卵巣がんにおけるbevacizumabの治療ベネフィット（Abstract No. LBA5006 and5007）

新たに診断された卵巣がんに対するbevacizumab使用に関する初期データから再発リスクの高い女性の生存率に関する有益性が示唆された

Initial data on use of bevacizumab for newly diagnosed ovarian cancer suggests survival benefit for women at high risk of recurrence

第47回ASCOで報告された無作為化Phase IIIトライアルの生存率に関する中間データから、新たに診断された卵巣がん患者に対する標準的なカルボプラチンおよびパクリタキセル化学療法へのbevacizumab併用は、特により進行の速い患者において、化学療法のみの治療と比較し有益である可能性が示唆された。ICON7スタディにおいて、新たに診断された、高リスクまたは進行上皮性卵巣がん、原発性腹膜がん、または卵管がん患者を6サイクルの化学療法単独、または同様の化学療法とbevacizumabの同時併用を受けその後ベバシズマブ単独療法を12ヵ月受ける群に無作為に割り付けた。フォローアップ期間中央値28ヵ月後、死亡は標準治療群よりもbevacizumab群において少なかった（それぞれ178対200、p=0.11）。再発リスクの最も高い患者においてあらかじめ計画されていたサブグループ解析では、36%の死亡リスク低下が認められた（p=0.0002）。やはりASCO学会で発表されたOCEANSスタディでは、bevacizumabとプラチナ製剤ベースの化学療法の併用により、再発性卵巣がん、腹膜がん、および卵管がんの無増悪生存期間が延長した。

Full Text

Interim survival data from a randomized Phase III trial reported at the American Society of Clinical Oncology's 47th Annual Meeting suggested that adding bevacizumab (Avastin) to standard carboplatin and paclitaxel chemotherapy for treatment of newly diagnosed ovarian cancer patients may offer benefit over treatment with chemotherapy alone, particularly for patients with more aggressive disease.

In the ICON7 study, 1,528 women with newly diagnosed high-risk or advanced epithelial ovarian, primary peritoneal or fallopian tube cancer were randomized to receive 6 cycles of chemotherapy alone, or the same chemotherapy concurrently with bevacizumab followed by single agent of bevacizumab for a total duration of 12 months. First results presented at last year's ESMO Annual Meeting reported a progression-free survival (PFS) benefit for adding bevacizumab to standard chemotherapy.

To further inform consideration of a licensing application, an interim analysis of overall survival was requested by regulatory authorities - the U.S. Food and Drug Administration and the European Medicines Agency. After a median follow-up of 28 months, there were fewer deaths in the bevacizumab group than the standard therapy group (178 versus 200, respectively). This represents a 15 percent overall reduction in risk of death, but was not statistically significant.

The ICON7 investigators also conducted a planned subgroup analysis looking at the results in patients at highest risk of recurrence - those with stage III ovarian cancer who were left with more than 1 cm of tumor after surgery and all stage IV patients who had surgery. In this subgroup, the reduction in risk of death was 36 percent (79 deaths versus 109 deaths in the standard therapy group). This result reached statistical significance (P=.0002).

"It's too early to reach firm conclusions about the full extent of the overall survival benefit of adding bevacizumab to the treatment regimen for newly diagnosed ovarian cancer, but it does seem very promising, particularly for patients at high risk of recurrence," said Gunnar Kristensen, M.D., Ph.D., one of the lead investigators of this study and Senior Consultant in the Department for Gynecologic Oncology, Norwegian Radium Hospital, Oslo, Norway. "We don't have complete answers to all our questions today; we will have to wait for final results of the trial which are expected in about two years."

In another trial also presented at ASCO, the randomized Phase III OCEANS study of bevacizumab in combination with platinum-based chemotherapy showed that women with recurrent ovarian cancer who took bevacizumab lived significantly longer without their disease getting worse. A 52% reduction in the risk of disease progression was seen.

"Women taking bevacizumab lived for longer periods without disease progression and without having to go back on chemotherapy," said Carol Aghajanian, M.D., lead study author and Chief, Gynecologic Medical Oncology Service, Memorial Sloan-Kettering Cancer Center in New York. "This is good news for women with these cancers, as we are increasingly able to treat ovarian cancer as a chronic disease."

The results from OCEANS show that after a median follow-up of 24 months, median progression-free survival was 12.4 months for the patients in the bevacizumab group, compared to 8.4 months for patients who had chemotherapy alone. In addition, 79 percent of women treated with bevacizumab in combination with chemotherapy had significant tumor shrinkage, compared to 57 percent treated with chemotherapy alone. The duration of response was also longer for the patients in the bevacizumab group (10.4 months versus 7.4 months).

The multicenter study randomized 484 patients to receive bevacizumab, an anti-VEGF monoclonal antibody, and chemotherapy (carboplatin and gemcitabine) or a placebo and the same chemotherapy regimen. Bevacizumab or placebo was continued after the completion of chemotherapy until the time of disease progression.

The side effects of bevacizumab were consistent with those seen in previous studies. No gastrointestinal perforations were seen in the OCEANS trial.

The investigators said the next step in this work is to evaluate the role of bevacizumab in combination with chemotherapy for platinum-resistant disease, and to combine bevacizumab with other emerging novel therapies such as PARP inhibitors.

"The data from OCEANS demonstrate a clear response from bevacizumab in these cancers," Dr. Aghajanian said. "These are very meaningful results for patients for whom there are currently limited treatment options available."

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