treatment includes surgery, chemotherapy and radiotherapy. Medicines that help the body's immune system fight cancer are also used. Yet, treatments can cause side effects, do not work for everyone, or stop working as time passes. So, new treatments are needed, especially for cancers that have grown and cannot be removed with surgery or that have spread to other parts of the body.

Inavolisib is an experimental drug. This means health authorities have not approved it for treating cancer. Inavolisib blocks a signal that cancer cells use to grow and multiply. This signal is called the PI3K pathway. In some cancers, the *PIK3CA* gene has changed or mutated. This *PIK3CA* mutation affects the PI3K pathway. As a result, cells grow and multiply more than normal. Researchers think that adding inavolisib to paclitaxel chemotherapy may improve treatment of certain cancers.

This clinical trial aims to test the safety of inavolisib and how well it works together with paclitaxel at different doses. Researchers will also look at how the body reacts to inavolisib plus paclitaxel. The trial will be in people with cancers that have grown or spread.

2. How does the CO42800 clinical trial work?

This clinical trial is recruiting people with solid tumour cancers that have grown or spread. People can take part if previous treatment has not worked, or it caused unacceptable side effects. People who take part in this clinical trial (participants) will be given the clinical trial treatment inavolisib plus paclitaxel for as long as it can help them. Treatment will be given in 'cycles' – a cycle is the treatment and recovery time, and each cycle will last 28 days. The clinical trial doctor will see participants 6 times in Cycle 1 then 4 times in all later cycles. Participants who stop having paclitaxel (for example, because it caused unacceptable side effects) may continue taking inavolisib and will be seen once a month. These hospital visits will include checks to see how participants respond to the treatment and any side effects they may have. Total time of participation in the clinical trial could range from 6 months to around 2 years, or longer if they benefit from the clinical trial treatment. Participants can stop trial treatment and leave the clinical trial at any time.

3. What are the main endpoints of the CO42800 clinical trial?

The main clinical trial endpoints (the main results measured in the trial to see how safe inavolisib together with paclitaxel is) are the maximum doses that can be given without unacceptable side effects, and the number and seriousness of any side effects.

The other clinical trial endpoints include:

- Number of participants whose cancers get smaller and the amount of time this lasts if the cancer then grows or spreads
- Number of participants whose cancers get smaller or stay the same size for at least 6 months after treatment
- The amount of time between the start of the trial treatment and participants' cancer possibly growing or spreading
- How the body breaks down and reacts to inavolisib when given with paclitaxel

4. Who can take part in this clinical trial?

People can take part in this trial if they are at least 18 years old. Participants that can become pregnant must agree to not have heterosexual sex or to use a reliable birth control method (and their male partners must use a condom with spermicide unless sterilization is confirmed) during the trial, for 6 months after the final dose of paclitaxel and 2 months after the final dose of inavolisib. During the trial and for up to 4 months after the final dose of paclitaxel and/or inavolisib, male participants must not donate sperm, must not have sex or use a condom plus another reliable birth control method if their partner is able to become pregnant, and those with pregnant partners must not have sex or use a condom. Participants must also agree to have a blood sample taken. People may not be able to take part in this trial if they have been given certain treatments or could not tolerate paclitaxel. People with diabetes and certain other diseases, infections or cancer that has spread to the brain and spinal cord may also not be able to take part.

5. What treatment will participants be given in this clinical trial?

Everyone who joins this clinical trial will be given treatment in 28-day cycles, as follows:

- Inavolisib, given as a tablet(s) (to be swallowed) daily
- Paclitaxel, given as an infusion (into the vein) on Days 1, 8, and 15 of each cycle and also optionally on Day 22 for each cycle

This is an open-label trial, which means everyone involved, including the participant and the clinical trial doctor, will know the clinical trial treatment the participant has been given.

6. Are there any risks or benefits in taking part in this clinical trial?

The safety or effectiveness of the experimental treatment or use may not be fully known at the time of the trial. Most trials involve some risks to the participant. However, it may not be greater than the risks related to routine medical care or the natural progression of the health condition. People who would like to participate will be told about any risks and benefits of taking part in the clinical trial, as well as any additional procedures, tests, or assessments they will be asked to undergo. All of these will be described in an informed consent document (a document that provides people with the information they need to decide to volunteer for the clinical trial).

Risks associated with the clinical trial drugs

Participants may have side effects (an unwanted effect of a drug or medical treatment) from the drugs used in this clinical trial. Side effects can be mild to severe, even life-threatening, and vary from person to person. Participants will be closely monitored during the clinical trial; safety assessments will be performed regularly.

Participants will be told about the known side effects of inavolisib and paclitaxel and possible side effects based on human and laboratory studies or knowledge of similar drugs. Inavolisib will be given as a tablet (to be swallowed) and paclitaxel as an infusion into the vein (intravenous infusion). Participants will be told about any known side effects of swallowing tablets and intravenous infusions.

