Alpelisib and fulvestrant in people with HR+, HER2– advanced breast cancer with PIK3CA mutations and who were previously treated with chemotherapy or endocrine therapy: A new analysis from the BYLieve study

Summary

- BYLieve is an ongoing study investigating how efficacious alpelisib plus endocrine therapy (ET) is in treating participants who have HR+, HER2– ABC with PIK3CA mutations and who had their tumors grow or spread while taking previous therapies.
- The BYLieve study has 3 different groups of participants who have HR+, HER2– ABC with PIK3CA mutations. Participants in Group A received alpelisib plus fulvestrant, those in Group B received alpelisib plus letrozole. Both drug combinations were effective in participants who took a CDK4/6 inhibitor with ET (either an aromatase inhibitor in Group A or fulvestrant in Group B) immediately before enrolling.1,2
- Participants in Group C also received alpelisib plus fulvestrant but were a more heterogeneous group who previously took chemotherapy, ET alone, or ET in combination with a targeted treatment (except a CDK4/6 inhibitor with an aromatase inhibitor) immediately prior to the study. This document explains new results from this group.
- These new results can help guide decisions when selecting the next therapy after a tumor grows or spreads during chemotherapy or while taking ET.

What are PIK3CA mutations?

- PIK3CA is a gene that, when altered, can promote tumor growth.
- PIK3CA mutations occur in about 4 out of 10 people who have 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 stops the growth or spread of breast cancer tumors with PIK3CA mutations.
- 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, such as fulvestrant.
- The SOLAR-1 study established that alpelisib plus fulvestrant was effective in treating people with HR+, HER2– ABC with PIK3CA mutations.4

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.

Results from Group A and B demonstrated that alpelisib plus ET was effective and safe for people with HR+, HER2– ABC with PIK3CA mutations.5

What do the new data from Group C in BYLieve show?

- There were 126 participants in Group C.
- The group consisted of 125 women and 1 man.
- The youngest person in this group was 31 years of age, and the oldest was 84.

Most participants received at least 2 treatments for ABC before enrolling in the study, and about one third had 3 prior treatments.

Almost half of the participants had chemotherapy.

Almost all participants had ET before enrolling in the study.

- After 6 months, approximately 49 in 100 participants did not have their tumors grow or spread further and continued to take alpelisib with fulvestrant.
- Half of the participants did not experience tumor growth or spread for approximately 5 and a half months.
- Approximately 65 in 100 participants had tumors that became smaller in response to alpelisib with fulvestrant.

What side effects did participants in Group C experience?

- The most common grade 3 and grade 4 side effects were high blood sugar, diarrhea, and nausea. These side effects were easily identified and treated.
  - 65.1% of participants had high blood sugar.
  - 23.8% of participants had high blood sugar that was grade 3 or above.
  - 52.4% of participants had diarrhea.
  - 3.2% of participants had diarrhea that was grade 3 or above.
  - 40.5% of participants had nausea.
  - 2.4% of participants had nausea that was grade 3 or above.

- These effects were similar to those previously seen in the SOLAR-1 study and in Group A and Group B of the BYLieve study.
- Antiadipose medicine, high blood sugar medicine (like metformin), and anti-rash medicine (like antihistamines) and dose modifications of alpelisib helped to treat and manage these side effects.

What additional results are available from this analysis of Group C?

- In a subset of participants (approximately 70% of participants analyzed), researchers measured the levels of circulating tumor DNA (ctDNA) in the bloodstream that were released from ABC tumors of participants.
  - Participants with less ctDNA in their bloodstream lived longer without their tumors growing or spreading further throughout their body (also referred to as progression-free survival, or PFS) than those who had more ctDNA in their bloodstream.
  - Researchers also studied whether mutations in another gene, called ESR1, affect how long participants live without their tumors growing or spreading.
  - Those who had no ESR1 mutations had longer median PFS than those who had ESR1 mutations.

Medium progression-free survival

High ctDNA: 5.4 months

Low ctDNA: 16.7 months

ESR1-mutated: 6.3 months

ESR1-nonmutated: 8.3 months

What are ESR1 and endocrine therapy?

- ESR1 is a targeted therapy tested in the SOLAR-1 study that slows the growth of PIK3CA-mutated breast cancer9
- Endocrine therapy (ET) is a type of treatment that is used to treat cancer.
- The study showed that taking alpelisib together with fulvestrant (a type of ET) increased by about 5 months the length of time people lived without their PIK3CA-mutated tumors growing or spreading.
- In this group, participants who had tumors with PIK3CA mutations had their cancer grow or spread while receiving chemotherapy or ET as their last prior medicine before the study. Most participants had at least 2 prior therapies before enrolling in this group.
- The results from Group C show that alpelisib taken with fulvestrant was a beneficial treatment option in these participants who have HR+, HER2– ABC with PIK3CA mutations, regardless of ctDNA levels in the bloodstream or presence of ESR1 mutations.

Conclusions

- In Group C from the BYLieve study, participants with HR+, HER2– ABC with PIK3CA mutations had their cancer grow or spread while receiving chemotherapy or ET as their last prior medicine before the study. Most participants had at least 2 prior therapies before enrolling in this group.
- The results from Group C show that alpelisib taken with fulvestrant was a beneficial treatment option in these participants who have HR+, HER2– ABC with PIK3CA mutations, regardless of ctDNA levels in the bloodstream or presence of ESR1 mutations.

Glossary

- ABC—Advanced breast cancer, or a type of breast cancer that has spread to other parts of the body.
- All-grade—All side effects, regardless of the severity.
- Alpelisib—A targeted therapy tested in the SOLAR-1 study that slows the growth 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.
- Chemotherapy—A type of treatment that is used to treat cancer.
- ctDNA—DNA found in the bloodstream that has been released from dead or broken tumor cells.
- DNA—Material that carries genetic information in the form of genes.
- Endocrine therapy (ET)—A type of medicine that is combined with a CDK4/6 inhibitor as first-line treatment for HR+, HER2– ABC (also called hormone therapy).
- ESR1—Mutations in this gene can cause tumors to be unresponsive to ET.
- 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.
- Letrozole—a type of ET used in HR+, HER2– ABC.
- Genes—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 type of ET, or hormone therapy, used in HR+, HER2– ABC.
- Mutation—A change in the PROCA gene that can cause tumors to grow or spread.
- SOLAR-1 study—This study showed that taking alpelisib together with fulvestrant (a type of ET) increased by about 5 months the length of time people lived without their PIK3CA-mutated tumors growing or spreading.
- ctDNA mutations—A change in the PROCA gene that can cause tumors to grow or spread.
- Progression-free survival (PFS)—How long participants have their disease controlled without their tumors growing or spreading further throughout their body.

- PIK3CA mutations—A change in the PROCA gene that can cause tumors to grow or spread.

References

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