分子標的薬の併用により卵巣がんの予後が改善する（Abstract: LBA5500）

新規分子標的薬の併用は再発卵巣がん患者の無増悪生存期間を有意に延長させる

New targeted drug combination significantly increases progression-free survival in women with recurrent ovarian cancer

2つの経口治験薬、PARP阻害薬olaparibおよび抗血管新生薬cediranibの併用は、再発プラチナ製剤感受性卵巣がんまたは*BRCA*遺伝子変異のある卵巣がんに対し、olaparib単剤よりも有意に有効である。再発プラチナ製剤感受性高悪性度漿液性卵巣がんまたはBRCA変異陽性卵巣がん患者90人がolaparib単剤群またはolaparibとcediranib併用群にランダムに割り付けられた。患者には再発卵巣がんに対する抗血管新生薬やPARP阻害薬による前治療歴はなかった。腫瘍縮小率はolaparib単剤群に比べ併用群において著明に高かった（80%対48%）。併用群患者5人およびolaparib単剤群患者2人が完全寛解した。併用療法は疾患の増悪を実質的に遅延させ、無増悪生存期間はolaparib単剤群の9か月に対し、併用群では17.7か月であった。プラチナ製剤感受性患者における標準的な化学療法の過去のトライアルでは、無増悪生存期間は8～13か月であった。この第II相研究の結果は、第50回American Society of Clinical OncologyのLate Breaking sessionで発表された。

Full Text

Findings from a federally funded, NCI-sponsored phase II study suggest that the combination of two investigational oral drugs, the PARP inhibitor olaparib and the anti-angiogenesis drug cediranib, is significantly more active against recurrent, platinum chemotherapy-sensitive disease or ovarian cancer related to mutations in *BRCA* genes than olaparib alone. The progression-free survival was 17.7 months with the combination treatment vs. nine months with olaparib alone.

"The significant activity that we saw with the combination suggests that this could potentially be an effective alternative to standard chemotherapy," said lead study author Joyce Liu, M.D., M.P.H., an instructor in medical oncology at Dana-Farber Cancer Institute in Boston, MA. "At the same time, this approach is not yet ready for clinical practice as neither of these drugs is currently FDA approved for ovarian or any other cancer. We also need additional clinical trials to confirm the findings of this study to see how this combination compares to standard treatment."

This study is the first time a combination of a PARP inhibitor and an anti-angiogenic drug has ever been explored in a clinical trial for ovarian cancer. It confirms preclinical research that suggested that olaparib and cediranib synergize. Dr. Liu and her colleagues designed this trial to confirm, in a clinical setting, that the combination of these two drugs was more active than the single drug olaparib alone.

As many as 80 percent of women with high-grade serous ovarian cancer experience a relapse after initially responding to chemotherapy. When the cancer comes back, it is more difficult to treat, because it will have metastasized to the pelvis and abdomen, or even the lungs. The current standard treatment for recurrent ovarian cancer is chemotherapy, which often causes significant side effects. Even in the setting of initial response, resistance to chemotherapy eventually develops. Therefore, researchers have been exploring alternate regimens using targeted drugs, with the goal of overcoming such treatment resistance.

Ninety women with recurrent, platinum-sensitive, high-grade serous or BRCA mutation-related ovarian cancer were randomly assigned to treatment with olaparib alone or olaparib plus cediranib. The women had no prior treatment with anti-angiogenic drugs in the setting of recurrent ovarian cancer or PARP inhibitors.

Tumor shrinkage rates were markedly higher in the combination arm than in the olaparib arm (80 vs. 48 percent). Five patients in the combination arm and two patients in the olaparib alone arm had a complete remission. The combination treatment substantially delayed disease progression, with a progression-free survival of 17.7 months compared to nine months for olaparib alone. Past trials of standard chemotherapy in the platinum-sensitive setting have demonstrated progression-free survival times between eight and 13 months.

Although certain side effects — high blood pressure, fatigue, and diarrhea — occurred more frequently in the combination arm, they were usually controllable by symptom management and dose reductions as needed.

Prior trials have suggested that PARP inhibitors tend to have the most activity in women who have either platinum-sensitive ovarian cancer or BRCA mutations in their tumors. An exploratory analysis from this study suggests that the combination treatment appears to also be active in patients without a known BRCA-mutation. Dr. Liu remarked that it is reasonable to explore whether the combination treatment would be effective in women with platinum-resistant disease as well.

"The combination of cediranib plus olaparib resulted in a significantly higher response rate, though at the expense of higher toxicity. Whether this response translates into gains in survival needs further follow-up," said Don S. Dizon M.D., FACP, ASCO Expert. "However, this combination represents an oral, non-chemotherapy-based combination treatment option for women with high-grade serous or BRCA-mutation related ovarian cancers and definitely warrants further study."

This study was supported by the National Cancer Institute, National Institutes of Health.

ASCO2014特集