Lay Language Summary

PATHFINDER

Ipatasertib with non-taxane chemotherapy for taxane-pretreated unresectable locally advanced or metastatic triple-negative breast cancer

IMPORTANT:

- The document contains the summary of a clinical trial, and its sole purpose is to communicate the results of it to the general public.
- This document is not intended to promote recruitment or provide medical advice.
- The results reflected in this document may contradict those of other trials.
- It is not recommended to make decisions based on the information collected in this document; it should always be consulted with a medical professional beforehand.

ABOUT THIS SUMMARY

SPONSOR: MEDICA SCIENTIA INNOVATION RESEARCH S.L.

TUMOR TYPE: Triple-Negative Breast Cancer (TNBC)

MEDICINE(S) STUDIED: Ipatasertib and non-taxane chemotherapy

DATES OF STUDY: July 2020 to November 2022

TITLE OF THIS STUDY: Ipatasertib with non-taxane chemotherapy for taxane-pretreated unresectable locally advanced or metastatic triple-negative breast cancer

DATE OF THIS REPORT: May 2024

STUDY FUNDER: F. Hoffman - La Roche

CLINICAL TRIALS.GOV: NCT04464174

The content for this document was finalised by **Medica Scientia Innovation Research (MEDSIR) - Oncoclínicas&Co** on the 10th of May of 2024. The information in this summary does not include additional information available after this date.

What was the purpose of this study?

Ipatasertib is drug that inhibits AKT, a protein known to be key for tumor growth and survival. Particularly when it is combined with other anti-cancer medications, it has shown considerable effectiveness against various cancer types, such as breast, prostate, and ovarian cancers.

To date, the efficacy of ipatasertib has been evaluated when paired with taxane chemotherapy, anti-HER2 targeted therapy, immunotherapy, endocrine therapy, and PARP inhibitors. The PATHFINDER study aimed to evaluate the safety and tolerability (main objective), as well as the preliminary efficacy (secondary objective) of ipatasertib in combination with non-taxane chemotherapy in patients with advanced triple negative breast cancer (TNBC) who had previously experienced tumor progression after treatment with taxane chemotherapy.

What did researchers want to find out?

When a new treatment shows promise, it is essential to thoroughly investigate its safety and effectiveness, especially when used alongside other treatments or at different stages of treatment, from first diagnosis to tumors progressing after initial medication. The PATHFINDER study was developed with this purpose. It was an exploratory study, meaning it did not start with a specific hypothesis to test. Instead, its goal was to evaluate the safety and tolerability of combining ipatasertib with three different non-taxane chemotherapy. These combinations included ipatasertib with either capecitabine (arm A), eribulin (arm B), or carboplatin+gemcitabine (arm C). Initially, a safety phase involving only three patients per combination was conducted. If any serious side effects occurred, treatment dose was reduced or stopped. However, if the combinations were well tolerated, treatment proceeded, and safety was further evaluated with more patients. Simultaneously, the preliminary efficacy of the treatment combinations was also evaluated.

When and where did the studies take place?

From July 30th, 2020, through November 11th, 2022, a total of 74 participants were screened at 11 hospitals in Spain. Ultimately, 54 participants were enrolled and assigned to the different treatment arms of the study: 22 participants in arm A, 25 participants in arm B, and 7 participants in arm C.

What were the results of the study?

Overall, the safety profile in arm A and arm B was found to be acceptable, with 27.3% and 68% of side effects appearing after treatment initiation (TEAEs), respectively. Notably, among the 68% of TEAEs in arm B, 20% of them were attributed to neutropenia, a slightly toxic side effect. In contrast, the combination tested in arm C was deemed intolerable, with 100% of TEAEs. No treatment-related deaths were reported in any treatment arm.

Regarding efficacy, these treatments showed modest clinical activity, measured with different efficacy outcomes, such as the time a patient's disease remains stable without getting worse during treatment (progression-free survival) or the time from the start of treatment until the patient's death from any cause (overall survival). Interestingly, two patients, one from arm A and another from arm B, showed prolonged responses lasting over 30 months. Notably, the combination of ipatasertib+eribulin showed improved progression-free survival compared to previous studies evaluating eribulin treatment alone.

What were the main medical conclusions?

The PATHFINDER study revealed that combining ipatasertib with capecitabine and eribulin has an acceptable safety profile in patients with advanced TNBC whose tumor had progressed after previous taxane chemotherapy. However, adding ipatasertib alongside carboplatin plus gemcitabine proved to be intolerable. Additionally, the combination of ipatasertib and eribulin demonstrated encouraging efficacy, warranting further investigation.

Where I can find more information?

Your doctor can help you understand more about this study and the results. Speak to your doctor about the treatment options available in your country. You should not make changes to your care based on the results of this or any single study. Keep taking your current treatment unless instructed by your doctor.

For more details, please visit:
https://www.medsir.org/pathfinder-clinical-trial

The full scientific report of this study is available online at:
www.clinicaltrials.gov

Thank you who took part in the study

If you took part in this study, **Medica Scientia Innovation Research (MEDSIR) - Oncoclínicas&Co**, as the Sponsor, extends its gratitude for your participation. This overview will outline the findings of the study. If you have any queries regarding the study or its outcomes, please reach out to the doctor or staff at your study location.

About Oncoclínicas & CO

Oncoclínicas - the largest cancer care group in Latin America - has a specialized, innovative model that focuses on the entire oncology care process, combining operational efficiency, humanized service and high specialization, through a medical team made up of more than 2,600 professionals, who mainly specialize in oncology. With the mission of making cancer treatment accessible to everyone in the country, it offers a complete operational system made up of outpatient clinics integrated with highly complex oncology centers. It currently has 134 units in 35 Brazilian cities, providing access to cancer care in all regions where it operates, with the quality standards of the best cancer centers in the world.

Through technology, precision medicine and genomics, Oncoclínicas ensures effective results and facilitates access to oncology treatment and has performed more than 595,000 treatments in the last 12 months alone. It is the exclusive partner in Brazil of the Dana-Farber Cancer Institute, an affiliate of Harvard Medical School and one of the most prestigious cancer research and treatment centers in the world. The Group also owns Boston Lighthouse Innovation, a bioinformatics company based in Cambridge, USA, and holds shares in MEDSIR, a Spanish company dedicated to the development and management of clinical trials for independent cancer research. The company is also developing projects in collaboration with the Weizmann Institute of Science in Israel, one of the world's most prestigious multidisciplinary scientific and research institutions, whose international board includes Bruno Ferrari, founder and CEO of Oncoclínicas.

For further information: www.grupooncoclinicas.com

ABOUT MEDSIR

Founded in 2012, MEDSIR works closely with its partners to drive innovation in oncology research. Based in Spain and the United States, the company manages all aspects of clinical trials, from study design to publication, utilizing a global network of experts and integrated technology to streamline the process. The company offers proof-of-concept support and a strategic approach that helps research partners experience the best of both worlds from industry-based clinical research and investigator-driven trials. To promote independent cancer research worldwide, MEDSIR has a strategic alliance with Oncoclínicas, the leading oncology group in Brazil with the greatest research potential in South America. Learn how MEDSIR brings ideas to life: www.medsir.org