HER2陽性転移性乳がんにおける重要な進歩（Abstract # S5-5）

CLEOPATRA: 二重HER2遮断は転移性乳がん患者の無増悪生存期間を有意に延長する

CLEOPATRA: Dual HER2 blockade significantly extends progression-free survival in metastatic breast cancer

トラスツズマブとドセタキセルの併用化学療法にpertuzumabを追加することによりHER2陽性転移性乳がん患者の無増悪生存期間中央値が6.1ヵ月延長したとの研究結果が、2011年CTRC-AACRサンアントニオ乳がんシンポジウムで発表されNew England Journal of Medicineに掲載された。研究者らはCLEOPATRA（CLinical Evaluation Of Pertuzumab And TRAstuzumab[Pertuzumabとトラスツズマブの臨床的評価]）として知られる国際phase 3、二重盲検、無作為化トライアルを行った。このトライアルでは808人の患者をトラスツズマブとドセタキセルの併用化学療法にpertuzumabまたはプラセボを追加する群に無作為に割り付けた。無増悪生存期間は、pertuzumab群で18.5ヵ月であったのに対しプラセボ群では12.4ヵ月であった―増悪リスクは38%低下した。客観的奏効率（少なくとも30%の腫瘍縮小）は、併用化学療法にpertuzumabを追加することにより80.2%であったのに対し、併用化学療法単独では69.3%であった。生存期間に関する成績は不完全ではあるが、3剤併用群では402人中69人が死亡し、2剤併用群では406人中96人が死亡した。3剤併用療法の忍容性は高かった。Pertuzumabは"二量体化阻害剤"と呼ばれる新たなクラスの初めての薬剤である。

Full Text

Adding pertuzumab to a combination of trastuzumab and docetaxel chemotherapy extended progression-free survival by a median of 6.1 months in patients with metastatic HER2-positive breast cancer compared with patients who received the combination therapy with placebo according to research presented at the 2011 CTRC-AACR San Antonio Breast Cancer Symposium and published in the New England Journal of Medicine.

Researchers conducted an international phase 3, double-blind, randomized trial, known as CLEOPATRA (CLinical Evaluation Of Pertuzumab And TRAstuzumab), in which they randomly assigned 808 patients to receive trastuzumab and docetaxel chemotherapy with pertuzumab or placebo. Progression-free survival (PFS) was 18.5 months for patients who received pertuzumab compared with 12.4 months for patients who received placebo - a 38 percent reduction in risk for progression.

The findings represent a significant advance in the treatment of this advanced breast cancer, said senior researcher José Baselga, M.D., Ph.D., professor in the department of medicine at Harvard Medical School, associate director of the Massachusetts General Hospital Cancer Center and chief of hematology/oncology at Massachusetts General Hospital.

"This is huge. It is very uncommon to have a clinical trial show this level of improvement in PFS," said Baselga. "Most metastatic patients with HER2-positive breast cancer eventually stop responding to trastuzumab, so the fact that we now have an agent that can be added to current treatment to delay progression is very exciting. With the advent of trastuzumab and now pertuzumab, we have come a very long way in treating a type of breast cancer that once had a very poor prognosis."

Pertuzumab is designed to work in combination with trastuzumab as a dual blockade of the HER2 growth factor, which fuels about one third of all breast tumors. Both drugs are monoclonal antibodies that bind to the HER2 receptor protein in different locations. Pertuzumab's role is to prevent the receptor from linking to HER3 and therefore forming a "dimer" that further signals tumor growth - making pertuzumab the first in a new class of drugs called "dimerization inhibitors," Baselga said. "These two agents offer a dual HER2 blockade, shutting down different mechanisms responsible for HER2 signaling."

Adding pertuzumab to the combination therapy resulted in an objective response rate (tumor shrinkage of at least 30 percent) of 80.2 percent compared with 69.3 percent for the combination therapy alone.

Although survival outcomes are not mature, Baselga reported 69 deaths among the 402 patients treated with the three-drug combination and 96 deaths among the 406 patients who received two drugs.

He added that the three-drug combination is "remarkably safe and well tolerated. Only minimal side effects were seen with the addition of pertuzumab." Some of those effects were grades 1 and 2 diarrhea and neutropenia, but no additional cardiac toxicity was seen, he said.

Enrollment is already underway in a new double-blind, randomized clinical trial, APHINITY, to test the use of pertuzumab as adjuvant treatment for early-stage HER2-positive breast cancer. "It is in that setting that you can really cure patients," Baselga said.

TOPICS