新たな分子標的治療は進行乳がんの増殖を遅らせる(Abstract LBA1006)

SANDPIPER：PI3K阻害剤は、転移性乳がんを有する閉経後女性において、がんの増殖を遅らせるのに成功した

SANDPIPER: PI3K inhibitor successfully slows cancer growth in postmenopausal women with metastatic breast cancer

2018 ASCO Annual Meetingにおいて取り上げられた第III相臨床試験において、新たな分子標的薬taselisibを標準的なホルモン療法薬フルベストラントに上乗せすることにより、ホルモン療法単独に比べ進行乳がんの増殖が2か月遅延し、がん増悪の確率が30% 低下した。SANDPIPER試験における奏効率は、taselisibを上乗せすることにより2倍以上になった（28 vs. 11.9%）。全生存率のデータはまだ得られていない。Taselisibは一般的なPIK3CA遺伝子変異を標的とし、比較的新たなクラスのPI3K阻害薬において初めてのそして最も有望な治療である。

Full Text

In a phase III clinical trial, a new targeted medicine, taselisib, combined with standard hormone therapy fulvestrant, halted the growth of advanced breast cancer growth by 2 months longer than hormone therapy alone, and decreased the chance of cancer worsening by 30%. Taselisib targets a common genetic abnormality in breast cancer – PIK3CA gene mutation – and is the first and most potent treatment in a relatively new class of PI3K inhibitors, according to the authors.

The study is featured in a presentation at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting.

"About 40% of all patients with advanced breast cancer estrogen receptor positive have PIK3CA mutations, which means they could benefit from taselisib," said lead study author José Baselga, MD, PhD, FASCO, the Physician-in-Chief at Memorial Sloan Kettering Cancer Center in New York. "Our findings are proof that that targeting this pathway in breast cancer is effective. However, the benefit to patients was more modest than we had hoped for, and there is a risk of considerable side effects with the addition of taselisib."

Taselisib is the first medicine that specifically blocks the type of PI3K protein (PI3Kalpha) that is mutated in estrogen receptor-positive breast cancers. Taselisib has also shown promising clinical benefit in early trials of patients with head and neck and certain gynecologic cancers.

The SANDPIPER trial is the first and largest phase III clinical trial of taselisib, according to the authors. The trial enrolled 516 postmenopausal women with locally advanced or metastatic ER-positive, HER2-negative metastatic breast cancer that worsened or recurred despite initial hormone treatment with aromatase inhibitors. Women were randomly assigned to receive fulvestrant and placebo (176 women) or fulvestrant and taselisib (340 women).

Women who received taselisib and fulvestrant had a 30% lower chance of cancer worsening than those who received fulvestrant and a placebo, and taselisib extended the time until the cancer worsened by a median of two months (7.4 months with taselisib and fulvestrant vs. 5.4 months with fulvestrant and placebo). The response rate to treatment was more than doubled when taselisib was added (28% vs. 11.9%). Overall survival data are not yet available.

The most common severe side effects for patients who received taselisib were diarrhea, high blood sugar, and colitis. Due to side effects, 17% of women who received taselisib stopped treatment early, compared to only 2% of those who did not receive the targeted therapy.

"We now know that it's possible to target this common breast cancer mutation, and it's heartening to see that a new therapy can provide some benefits to women with advanced breast cancer. However, because the treatment has side effects, doctors will have to weigh its benefits and risks with their patients," said ASCO Expert Harold Burstein, MD, PhD, FASCO.

When they looked at outcomes by geographic area, the researchers noted that taselisib provided more benefit to study participants who received treatment in North America and Europe, where cancer worsening was delayed by a median of 3.5 months (7.9 with taselisib plus fulvestrant vs. 4.5 months with only fulvestrant). In other countries including Eastern Europe and Latin America, taselisib appeared to provide very little or no added benefit. More research is needed understand the reasons for this discrepancy.

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