Potential benefits associated with the clinical trial

Participants' health may or may not improve from participation in the clinical trial. Still, the information collected may help other people with similar medical conditions in the future.

Inclusion Criteria:

- Signed Informed Consent Form
- Aged over 18 years and over
- Evaluable or measurable disease per RECIST, v1.1
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Life expectancy of >12 weeks
- Adequate hematologic and organ function within 14 days prior to initiation of study treatment, defined by the following:
    - Absolute neutrophil count 1500/µl
    - Hemoglobin #9 g/dl
    - Platelet count #100,000/l
    - Fasting glucose <126 mg/dL or <7 mmol/l and glycosylated hemoglobin (HbA1C) 5.7% or <39 millimoles per mole (mmol/mol)
    - Total bilirubin <1.5 upper limit of normal (ULN)
    - Serum albumin #2.5 g/dl or 25 g/l
    - AST and ALT #2.5 ULN with the following exception: patients with documented liver metastases may have AST and ALT #5.0 ULN.
    - Serum creatinine 1.5 ULN or creatinine clearance #50 ml/min on the basis of the Cockcroft-Gault glomerular filtration rate estimation
    - International normalized ratio (INR) <1.5 x upper limit of normal (ULN) and activated partial thromboplastin time (aPTT) <1.5 x ULN
- Consent to provide fresh (preferred) or archival tumor tissue specimen. It is preferred that the specimen be from the most recently collected and available tumor tissue, and whenever possible, from a metastatic site of disease.
- Consent to provide a freshly collected pre-treatment blood sample.
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use a highly effective form of contraceptive method with a failure rate of 1% per year in combination with use of male condom with spermicide (for male partners), unless male sterilization has been confirmed.

- For men: agreement to remain abstinent (refrain from heterosexual intercourse) or use highly effective contraceptive measures, and agreement to refrain from donating sperm.

Inclusion Criteria Specific to Patients Enrolling in Part 1, Arm A:

- Histologically documented, locally advanced, recurrent, or metastatic, incurable solid tumor malignancy that has progressed after available standard systemic therapies; or for whom standard therapy has proven to be ineffective or intolerable; or for whom a clinical trial of an investigational agent is a recognized standard of care. If there are other available SOC therapies, these will be discussed with the patient and documented before informed consent is obtained.

Inclusion Criteria Specific to Patients Enrolling in Part 2, Arm A Expansion Cohorts:

- Histologically documented, locally advanced, recurrent, or metastatic, incurable solid tumor malignancy with a known PIK3CA mutation that has progressed after at least one available standard systemic therapy in the metastatic setting.
  - Cohort 1 (HNSCC): Histologically or cytologically confirmed recurrent and/or metastatic HNSCC that has been previously treated with systemic therapy in the recurrent and/or metastatic setting, which may include immunotherapy and/or chemotherapy with or without cetuximab.
  - Cohort 2 (ovarian cancer): Persistent or recurrent epithelial ovarian, fallopian tube, or primary peritoneal tumors that have been previously treated with up to 4 prior regimens in the recurrent and/or metastatic setting, being at least one platinum-based. Patients may have received bevacizumab and/or poly-ADP ribose polymerase (PARP) inhibitors.
  - Cohort 3 (TNBC): Histologically or cytologically confirmed adenocarcinoma of the breast that is locally advanced or metastatic, not amenable to surgical or radiation therapy with curative intent, which has progressed after all available standard therapies, or for which standard therapy has proven to be ineffective or intolerable.
  - Cohort 4 (endocrine resistant/refractory HR-positive, HER2 negative breast cancer): Histologically or cytologically confirmed adenocarcinoma of the breast that is locally advanced or metastatic and is not amenable to surgical or radiation therapy with curative intent and has progressed after all available endocrine-based standard therapies in the locally advanced/metastatic setting or for which endocrine-based standard therapy has proven to be ineffective or intolerable.
- Confirmation of biomarker eligibility: valid results from central testing of blood or local testing of blood or tumor tissue documenting PIK3CA-mutated tumor status is required for patients enrolling to Part 2, Arm A, expansion cohorts.

Exclusion Criteria:

- Metaplastic breast cancer
- Any history of leptomeningeal disease
- Type 2 diabetes requiring ongoing systemic treatment at the time of study entry; or any history of Type 1 diabetes
- Inability or unwillingness to swallow pills
- Malabsorption syndrome or other condition that would interfere with enteral absorption
- Known and untreated, or active CNS metastases (progressing or requiring anticonvulsants or corticosteroids for symptomatic control).
- Uncontrolled pleural effusion or ascites requiring recurrent drainage procedures twice per month or more frequently
- Any active infection that, in the opinion of the investigator, could impact patient safety; or, serious infection requiring IV antibiotics within 7 days prior to Day 1 of Cycle 1

