

[Triple Negative Breast Cancer](#)[Metastatic Breast Cancer](#)[Breast Cancer Er-Positive](#)[Breast CancerHER2-Positive Breast Cancer](#)

**A clinical trial to look at how safe new treatment combinations are and how well they work for people with breast cancer that has grown and cannot be removed with surgery, or has spread in the body**

A Study Evaluating the Efficacy and Safety of Multiple Treatment Combinations in Patients With Metastatic Triple-Negative Breast Cancer (Morpheus-pan-BC)

**Trial Status**  
**Recruiting**

**Trial Runs In**  
**9 Countries**

**Trial Identifier**  
**NCT03424005 2023-503629-20-00**  
**CO40115**

*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/II, open-label, multicenter, randomized umbrella study evaluating the efficacy and safety of multiple treatment combinations in patients with metastatic breast cancer (MORPHEUS-panBC)

## ***Trial Summary:***

This is an umbrella study evaluating the efficacy and safety of multiple treatment combinations in participants with metastatic or inoperable locally advanced breast cancer. The study will be performed in two stages. During Stage 1, four cohorts will be enrolled in parallel in this study: Cohort 1 will consist of Programmed death-ligand 1 (PD-L1)-positive participants who have received no prior systemic therapy for metastatic or inoperable locally advanced triple-negative breast cancer (TNBC) (first-line [1L] PD-L1+ cohort). Cohort 2 will consist of participants who had disease progression during or following 1L treatment with chemotherapy for metastatic or inoperable locally-advanced TNBC and have not received cancer immunotherapy (CIT) (second-line [2L] CIT-naïve cohort). Cohort 3 will consist of participants with locally-advanced or metastatic HR+, HER2-negative disease with PIK3CA mutation who may or may not have had disease progression during or following previous lines of treatment for metastatic disease (HR+cohort). Cohort 4 will consist of participants with locally-advanced or metastatic HER2+ /HER2-low disease with PIK3CA mutation who had disease progression on standard-of-care therapies (HER2+ / HER2-low cohort). In each cohort, eligible participants will initially be assigned to one of several treatment arms (Stage 1). In addition, participants in the 2L CIT-naïve cohort who experience disease progression, loss of clinical benefit, or unacceptable toxicity during Stage 1 may be eligible to continue treatment with a different treatment combination (Stage 2), provided Stage 2 is open for enrollment.

Hoffmann-La Roche  
Sponsor

Phase 1/Phase 2  
Phase

NCT03424005 2023-503629-20-00 CO40115  
Trial Identifiers

## Eligibility Criteria:

Gender <b>All</b>	Age <b># 18 Years</b>	Healthy Volunteers <b>No</b>
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### 1. Why is the MORPHEUS-panBC clinical trial needed?

Breast cancer can be challenging to treat if it has spread to nearby tissues and cannot be removed with surgery (known as 'locally advanced unresectable breast cancer') or if it has spread to other parts of the body (known as 'metastatic breast cancer'). Standard treatment includes chemotherapy (such as capecitabine, nab-paclitaxel and carboplatin) and/or hormone or targeted treatments (such as atezolizumab) depending on the type of breast cancer a person has.

New treatment combinations are needed to improve health outcomes for people with locally advanced unresectable or metastatic breast cancer. New treatment combinations are not currently approved as standard for treating breast cancer.

This clinical trial aims to compare the effects, good or bad, of new treatment combinations in people with locally advanced unresectable or metastatic breast cancer.

### 2. How does the MORPHEUS-panBC clinical trial work?

This clinical trial is recruiting people with certain types of locally advanced unresectable or metastatic breast cancer. People can take part if they also fit other criteria to join a treatment group.

People who take part in this clinical trial (participants) will be given the clinical trial treatment for as long as it can help them unless they have unacceptable side effects. The clinical trial doctor will see them regularly. These hospital visits will include checks to see how the participant responds to the treatment, and any side effects they may have. The total time of participation in the clinical trial may be 1–2 years for treatment, plus follow-up time after the last dose of treatment to check for any side effects. Participants who have cancer that gets worse while they are being given a particular clinical trial treatment, or who have unacceptable side effects, may be able to be given a different treatment in this clinical trial if they meet the criteria. Participants can stop trial treatment and leave the clinical trial at any time.

### **3. What are the main endpoints of the MORPHEUS-panBC clinical trial?**

The main clinical trial endpoint (the main result measured in the trial to see if the drug has worked) is the number of participants whose cancer shrinks or disappears during treatment (objective response rate).

