進行ER陽性乳がんの新たな治療オプション（Abstract # S1-6）

治験薬とレトロゾールの併用は転移性ER陽性乳がんにおいて臨床的有益性を示した

Combination of investigational agent and letrozole demonstrated clinical benefit in metastatic ER-positive breast cancer

治験薬PD 0332991とレトロゾールの併用は進行エストロゲン受容体陽性乳がんの無増悪生存期間中央値を有意に改善したとの第Ⅱ相試験の結果が2012 CTRC-AACRサンアントニオ乳がんシンポジウムで発表された。PD 0332991は、細胞周期進行を阻害することにより細胞DNA合成を阻害する新たな選択的経口サイクリン依存性キナーゼ（CDK）4/6阻害剤である。研究者らは、転移性エストロゲン受容体（ER）陽性乳がんの閉経後女性66人を、PD 0332991とレトロゾールの併用群またはレトロゾール単独群に無作為に割り付けた。無増悪生存期間は併用群で26.1か月であったのに対しレトロゾール単独群では7.5か月であった。測定可能な疾患を有する患者における奏効率は併用群で45%であり、レトロゾール単独群では31%であった。臨床上の有益率は併用治療群で70%であり、レトロゾール単独群で44%であった。サイクリンD1増幅またはp16傷害のバイオマーカーをレトロスペクティブに解析した結果、ER陽性はPD 0332991の有益性を最も受けやすい患者を選択するのに必要な唯一のバイオマーカーであることが明らかにされた。

Full Text

The combination of the investigational agent PD 0332991 and letrozole significantly improved median progression-free survival in patients with advanced estrogen receptor-positive breast cancer, according to phase II results presented at the 2012 CTRC-AACR San Antonio Breast Cancer Symposium.

"We are very encouraged by this improvement in progression-free survival," said Richard S. Finn, M.D., associate professor of medicine at the Jonsson Comprehensive Cancer Center at the University of California, Los Angeles.

PD 0332991, which is being developed by Pfizer Inc., is a novel oral selective inhibitor of cyclin-dependent kinase (CDK) 4/6, which prevents cellular DNA synthesis by blocking cell cycle progression, Finn said. Previously published preclinical data have suggested that CDK 4/6 inhibition may play a role in the treatment of some breast cancers.

In the first part of this two-part, phase Ⅱ study, Finn and colleagues randomly assigned 66 postmenopausal women with metastatic estrogen receptor (ER)-positive breast cancer to either the combination of PD 0332991 and letrozole or to letrozole alone. The second part of the study involved 99 patients with ER-positive cancers determined by screening to have certain genomic alterations, specifically cyclin D1 amplification and/or p16 loss, according to Finn.

Results showed that progression-free survival was 26.1 months for those in the combination arm versus 7.5 months for patients treated with letrozole alone. There was also a 45 percent response rate with the combination treatment versus 31 percent with letrozole alone in patients with measurable disease. The clinical benefit rate was 70 percent with the combination treatment and 44 percent with letrozole alone.

The combination of PD 0332991 and letrozole was also well tolerated. The most common adverse events were neutropenia, leukopenia, anemia and fatigue. "Importantly, this was uncomplicated neutropenia," Finn said. "There was no evidence of febrile neutropenia."

Further, after retrospectively analyzing the biomarkers for cyclin D1 amplification or p16 loss, the researchers found that "ER positivity was the only biomarker we really needed to select patients who were most likely to benefit from PD 0332991," he said.

"If these results are verified in a large, phase III study this could establish PD 0332991 as an important new treatment option for advanced ER-positive breast cancer in a frontline setting."

TOPICS