- Any concurrent ocular or intraocular condition (e.g., cataract or diabetic retinopathy) that, in the opinion of the investigator or study ophthalmologist, would require medical or surgical intervention during the study period to prevent or treat vision loss that might result from that condition
- Active inflammatory (e.g., uveitis or vitritis) or infectious (e.g., conjunctivitis, keratitis, scleritis, or endophthalmitis) conditions in either eye or history of idiopathic or autoimmuneassociated uveitis in either eye
- Patients requiring any daily supplemental oxygen
- History of or active inflammatory disease (e.g., Crohn's disease or ulcerative colitis), or any active bowel inflammation (including diverticulitis). Patients currently receiving immunosuppressants (e.g., sulfasalazines) are considered to have active disease; therefore, they are ineligible.
- Symptomatic hypercalcemia requiring continued use of bisphosphonate or denosumab therapy
- Clinically significant history of liver disease, including severe liver impairment (Child-Pugh Class B/C), viral or other hepatitis, current alcohol abuse, or cirrhosis
- Known HIV infection
- Any other diseases, active or uncontrolled pulmonary dysfunction, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug, that may affect the interpretation of the results, or renders the patients at high risk from treatment complications
- Significant traumatic injury or major surgical procedure within 4 weeks prior to initiation of study treatment
- Radiation therapy (other than palliative radiation to bony metastases) as cancer therapy within 4 weeks prior to initiation of study treatment
- Palliative radiation to bony metastases within 2 weeks prior to initiation of study treatment
- Unresolved toxicity from prior therapy, except for the following: Alopecia Grade 1 and peripheral neuropathy
- Inability to comply with study and follow-up procedures
- History of other malignancy within 5 years prior to screening, with the exception of patients with a negligible risk of metastasis or death and/or treated with expected curative outcome (such as appropriately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, localized prostate cancer, ductal carcinoma in situ, or Stage I uterine cancer)
- History of or active ventricular dysrhythmias or congestive heart failure requiring medication or coronary heart disease that is symptomatic
- Clinically significant electrolyte abnormalities (e.g., hypokalemia, hypomagnesemia, hypocalcemia)
- Congenital long QT syndrome or QT interval corrected with Fridericia's formula (QTcF) 470 ms demonstrated by at least two ECGs 30 minutes apart, or family history of sudden unexplained death or long QT syndrome
- Current treatment with medications that are well known to prolong the QT interval
- Allergy or hypersensitivity to components of the inavolisib formulation and paclitaxel
- Pregnancy, lactation, or intention to become pregnant or fathering a child during the study
- Women of childbearing potential (including those who have had a tubal ligation) must have a negative serum pregnancy test result within 14 days prior to initiation of study treatment.

Exclusion Criteria Specific to Patients Enrolling Part 1, Arm A:

- History of prior significant toxicity related to a PI3K, AKT, or mTOR inhibitor requiring discontinuation of treatment. Patients may have received prior treatment with a PI3K, AKT, or mTOR inhibitor
- History of prior significant toxicity related to paclitaxel treatment requiring discontinuation of treatment. Patients may have received prior treatment with paclitaxel
- Treatment with chemotherapy, immunotherapy, or biologic therapy as anti-cancer therapy within 21 days prior to initiation of study treatment, except for the following: Kinase inhibitors, approved by regulatory authorities, may be used up to 2 weeks prior to initiation of study treatment, provided any drug-related toxicity has resolved up to Grade 1 and prior approval is obtained from the Medical Monitor. Treatment with an investigational agent within 3 weeks or five half-lives prior to initiation of

study treatment, whichever is shorter. A shorter washout period may be allowed if the patient has adequately recovered from any clinically relevant toxicity and with prior approval from the Medical Monitor.
- Prior anti-cancer therapy that fulfills the following criteria: High dose chemotherapy requiring stem-cell support; Irradiation to 25% of bone marrow-bearing areas

Exclusion Criteria Specific to Patients Enrolling Part 2, Arm A:

- History of prior significant toxicity related to a PI3K, AKT, or mTOR inhibitor requiring discontinuation of treatment.
- Prior treatment with any PI3K-specific inhibitor
- History of prior significant toxicity related to paclitaxel treatment requiring discontinuation of treatment. Patients may have received prior treatment with paclitaxel
- Treatment with chemotherapy, immunotherapy, or biologic therapy as anti-cancer therapy within 21 days prior to initiation of study treatment, except for the following: Kinase inhibitors, approved by regulatory authorities, may be used up to 2 weeks prior to initiation of study treatment, provided any drug-related toxicity has resolved up to Grade 1 and prior approval is obtained from the Medical Monitor Treatment with an investigational agent within 3 weeks or five half-lives prior to initiation of study treatment, whichever is shorter
- Prior anti-cancer therapy that fulfills the following criteria: high dose chemotherapy requiring stem-cell support Irradiation to 25% of bone marrow-bearing areas