PARP阻害薬は再発性卵巣がんの生存率を改善する（Abstract No.5003）

維持療法およびPARP阻害薬は再発性卵巣がん治療において重要な役割を果たす可能性がある

Maintenance therapy and PARP inhibitors could play important roles in treatment of relapsed ovarian cancer

第47回ASCOで発表されたphase II無作為化トライアルの結果、経口PARP阻害薬を用いた維持療法により最も一般的なタイプの卵巣がん患者の無増悪生存期間が4ヵ月延長したことが示された。この多施設国際スタディでは高悪性度の重症卵巣がん患者265人をolaparibまたはプラセボ投与群に無作為に割り付けた。患者はプラチナ製剤を基本とした治療により完全寛解または部分寛解を達成した後、8週以内にトライアルに組み入れられた。無増悪生存期間（PFS）はolaparib投与群において生存期間中央値8.4ヵ月とプラセボ投与群の4.8ヵ月よりも有意に長かった。データ解析の時点で、olaparib群に割り付けられた患者の半分（68人）が再発せず内服を継続していたのに対し、プラセボ群のうちプラセボ内服を継続していたのはわずか16%（21人）であった―したがって、全生存期間データはまだ解析として使用できていない。嘔気、倦怠感、嘔吐、および貧血などの有害事象はolaparib群においてプラセボ群よりも多く認められたが、これらの多くは重度ではなかった。副作用を軽減するための投与量減量がこのスタディでは認められており、それはolaparib群において（23%）プラセボ群（7%）よりも多く認められた。

Full Text

A Phase II randomized trial showed that maintenance treatment with the oral PARP inhibitor drug olaparib improved progression-free survival by about four months in women with the most common type of relapsed ovarian cancer. This is the first randomized trial to demonstrate a benefit for maintenance therapy for recurrent ovarian cancer, and the first randomized trial in ovarian cancer of a PARP inhibitor - a novel class of molecularly targeted drugs.

The results of this study, if confirmed in larger trials, could lead to a new treatment approach for recurrent ovarian cancer in which drugs like olaparib are given over a long period of time to prevent recurrences or prolong remissions. This somewhat novel approach, called maintenance therapy, has already proven useful in lung cancer. Standard treatment for ovarian cancer includes platinum-based chemotherapy. After this regimen, patients are observed until recurrence, and then treated with another course of chemotherapy. While some tumors respond well to chemotherapy, the regimens are too toxic for patients to take continuously, and clinical trials haven't shown any benefit for extended courses of chemotherapy.

"A well-tolerated antitumor agent that could be used for months or perhaps years as maintenance therapy after standard chemotherapy could be a big step forward and ultimately extend survival," said lead author Jonathan A. Ledermann, M.D., principal investigator of the study and Professor of Medical Oncology at UCL Cancer Institute, University College London. "This study demonstrates proof of principle for the concept of maintenance therapy in ovarian cancer using a PARP inhibitor. Our progression-free survival difference was very impressive and better than we anticipated."

The multicenter, international study randomized 265 women with high-grade serous ovarian cancer to either olaparib or placebo. Patients were enrolled in the trial within 8 weeks of having achieved either a complete or partial response to platinum-based treatment. PARP inhibitors have been shown to work better in patients whose tumors have responded to platinum.

In the study, the progression-free survival (PFS) - the amount of time during and after treatment in which the cancer does not return - was significantly longer in the group receiving olaparib than the placebo group, with a median of 8.4 months versus 4.8 months. At the time of data analysis, half the patients randomized to olaparib (68 patients) had not relapsed and were still receiving the drug, while only 16 percent (21 patients) remained on placebo - so overall survival data were not yet available for analysis.

Adverse events were more commonly reported in the group receiving olaparib than placebo, including nausea, fatigue, vomiting, and anemia, but the majority of these were not severe. Dose reductions to manage side effects were allowed in the study and were more prevalent in the olaparib group (23 percent) compared to the placebo group (7 percent).

Olaparib inhibits the enzyme Poly ADP ribose polymerase (PARP), which is involved in DNA repair. Up to half of women with high-grade serous ovarian cancer - the most common type of ovarian cancer - may have a DNA repair deficiency that makes them more susceptible to treatment with PARP inhibitors.

A number of PARP inhibitors are in Phase II and Phase III clinical trials as single agents and in combination with standard chemotherapies and radiation in some types of breast and ovarian cancers believed to have DNA repair defects.

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