ソラフェニブは一部の進行の速い甲状腺がんの進行を抑制する（Abstract＃4）

DECISION:ソラフェニブはここ40年において治療抵抗性分化型甲状腺がんに対し有効であることが示された初めての薬剤である

DECISION: Sorafenib is first drug in four decades to be shown effective for treatment-resistant differentiated thyroid cancer

第49回American Society of Clinical Oncology年次集会で報告された第III相試験DECISIONの中間解析の結果、マルチターゲット阻害剤ソラフェニブは、標準的な放射性ヨード療法（RAI）に抵抗性の甲状腺分化がん患者の無増悪生存期間を延長することが示された。ソラフェニブは2つの別々の蛋白（Rafキナーゼおよび VEGF受容体キナーゼ）を阻害するマルチターゲット阻害剤である。このスタディにおいて、転移性、RAI抵抗性分化型甲状腺がん患者417人がソラフェニブまたはプラセボを投与される群に無作為に割り付けられた。患者は疾患が進行した際にはソラフェニブ群に切り替えることが許可されていた。無増悪生存期間中央値はソラフェニブ群で10.8か月であり、プラセボ群では5.8か月であった。30%以上の腫瘍縮小が認められたのはソラフェニブ群で12.2%、プラセボ群で0.5%であった。ソラフェニブ群ではさらに42%が6か月以上の病勢安定、病勢コントロール率は54%であったのに対し、プラセボ群の病勢コントロール率は34%であった。全生存期間のデータは完成していない。もし承認されれば、ソラフェニブは分化型甲状腺がんに対しこの40年で初めての新たな有効な薬剤となるであろう。

Full Text

A randomized phase III study, DECISION, finds that the targeted drug sorafenib stalls disease progression by five months in patients with metastatic differentiated thyroid cancer that has progressed despite standard radioactive iodine (RAI) therapy. If approved, sorafenib would become the first new active drug for this form of thyroid cancer in 40 years.

Differentiated thyroid cancer is the most common subtype of thyroid cancer, accounting for about 85 percent of the 60,000 thyroid cancer cases diagnosed each year in the United States. Although differentiated thyroid cancer generally has high cure rates following standard treatment – surgery and RAI– roughly 5-15 percent of patients develop RAI resistance. The only approved treatment for those patients, doxorubicin, is rarely used due to its low efficacy and high toxicity. This is the first time a kinase inhibitor has been assessed for this indication in a large clinical trial.

"After having no effective drugs for these patients for so many years, it is very exciting to find an oral drug that stops growth of the cancer for several months," said lead study author Marcia Brose, M.D., Ph.D., an assistant professor of otolaryngology and head and neck surgery in the Abramson Cancer Center and the Perelman School of Medicine at the University of Pennsylvania in Philadelphia, Pa. "For these patients, a longer progression-free survival means more months without hospitalization and invasive procedures to control pain and other symptoms. This is the first time we have had a systemic treatment that can help."

In this study, 417 patients with metastatic, RAI-resistant differentiated thyroid cancer were randomly assigned to receive sorafenib or placebo. Patients were allowed to cross over to the sorafenib arm upon disease progression. The median progression-free survival was 10.8 months in the sorafenib group vs. 5.8 months in the placebo arm. Tumor shrinkage of 30 percent or more was observed in12.2 percent and 0.5 percent of patients in the sorafenib and placebo arms, respectively. An additional 42 percent of patients in the sorafenib arm had stable disease for 6 months or longer for a disease control rate of 54 percent, compared with a disease control rate of 34 percent in the placebo arm. Overall survival data are not yet mature.

"Few good options exist for patients with these more aggressive thyroid cancers, so these findings offer renewed hope and momentum for patients and researchers alike. Sorafenib provides meaningful activity for these patients, nearly doubling progression-free survival. Future studies will help identify which patients can benefit most from this therapy, and how other targeted therapies may further improve the outcome for these patients," said Gregory Masters, M.D., ASCO spokesperson and head and neck cancers expert.

Further analysis of data from this clinical trial is planned to find markers that would help identify patients that respond well to sorafenib and those that may need additional therapy. Unfortunately, the disease will eventually progress after sorafenib treatment in most patients. Additional treatment options still need to be developed for use as second-line agents and beyond.

Sorafenib is a multi-targeted drug that blocks two distinct proteins – Raf kinase and VEGF receptor kinase –which control tumor cell division and growth of tumor blood vessels, respectively. The drug is already approved in the U.S. for the treatment of advanced kidney cancer and inoperable liver cancer.

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