治療により進行乳がんの進行が抑制される (Abstract LBA502)

PALOMA-3：新たな分子標的治療薬palbociclibはホルモン受容体陽性乳がんの進行を遅延させる

PALOMA-3: Novel targeted drug palbociclib slows progression of hormone receptor-positive breast cancer

前治療歴のあるエストロゲン受容体陽性ヒト上皮成長因子受容体2陰性（HR+/HER2-）進行乳がん患者において標準ホルモン療法（フルベストラント）にpalbociclibを併用することで疾患コントロール期間が2倍以上に延長したとのPALOMA-3スタディの結果が第51回American Society of Clinical Oncology年次集会で発表された。Palbociclibは、サイクリン依存性キナーゼ（CDKs）4および6の新規経口阻害薬で、画期的新薬である。先行研究から、CDK4およびCDK6はエストロゲン陽性乳房腫瘍の増殖を促進する重要な蛋白の一部であることが示されている。HR+/HER2-乳がんの女性がpalbociclibとフルベストラント併用またはプラセボとフルベストラント併用群にランダムに割り付けられた。全ての患者が初回ホルモン療法後に悪化または再発した転移がんを有しており、21%は閉経前であった。筆者らによると、PALOMA-3は分子標的治療薬の最初の登録研究の１つであり―若年、閉経前女性を含む進行乳がんにおけるホルモン療法併用スタディの1つである。この中間解析の時点で、疾患進行までの平均期間はpalbociclib群で9.2か月であったのに対しプラセボ群では3.8か月であった。閉経前女性と閉経後女性とで有益性は同等であった。今回の中間解析において有益性が認められたことから、トライアルは早期に中止となった。

Full Text

The phase III registration study PALOMA-3 reports that adding the investigational targeted agent palbociclib to standard hormonal therapy (fulvestrant) more than doubled the duration of disease control, delaying disease progression by roughly five months in women with previously treated, hormone receptor-positive, human epidermal growth factor receptor 2 negative (HR+/HER2-) advanced breast cancer. The study results were reported at the American Society of Clinical Oncology's 51st Annual Meeting.

This trial was stopped early based on efficacy seen in the interim analysis.
Approximately 75% of all breast cancers are hormone receptor-positive (HR+), HER2 negative,2 and palbociclib in combination with hormonal therapy could become a very effective treatment option after initial hormonal therapy for women with HR+, HER2- advanced breast cancer.

"After initial hormonal therapy stops working in metastatic breast cancer, the next step is typically chemotherapy, which can be effective, but the side effects are often very difficult for women," said lead study author Nicholas C. Turner, a consultant medical oncologist at The Royal Marsden and a team leader at The Institute of Cancer Research, London, United Kingdom. "This relatively easy-to-take new drug can substantially delay the point when women need to start chemotherapy, making this an exciting new approach for women."

Palbociclib is a novel, first-in-class oral drug that blocks cyclin dependent kinases (CDKs) 4 and 6. Prior research has shown that CDK4 and CDK6 are among the key proteins that fuel the growth of hormone receptor-positive breast tumors. Strong preclinical evidence supports combining CDK4 and CDK6 inhibitors with hormonal therapy. Fulvestrant is one of the most active hormone therapies for patients with HR+/ HER2- advanced breast cancer.

Women with HR+/HER2- breast cancer were randomly assigned to palbociclib with fulvestrant or placebo with fulvestrant. All patients had metastatic disease that had worsened or relapsed after initial hormonal therapy, and 21% were premenopausal. According to the authors, PALOMA-3 is one of the first registration targeted therapy–hormone therapy combination studies in advanced breast cancer to include younger, premenopausal women.

At the time of this interim analysis, the average time to disease progression was 9.2 months in the palbociclib arm compared to 3.8 months in the placebo arm. Comparable benefits were seen in pre- and postmenopausal women.

Longer follow-up is needed to determine the effect of palbociclib on overall survival. Quality of life data were collected and will be reported at a later date.
The palbociclib combination was generally well tolerated, with only 2.6% of patients having to stop treatment due to side effects, the most common being blood count abnormalities. Despite frequent occurrences of low white blood cell counts, the rates of a serious complication known as febrile neutropenia were very low (0.6%), the same in both treatment groups.

Another study known as PALOMA-2 is exploring the efficacy of palbociclib as a therapy for advanced breast cancer not previously treated with hormonal therapy. Dr. Turner noted that researchers are also looking at the possibility of using this therapy in women with early-stage hormone receptor-positive breast cancer.

Earlier this year, the FDA granted palbociclib accelerated approval for use in combination with letrozole for women with metastatic estrogen receptor positive (ER+), HER2- breast cancer who have not yet received hormonal therapy for their metastatic disease. The approval was granted based on results of a prior phase II study, PALOMA-1.

"For women with advanced breast cancer, it's remarkable to be able to stall disease progression and stave off the need for chemotherapy for months with a simple pill," commented ASCO Expert Don S. Dizon, M.D.. "In one of the most common forms of advanced breast cancer, palbociclib works in both older and younger women."

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