肺がんの進行に重要な役割を果たす二つのパスウェイを標的とする新たな治療薬（Abstract #: CRA8003）

分子標的治療薬vandetanibは進行非小細胞肺がん患者の無増悪生存期間を改善する

Targeted therapy vandetanib improves progression-free survival in patients with advanced non-small cell lung cancer

国際トライアルの結果、ドセタキセルに分子標的治療治験薬vandetanibを加えることにより、ファーストライン治療後に進行した進行非小細胞肺がん（NSCLC）患者の無増悪生存期間が改善することが示されたと第45回American Society of Clinical Oncology学会で発表された。VandetanibはNSCLCにおいて役割を果たすことが知られている二つの受容体（上皮増殖因子受容体[EGFR]および血管内皮増殖因子[VEGF]）の両方を標的とした初めての薬剤である。このスタディでは、既に化学療法で治療された患者1,391人をドセタキセルとvandetanib、またはドセタキセルとプラセボを投与する群に無作為に割り付けた。経過観察期間中央値12.8ヵ月後にvandetanib群の患者はプラセボ群と比較し疾患進行のリスクが21%低下した（無増悪生存期間中央値はvandetanib群で17.3週間、プラセボ群で14週間、p=0.001）。全生存期間には統計学的有意差はなかったが、奏功率の有意な改善が認められた（17%対10%、p=0.001）。またvandetanib治療によりがん自体による症状も軽減し症状増悪のリスクも22%低下した（p=0.002）。

Full Text

The results of an international trial have shown that adding the experimental targeted therapy vandetanib to docetaxel improves progression-free survival in patients with advanced non-small cell lung cancer (NSCLC) whose disease has progressed after first-line treatment. This is the first phase III study to show that adding a targeted therapy to second-line chemotherapy with docetaxel results in a clinical benefit for patients with advanced NSCLC. It is also the first phase III trial of vandetanib for NSCLC, which is being evaluated for certain types of thyroid cancer as well.

Vandetanib is a pill that targets two receptors already known to play a role in NSCLC - epidermal growth factor receptor (EGFR) and vascular endothelial growth factor (VEGF). These receptors are targeted separately by other drugs, but vandetanib is the first drug to target both.

In this study 1,391 patients who had previously been treated with chemotherapy were randomized to receive the docetaxel and vandetanib, or docetaxel and placebo. After a median follow-up of 12.8 months, patients in the vandetanib group had a 21 percent reduction in the risk of disease progression compared with patients in the placebo group. The median progression-free survival time was 17.3 weeks in the vandetanib arm versus 14 weeks in the control arm.

While there was no statistical difference in overall survival, a significant improvement in objective response rate was observed. Vandetanib treatment was also associated with an improvement in symptoms related to the underlying cancer and a 22 percent reduction in the risk that symptoms would worsen. For example, it took longer for patients in the vandetanib group to report that their disease symptoms, such as cough, weight loss, and difficulty breathing, had worsened.

Some side effects were more common in the vandetanib arm, including diarrhea (42 percent versus 33 percent in the placebo group), rash (42 percent versus 24 percent), and low white blood cell counts (32 percent versus 27 percent). Other side effects (nausea, vomiting, and anemia) were more common in the control group. About 22 percent of patients in the study discontinued vandetanib due to side effects, which is relatively low for a second-line therapy in advanced lung cancer.

"Clearly in a disease as heterogeneous as lung cancer the need to target multiple pathways has become clear - hence, this agent targeting two key pathways critical for NSCLC growth and metastasis is novel and could play a key role," said Roy S. Herbst, M.D., Ph.D., chief of thoracic medical oncology at the University of Texas M.D. Anderson Cancer center and the study's lead author. "The fact that more patients had an improvement in the symptoms from their lung cancer suggests that the drug could be important for the future management of this disease."

ASCO2009特集