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Lay Language Summary

PARSIFAL-LONG

Extended follow-up of hormone receptor-positive/HER2-negative advanced breast cancer patients treated with fulvestrant and palbociclib vs letrozole and palbociclib in the PARSIFAL study

Context

About 70-80% of newly diagnosed breast cancers are hormone receptor positive. Hormone receptor positive/HER2 negative (HR[+]/HER2[-]) breast cancer is characterized by breast tumors that are positive for estrogen receptors, progesterone receptors, or both; and have very low to no expression of HER2 receptors. When breast cancer starts to spread to other parts of the body, it is considered advanced breast cancer.

Cyclin dependent kinase 4/6 inhibitors are drugs that interrupt the growth of cancer cells and have transformed the treatment of HR[+]/HER2[-] advanced breast cancer. There are currently three CDK 4/6 inhibitors (Palbociclib, ribociclib, abemaciclib) that are approved by the FDA (USA) and EMA (Europe) in combination with hormone therapy for HR[+]/HER2[-] advanced breast cancer.

Presented at San Antonio Breast Cancer Symposium (SABCS) 2023

The PARSIFAL clinical trial assessed whether fulvestrant (a selective estrogen receptor degrader) or letrozole (an aromatase inhibitor that blocks estrogen production), was the optimal drug to be combined with palbociclib for the treatment of HR[+]/HER2[-] advanced breast cancer. The study involved a total of 486 patients and found no difference between the drugs in terms of the amount of time the treatment was able to prevent the breast cancer from getting worse, known as progression-free survival. This is relevant since letrozole is an oral medication whereas fulvestrant is administered through an injection in the muscle.

About PARSIFAL-LONG

PARSIFAL-LONG, is a 5-year extended follow-up of the PARSIFAL study. In this analysis, the primary goal was to assess the overall survival, or the time from enrollment to death from any cause, between the two groups. In addition, the study assessed the extended progression-free survival (time from randomization until the disease getting worse), the overall survival (time from randomization until death) from the combined groups, and the post progression effectiveness or the how well the treatment worked in terms of the time from disease worsening after the first treatment to death of any cause. As exploratory analysis, this extended follow-up also aimed to determine if having an early progression (the disease getting worse in under 12 months while on treatment) could be an indicator of resistance to therapy.

Patients who participated

This study included 389 patients from 32 of the original 47 sites. This represents 80% of all patients initially included in the PARSIFAL. Of note, the centers in this analysis were the ones that included all patients at the given site and had to have obtained a new informed consent, when applicable and depending on each country's regulations. Patient characteristics in the PARSIFAL-LONG analysis were similar to those included in the PARSIFAL analysis.

What were the results?

At this extended analysis, the results show that there were still no observed differences in either overall time to death or time to disease worsening when palbociclib was combined with either letrozole or fulvestrant. Given that there was no difference between groups, they were combined, and it was determined that the progression-free survival was 33.2 months, and the overall survival was 65.4 months. There were 86 patients (12.8%) that had a progression within the first year on treatment, with a progression-free survival of 24 months and an overall survival of 7 months. The remaining patients were progression-free at 12 months and had better outcomes, since the time until their disease got worse or until they died were much higher (49.8 months and 81.5 months, respectively). Patients who experienced a progression during the 5-year follow-up were then assessed based on the time that they progressed. Those who progressed within the first year had an overall survival of 18 months compared to 27 months for patients that progressed after a year.

Conclusions

This extended analysis further confirmed that there is no difference between letrozole or fulvestrant when combined with palbociclib. Additionally, the progression-free survival and overall survival were consistent with those of the other CDK4/6 inhibitor-based regimens when used as the first treatment option for patients with HR[+]/HER2[-] advanced breast cancer. Progression within the first year may also be indicative of a less favorable outcome.