新たな複数分子を標的とした分子標的薬は骨転移病変を縮小または除去する（Abstract No.3010）

経口METおよびVEGFR2阻害薬は複数の進行固形がんに対し有意な有効性を有する

An oral inhibitor of MET and VEGFR2 has significant effect on several advanced solid tumors

経口METおよびVEGFR2（多くのがんの発現や増殖に関係するキナーゼ）阻害薬Cabozantinib（XL184）は様々な進行がんを有する患者において強力な有効性を有することが、第47回ASCOで発表されたPhase IIトライアルの結果示された。骨転移を有するまたは有さない進行固形がん患者がcabozantinibを12週間にわたり内服した。このトライアルは、部分寛解をした患者は内服を継続し、疾患が安定している患者はcabozantinibまたはプラセボに無作為に割り付けられ、疾患が進行した患者はトライアルから外れるといった、“中断”トライアルとしてデザインされた。様々なタイプのがんを有する評価可能であった患者398人における奏効率は9%（398人中34人）であった。12週後のコントロール率（部分寛解および疾患の安定）が最も高かったのは肝がんの76%（29人中22人）であり、前立腺がんで71%（100人中71人）、卵巣がんでは58%（51人中32人）であった。骨転移を有する68人（乳がん、前立腺がんおよびメラノーマ）中59人が部分寛解または、しばしば有意な疼痛軽減や他のがん関連症状の改善に結びつく骨スキャン上の完全な病変消失を来した。

Full Text

Cabozantinib (XL184) - an oral inhibitor of MET and VEGFR2, kinases involved in the development and progression of many cancers - showed strong responses in patients with various advanced cancers in a Phase II trial. The drug demonstrated particularly high rates of disease control for advanced prostate, ovarian and liver cancers, which are historically resistant to available therapies. The drug also fully or partially eliminated bone metastases in patients with breast and prostate cancers and melanoma.

"Cabozantinib appears to have significant effects on several treatment-resistant tumors, as well as impressive effects on bone metastases. In addition, these effects are associated with rapid improvement in pain, a reduction in opiate narcotic requirements and improvement in anemia," said lead author Michael S. Gordon, M.D., a medical oncologist at Pinnacle Oncology Hematology in Scottsdale, AZ. "The implications of these results are very exciting-it is unusual to find a targeted therapy, absent of a molecular mutation in tumors, that works in bony disease and has this activity."

To be eligible for the study, patients had to have advanced, progressive solid tumors, with or without bone metastases. Of 398 evaluable patients (of 483 enrolled in the trial), 39 percent had bone metastases at baseline. Patients received cabozantinib over 12 weeks. The trial was designed as a "discontinuation" trial, in which those who had partial responses stayed on the drug; those with stable disease were randomized to cabozantinib or placebo; and patients with progressive disease were removed from the trial. This novel type of clinical trial design more quickly evaluates the disease-stabilizing activity of growth-inhibitory agents like cabozantinib, compared to the traditional model of randomizing all patients to either the experimental arm or placebo.

Among 398 patients evaluable with all types of cancer included in the trial, the response rate was 9 percent (34 of 398). The highest disease control rates (partial response and stable disease) at week 12 were 76 percent for liver cancer (22 of 29 patients), 71 percent for prostate cancer (71 of 100 patients), and 58 percent for ovarian cancer (32 of 51 patients).

Fifty-nine of 68 patients with bone metastases (including patients with breast and prostate cancers and melanoma) experienced either partial or complete disappearance of the cancer on bone scans, often with significant pain relief and other improved cancer-related symptoms.

The reduction of bone metastases and pain relief was an unexpected finding in this study, Dr. Gordon said. Independent review by radiologists confirmed that bone metastases disappeared in the majority of patients who had bone metastases when they entered the study. The majority of these patients had castration-resistant prostate cancer (CRPC), but patients with breast cancer and melanoma also had disappearance of bone metastases. Bone metastases greatly contribute to morbidity and mortality in patients with these types of cancer, which typically spread to the bone.

Due to these results, the study has been expanded to include more CRPC patients. Similarly, the high rate of lasting responses in ovarian cancer patients led researchers to also expand the study to evaluate the drug's effect on patients with a particularly resistant form of the disease known as platinum resistant/refractory ovarian cancer.

This study expansion results will help determine the design of future Phase III trials, which will assess whether the drug extends patients lives or has other longer-term benefits among patients with specific cancer types. At present, cabozantinib is being investigated for use as a single agent. Additional studies will evaluate the efficacy and tolerability of appropriate combinations with other agents for future indications.

The most common grade three or above adverse events were fatigue (9 percent) and hand-foot syndrome (8 percent). Dose reductions were required in 41 percent of patients due to side effects; 12 percent were removed from the trial for adverse events.

ASCO2011特集

[News 01]
HPV検査単独の方がパップ検査よりも優れているようである

[News 02]
新たな複数分子を標的とした分子標的薬は骨転移病変を縮小または除去する

[News 03]
全ての男性が頻回のPSAスクリーニングを必要とするわけではない

[News 04]
CA-125と経膣エコーによるスクリーニング法は有効ではない

[News 05]
喫煙の乳がんに対するリスクのエビデンスがさらに得られた

[News 06]
PARP阻害薬は再発性卵巣がんの生存率を改善する

[News 07]
新たな化学療法レジメンにより高リスクALLの生存率が改善する

[News 08]
長期のイマチニブ投与により高リスクGIST患者の生存期間が延長される

[News 09]
BRAF阻害剤は転移性メラノーマの生存率を改善する

[News 10]
治療により小児神経芽腫の生存率が改善する

[News 11]
メラノーマのファーストライン治療としてipilimumabは有効である

[News 12]
エキセメスタンは健常女性の乳がんリスクを軽減させる

[News 13]
卵巣がんにおけるbevacizumabの治療ベネフィット

[News 14]
前立腺がん循環腫瘍細胞は生存期間と相関する

[News 15]
リンパ節への放射線照射は早期乳がんの予後を改善する

[News 16]
肺がんに対する維持療法は無増悪生存期間を改善する

[News 17]
アジュバント化学療法を早く開始するのが最適なようである

[News 18]
薬物により骨髄線維症の奏効率が改善する

[News 19]
抗体製剤はALLに対し有効である