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Lay Language Summary

transFAL

Prospective evaluation of predictive biomarkers for palbociclib and endocrine therapy benefit in hormone receptor (HR)-positive [+]/human epidermal growth factor receptor 2 (HER2)-negative|-] advanced breast cancer patients from PARSIFAL clinical trial: The transFAl sub-study.

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.

MEDICINE(S) STUDIED: Palbociclib + letrozole or fulvestrant in HR[+]/HER2[-] advanced breast cancer

TITLE OF THIS STUDY: Prospective evaluation of predictive biomarkers for palbociclib and endocrine therapy benefit in hormone receptor (HR)-positive [+]/human epidermal growth factor receptor 2 (HER2)-negative|-] advanced breast cancer patients from PARSIFAL clinical trial: The transFAI sub-study.

DATE OF THIS REPORT: March 2024

PHARMACEUTIC PARTNERS: PFIZER S.L.U.

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Context

Breast cancer is the most frequently diagnosed cancer in women, with an estimated global incidence of 2.21 million cases reported in 2020. Within breast cancer, there are multiple subtypes that have different behaviors and outcomes. One common type of breast cancer is one that has 1 or 2 hormone receptors (HR positive (HR[+]) and little to no receptors for HER2 (HER2-negative (HER2[-]), which is known as HR+/HER2- breast cancer. Additionally, breast cancer can be categorized as “advanced” when it has spread from the breast to other parts of the body.

Drugs that inhibit cyclin-dependent kinases 4 and 6 (CDK4/6) in combination with treatments that add, block, or remove hormones (endocrine therapy) is the standard first treatment for patients that have this subtype of breast cancer known as HR[+]/HER2[-] advanced breast cancer. However, despite this being the standard of care, there is still subset of patients that do not respond to this treatment. To better understand differences in response to treatment, many studies have evaluated different biomarkers (a measurable indicator that provides information about biological processes, conditions, or diseases) that could help identify which patients are more likely to have a benefit. Unfortunately, these studies have mostly been unsuccessful, and whether a patient is HR+ remains the only validated indication that a patient should receive a CDK4/6 inhibitor plus endocrine therapy.

About the transFAL study

The transFAL study, was a set of exploratory studies with the aim of uncovering biomarkers of response or resistance to palbociclib- (a CDK 4/6 inhibitor) plus endocrine therapy-based regimens. To do this, analysis was done on samples from the PARSIFAL study, a clinical trial that evaluated which endocrine therapy (fulvestrant or letrozole) was the optimal partner for palbociclib. PARSIFAL found that both treatments had comparable results, therefore both groups could be used in the exploratory analysis. transFAL consisted of analysis of both tissue samples and blood samples. The participants of the PARSIFAL study were defined as resistant or sensitive to treatment based or their progression-free survival (PFS), or the amount of time during and after treatment that the patient lived with the disease not getting any worse.

For the tissue analysis, were categorized as resistant to treatment if the disease got worse in the first 12 months after treatment began and patients with a PFS longer than 12 months were considered sensitive to treatment.

Multiple biomarkers were assessed in the PARSIFAL tissue samples, but none of them demonstrated a significant association with a clinical benefit. When patients were grouped into categories of high versus low expression of the corresponding biomarkers, it was found that low expression of CDK6 (a protein that plays a key role in the cell cycle relgulation) and Ki67 (a prognostic factor predicting relapse-free and overall survival in breast cancer patients) were associated with a longer time in which patients did not experience their cancer getting worse and a longer length of time that patients remained alive (overall survival). Proteomics studies, or the studies on the structure and function of proteins, were also carried out on the tissue samples, but no difference was found between resistant and sensitive participants.

transFAL also evaluated blood samples from participants. As a tumor grows, the cells die and are replaced, and during this process the dead cells release their contents, including DNA, into the bloodstream. This DNA can be measured and is known as circulating tumor DNA (ctDNA). In the transFAL substudies, ctDNA was evaluated between resistant (PFS < 9 months) and sensitive (PFS >31 months) participants. Mutations in TP53 (tumor suppressor gene) was associated with a shorter PFS, whereas MTOR (regulates cell proliferation and death) and GNAS (gene that encodes a protein responsible for transmembrane signal transduction) were correlated with longer PFS. It was also found that patients with a larger amount of ctDNA at baseline were more likely to be resistant to treatment.

In the transFAL exploratory substudies, we found that high expression of Ki67 and CDK6, and high ctDNA density at baseline were all associated with shorter PFS and OS. These findings could help guide future studies that aim to determine mechanisms of resistance to CDK4/6 inhibitors. The pursuit of biomarkers that can guide treatment decisions is crucial for the advancement of personalized medicine.

Where I can find more information about the study?

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.

Thank you to the people who took part in the study

If you took part in this study, **MEDSIR**, 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 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.