Effect on alpelisib benefit of having 6 months or less or more than 6 months of prior cyclin-dependent kinase 4/6 inhibitor therapy in people with HR+, HER2–, PIK3CA-mutated advanced breast cancer: An update from the BYLieve study

Summary
- BYLieve was an ongoing study that looks at how well alpelisib plus endocrine therapy (ET) works in participants with HR+, HER2– ABC whose tumors have PIK3CA mutations and who had prior CDK4/6 inhibitor-based treatment for up to 6 months, or for more than 6 months, before entering the study.
- The BYLieve study had 3 different groups. Two of those groups included participants who took a CDK4/6 inhibitor plus ET immediately before enrolling and then received alpelisib plus fulvestrant (Group A) or alpelisib plus letrozole (Group B) as next treatment.
- Alpelisib plus ET was previously demonstrated to be effective and safe in both groups.
- A previous analysis based on the median length of time participants had prior CDK4/6 inhibitor-based treatment indicated that longer or shorter treatment duration might matter.
- This document explains the results of an analysis from Group A and Group B that studied whether participants responded differently to alpelisib plus ET depending on whether they had prior CDK4/6 inhibitor-based treatment for up to 6 months, or for more than 6 months, before entering the BYLieve study.

What are PIK3CA mutations?
- PIK3CA is a gene that, when altered, can promote tumor growth.
- PIK3CA mutations are found in 4 out of 10 people with HR+, HER2– ABC.
- These people may stop responding to treatment sooner and/or may not live as long as people who do not have PIK3CA mutations.

What is alpelisib and endocrine therapy?
- Alpelisib is a targeted therapy that specifically targets breast cancer tumors with PIK3CA mutations by stopping their growth and their ability to spread throughout the body.
- Endocrine therapy (ET) helps stop or slow down the growth of breast cancer tumors that depend on hormones to grow.
- Types of ET include aromatase inhibitors, such as letrozole, and estrogen receptor antagonists, like fulvestrant.
- The SOLAR-1 study established that alpelisib plus fulvestrant was effective in treating participants with HR+, HER2– ABC with PIK3CA mutations.

What is the BYLieve study?
- BYLieve investigates how well alpelisib plus ET works in 3 different groups of participants who have HR+, HER2– ABC with PIK3CA mutations and who had their tumors grow or spread while taking previous therapies.
- Many participants in BYLieve took a CDK4/6 inhibitor together with ET, which is a common treatment for HR+, HER2– ABC prior to entering the study.

How was this analysis done?
- Participants in Group A and Group B were divided into 2 subgroups:
  - 6 months’ or less subgroup: Those who took prior CDK4/6 inhibitor-based treatment for up to 6 months before entering BYLieve.
  - More than 6 months’ subgroup: Those who took prior CDK4/6 inhibitor-based treatment for more than 6 months before entering BYLieve.
- Duration of prior CDK4/6 inhibitor-based treatment
  - Group A
    - 6 months or less: 26
    - More than 6 months: 100
  - Group B
    - 6 months or less: 32
    - More than 6 months: 91
- Based on participants with information available on their prior CDK4/6 inhibitor-based treatment duration.

What do the new data from this analysis of BYLieve show about participants in Group A and Group B who had 6 months or less or more than 6 months of prior CDK4/6 inhibitor-based treatment?
- The vast majority of participants in each subgroup in both Group A and Group B had disease spread to the bones and internal organs, all participants were women, and the median age was about 60 years old.
- In other reports of the BYLieve study, results indicated that the median PFS was 7.3 months for Group A and 5.7 months for Group B.
- In Group A, researchers found that participants in either subgroup, 6 months or less or more than 6 months of prior CDK4/6 inhibitor-based treatment, derived benefit from alpelisib plus fulvestrant.
- In Group B, researchers found similar PFS between both subgroups.

What side effects did participants experience in the 6 months’ or less or more than 6 months’ duration of prior CDK4/6 inhibitor-based treatment subgroups?
- The side effects observed in both subgroups were consistent with those of the entire group of participants in Group A and Group B.
- Hyperglycemia, diarrhea, and nausea were the most frequently observed side effects across the subgroups within both Group A and Group B.

Conclusions
- The results of this analysis suggest that alpelisib works in participants with HR+, HER2– ABC with PIK3CA mutations regardless of the duration of prior CDK4/6 inhibitor-based treatment.
- Alpelisib with ET may be a good candidate for treating those people who have HR+, HER2– ABC with PIK3CA mutations, even if they have a short response to their prior CDK4/6 inhibitor-based treatment, and may help delay the need for chemotherapy.

Glossary
- ABC—Advanced breast cancer, or a type of breast cancer that has spread to other parts of the body.
- Alpelisib—A targeted therapy tested in the SOLAR-1 study that slows the growth or spread of PIK3CA-mutated breast cancer.
- Aromatase inhibitor—A type of ET, or hormone therapy, used in HR+—HER2— ABC.
- CDK4/6 inhibitor—A medicine that is combined with ET as the standard of care for people with HR+—HER2— ABC.
- Endocrine therapy (ET)—A type of medicine that is combined with CDK4/6 inhibitor as first-line treatment for HR+—HER2— ABC (also called hormone therapy).
- Estrogen receptor antagonist—A type of ET, or hormone therapy, used in HR+—HER2— ABC.
- Fulvestrant—A type of ET used in HR+—HER2— ABC. In SOLAR-1, fulvestrant was given either alone or together with alpelisib.
- Gene—A portion of DNA that is responsible for the transmission of a specific characteristic to your children (for example, the color of your eyes or a family disease).
- HR+, HER2– ABC—A subtype of breast cancer whose tumor cells have hormone receptors, or HRs, but do not have a protein called HER2 or human epidermal growth factor receptor 2.
- Lactinost—A type of ET used in HR+—HER2— ABC.
- Median—The middle value in a set of measurements.
- PIK3CA—A mutation in the PIK3CA gene that can cause tumors to grow or spread.

References

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