The other clinical trial endpoints include:

- The length of time between the start of the trial and participants' cancer progressing (progression-free survival)
- The number of participants whose cancer stays the same, shrinks or disappears for at least 3 months during treatment, (disease control rate)
- How long participants live (overall survival)
- The length of time between participants' cancer starting to shrink to cancer progressing (duration of response)
- The number and seriousness of any side effects

### **4. Who can take part in this clinical trial?**

People can take part in this trial if they are at least 18 years old, have locally advanced unresectable or metastatic breast cancer, and can have a sample of breast cancer taken (known as a 'biopsy'). They must also meet certain criteria to join a particular treatment group, including the type of breast cancer they have – such as triple-negative breast cancer (TNBC), ER-positive or HER2-positive breast cancer – and which treatments they have been given before, if any.

People may not be able to take part in this trial if they have cancer that has spread to the brain or spinal cord and causes symptoms, certain medical conditions such as heart or lung diseases or certain infections, have had severe reactions to previous cancer treatment, or are pregnant or breastfeeding.

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

Everyone who joins this clinical trial will be placed into a treatment group that they fit the criteria for. The treatment group will depend on the participant's breast cancer type and any treatments they have received before.

Treatments will be given as combinations of pills (to be swallowed), injections under the skin, or infusions (into the vein) in treatment cycles – a treatment cycle is the period of treatment and recovery time before the next dose of treatment is given – a cycle is usually 3 or 4 weeks.

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 clinical trial drugs and possible side effects based on human and laboratory studies or knowledge of similar drugs. Participants will also be told about any known side effects of swallowing pills, being given injections under the skin (subcutaneous injections), or infusion into the vein (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:***

Patients must meet all of the following criteria to qualify for Stage 1 (all cohorts) and to qualify for Stage 2 (2L CIT-naïve cohort):

- Age  $\geq$  18 years at the time of signing Informed Consent Form
- ECOG Performance Status of 0 or 1
- Able to comply with the study protocol, in the investigator's judgment
- Metastatic or inoperable locally advanced breast cancer
- Measurable disease (at least one target lesion) according to RECIST v1.1
- Life expectancy  $\geq$  3 months, as determined by the investigator
- Tumor accessible for biopsy, unless archival tissue is available
- Availability of a representative tumor specimen that is suitable for biomarker analysis via central testing
- Adequate hematologic and end-organ function, defined by the following laboratory test results, obtained within 14 days prior to initiation of study treatment
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures and agreement to refrain from breastfeeding and donating eggs, as outlined for each specific treatment arm

- For men: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures, and agreement to refrain from donating sperm, as outlined for each specific treatment arm

## ***Exclusion Criteria:***

### Exclusion Criteria for Stage 1

- Prior treatment with T-cell co-stimulating or immune checkpoint blockade therapies, including anti-CTLA-4, anti-PD-1, and anti-PD-L1 therapeutic antibodies, CD40 agonists or interleukin-2 (IL-2) or IL-2-like compounds
- Treatment with investigational therapy within 28 days prior to initiation of study treatment
- Biologic treatment (e.g., bevacizumab) within 2 weeks prior to initiation of study treatment, or other systemic treatment for TNBC within 2 weeks or 5 half-lives of the drug (whichever is longer) prior to initiation of study treatment
- Adverse events from prior anti-cancer therapy that have not resolved to Grade  $\leq$  1 or better with the exception of alopecia of any grade and Grade  $\leq$  2 peripheral neuropathy
- Eligibility only for the control arm

### Exclusion Criteria for Stage 1 (both cohorts) and Stage 2 (2L CIT-naïve cohort)

- Uncontrolled pleural effusion, pericardial effusion, or ascites requiring recurrent drainage procedures (once monthly or more frequently)
- Uncontrolled tumor-related pain
- Symptomatic, untreated, or actively progressing central nervous system (CNS) metastases
- History of leptomeningeal disease
- Active or history of autoimmune disease or immune deficiency
- History of idiopathic pulmonary fibrosis, organizing pneumonia (e.g., bronchiolitis obliterans), drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest computed tomography (CT) scan. History of radiation pneumonitis in the radiation field (fibrosis) is permitted.
- Active tuberculosis
- Severe infection within 4 weeks prior to initiation of study treatment
- Treatment with therapeutic oral or IV antibiotics within 2 weeks prior to initiation of study treatment
- Significant cardiovascular disease
- Prior allogeneic stem cell or solid organ transplantation
- History of malignancy other than breast cancer within 2 years prior to screening, with the exception of those with a negligible risk of metastasis or death
- Treatment with systemic immunosuppressive medication (including, but not limited to, corticosteroids, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-tumor necrosis factor alpha agents) within 2 weeks prior to initiation of study treatment, or anticipation of need for systemic immunosuppressive medication during the course of the study
- Pregnancy or breastfeeding, or intention of becoming pregnant during the study