Alpelisib and fulvestrant in people with HR+, HER2– advanced breast cancer with PIK3CA mutations and who were previously treated with a CDK4/6 inhibitor and aromatase inhibitor: A new analysis from Group A of the BYLieve study

Summary
- BYLieve is a study that evaluates how well alpelisib plus endocrine therapy (ET) works in people with HR+, HER2– advanced breast cancer (ABC) with PIK3CA mutations and who had their tumors grow or spread while taking previous therapies.10
- Early results from Group A of the BYLieve study (6-month follow-up) showed that alpelisib taken with fulvestrant is effective in people who have ABC with PIK3CA mutations and whose tumors grew or spread while or after they took a CDK4/6 inhibitor together with a kind of ET called an aromatase inhibitor (AI) as their last prior medicine before enrolling in this study.11
- This summary explains results from BYLieve in the same group of people after an 18-month follow-up.12
- These results confirm how well alpelisib with fulvestrant still works, after a longer follow-up period, in people with HR+, HER2– ABC with PIK3CA mutations and were previously treated with a CDK4/6 inhibitor and Al.13

What is PIK3CA and why is it important?
- In HR+, HER2– ABC, mutations often occur in a gene called PIK3CA, which leads to an incorrectly produced protein called PI3Kα that makes the tumor grow and spread.1
- A PIK3CA mutation occurs in about 4 in 10 people who have HR+, HER2– ABC.1–4
  - These people may stop responding to treatment sooner and/or may not live as long as people who do not have PIK3CA mutations.1–4

How do alpelisib and endocrine therapy work?
- In people with tumors that have a PIK3CA mutation, alpelisib blocks PI3Kα, stopping the tumors’ growth and their ability to spread throughout the body.1
- Endocrine therapy, or ET, including aromatase inhibitors (eg, letrozole) and estrogen receptor antagonists (eg, fulvestrant) stop or slow down the growth of breast cancer tumors that depend on hormones to grow.4
- The SOLAR-1 study showed that taking alpelisib together with fulvestrant increased the length of time people lived without their tumors growing or spreading.13 The study also showed that half of those who took alpelisib together with fulvestrant lived almost 8 months longer than those who took fulvestrant only.1
- In SOLAR-1, only a few people were previously treated with a CDK4/6 inhibitor; at the time, not many CDK4/6 inhibitors were approved, but now they are commonly used to treat HR+, HER2– ABC.5

What is the BYLieve study?
- The BYLieve study is evaluating how well alpelisib + ET works in 3 different groups of people who had HR+, HER2– ABC with a PIK3CA mutation and who had their tumors grow or spread while taking prior treatments, including in people who took a CDK4/6 inhibitor + ET immediately before enrollment.12

Immediate prior treatment before BYLieve

<table>
<thead>
<tr>
<th>Group</th>
<th>CDK4/6 inhibitor + aromatase inhibitor</th>
<th>Alpelisib + fulvestrant</th>
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<tbody>
<tr>
<td>Group A</td>
<td>CDK4/6 inhibitor + fulvestrant</td>
<td>Alpelisib + fulvestrant</td>
</tr>
<tr>
<td>Group C</td>
<td>Chemotherapy, ET alone, or ET plus targeted treatment (except CDK4/6 inhibitor with an aromatase inhibitor)</td>
<td>Alpelisib + fulvestrant</td>
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Treatment during BYLieve

- This is an 18-month update about the group of people who had taken a CDK4/6 inhibitor together with an AI immediately prior to the study and were given alpelisib with fulvestrant in Group A of the BYLieve study.

What do the new data from BYLieve show about the combination of alpelisib + fulvestrant in people who previously took a CDK4/6 inhibitor together with an AI?1
- In this group, there were 127 people; all women.
- The youngest person in this group was 33 and the oldest was 83.

Hormone therapy side effects
- Most people received 1 treatment for their ABC before entering the study.13

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<table>
<thead>
<tr>
<th>Number treated</th>
<th>Number treated more than 1 treatment</th>
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<tr>
<td>127</td>
<td>19 in 100</td>
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After 18 months, around 22 in 100 people were alive and did not have their tumors grow or spread further when alpelisib and fulvestrant half of the people in the study did not experience tumor growth or tumor spread for a little over 7 months.

After 18 months, about 65 in 100 people were still alive, whether their tumors grew or spread or not while taking alpelisib and fulvestrant, half of the people in the study were still alive after 26 and a half months.

About 71 in 100 people had tumors that became smaller in response to alpelisib and fulvestrant.

Conclusions
- The efficacy and safety of alpelisib + fulvestrant were maintained with a longer follow-up of 18 months in participants in Group A of the BYLieve study with HR+, HER2– ABC with PIK3CA mutations, who previously had their cancer grow or spread while taking a CDK4/6 inhibitor together with an AI.13

Glossary
- ABC—Advanced breast cancer, or a type of breast cancer that has spread to other parts of the body.1
- Alpelisib—A targeted therapy tested in the SOLAR-1 study that slows the growth or spread of PIK3CA-mutated breast cancer.6
- Aromatase inhibitor (AI)—A type of ET, or hormone therapy, used in HR+, HER2– ABC.7
- CDK4/6 inhibitor—A medicine that is combined with ET as the standard of care for people with HR+, HER2– ABC.8
- Endocrine therapy (ET)—A type of medicine (also called hormone therapy) that is combined with a CDK4/6 inhibitor as first-line treatment for HR+, HER2– ABC.8
- Fulvestrant—A type of ET used in HR+, HER2– ABC.8 In SOLAR-1, fulvestrant was given either alone or together with alpelisib.9
- 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 2.10
- Letrozole—A type of ET used in HR+, HER2– ABC.8
- PIK3CA—A PI3Kα mutation that can cause tumors to grow or spread.11

References
6. Molin L, and others. AACR 2018; Abstract 4027 [poster].
7. Mayo Clinic, and others. ASCO 2019; Abstract 4458 [oral presentation].