進行性甲状腺がんにおいて新規分子標的薬は有効性が高い（Abstract: LBA6008）

Lenvatinibは進行性放射性ヨウ素治療抵抗性分化型甲状腺がん患者において高い奏効率を示す

Lenvatinib yields high response rates in patients with radioiodine-resistant, advanced differentiated thyroid cancer

SELECTスタディの結果、lenvatinibは標準的な放射性ヨウ素（RAI）療法に抵抗性の分化型甲状腺がんに対し有効性が高いことが示された。Lenvatinibは、VEGFR1-3、FGFR 1-4、PDGFR-β、KIT、およびRETなどのがん細胞内のいくつかの標的をブロックする経口チロシンキナーゼ阻害薬である。この薬剤は今、肝がん、肺がん、および腎がんや他のタイプの固形がんの治療に対する可能性を第II相および第III相試験において検証されている。今回のスタディにおいて、1年以内に増悪した進行性RAI治療抵抗性分化型甲状腺がんの患者392人が、lenvatinibまたはプラセボ群にランダムに割り付けられた。プラセボ群患者は疾患が増悪した時点でlenvatinib群へクロスオーバーすることが許可された。Lenvatinib群では約65%の患者に腫瘍縮小が認められたのに対し、プラセボ群ではわずか3%であった。奏効は多くが治療開始後2か月以内に認められた。無増悪生存期間中央値はプラセボ群よりもlenvatinib群において有意に長かった（18.3か月対3.6か月、p<0.001）。全生存期間中央値には到達しなかった。この第III相スタディは第50回American Society of Clinical OncologyのLate Breaking sessionで発表された。

Full Text

Findings from the SELECT phase III study show that lenvatinib is highly effective against differentiated thyroid cancer that is resistant to standard radioiodine (RAI) therapy. The new oral targeted drug delayed disease progression by 14.7 months, and nearly two thirds of patients experienced tumor shrinkage. The median overall survival has not been reached.

"We are confident that, based on our findings, lenvatinib will eventually become a standard treatment for radioiodine-resistant thyroid cancer," said lead study author Martin Schlumberger, M.D., a professor of oncology at the University Paris Sud in Paris, France. "As little as a year ago, this group of patients had no effective treatment options. It's remarkable that we now have two active drugs in this setting, both of them tyrosine kinase inhibitors."

Differentiated thyroid cancer is the most common subtype of thyroid cancer. Although differentiated thyroid cancer is generally curable with standard treatment – surgery and RAI – roughly 5-15 percent of patients develop RAI resistance.

Lenvatinib is an oral tyrosine kinase inhibitor that blocks several targets in a cancer cell, including VEGFR1-3, FGFR 1-4, PDGFR-β, KIT, and RET. It is being explored in phase II and phase III clinical trials as a potential treatment for liver, lung, and kidney cancers and other types of solid tumors.

In this study, 392 patients with advanced, RAI-resistant, differentiated thyroid cancer that had progressed within a year were randomly assigned to treatment with either lenvatinib or placebo. Patients on the placebo arm were allowed to cross over to the lenvatinib arm upon disease progression.

Approximately 65 percent of patients experienced tumor shrinkage in the lenvatinib arm, compared to only 3 percent in the placebo arm. The majority of responses occurred within two months of starting treatment. The median progression-free survival was 18.3 months in the lenvatinib arm vs. 3.6 months in the placebo arm. The median overall survival has not been reached.

The five most common side effects of lenvatinib were high blood pressure, diarrhea, decreased appetite, decreased weight, and nausea. Although the side effects necessitated dose reductions in 78.5 percent of patients, the benefit of lenvatinib persisted with decreased dose, Dr. Schlumberger noted.

"The progress we're seeing with targeted agents for uncommon cancers is encouraging," said Gregory A. Masters, M.D., ASCO Expert. "Patients with differentiated thyroid cancer have historically had limited options when the disease progresses despite radioactive iodine therapy. Now this new drug, lenvatinib, offers an effective option with reasonable side effects and can help patients live longer before the disease worsens."

This research was supported by Eisai Inc.

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