まれな腫瘍性関節疾患の治療に対する有望な結果（Abstract: 10503）

色素性絨毛結節性滑膜炎再発患者に対する新たな治療選択肢

New treatment option for patients with recurrent pigmented villonodular synovitis

2014年ASCO年次総会で発表された第1相試験の初期結果によると、新たな標的治療薬PLX3397は、まれな腫瘍性関節疾患である色素性絨毛結節性滑膜炎（PVNS）に対し有効なようである。今回のスタディは、他の可能な治療を行ったにもかかわらず疾患が進行した患者を評価した。単群第1相のこのスタディで、最初に治療された23人の患者の結果が報告されている。患者は進行PVNSで膝、足関節、足、または肘に腫瘍を有していた。ほとんどの患者が複数回の手術を受け、前治療として放射線治療および/またはイマチニブやニロチニブなどの他の分子標的治療薬による全身治療を受けた患者もいた。患者は疾患の増悪または薬剤への忍容性がなくなるまでスタディ参加を継続した。評価可能な患者14人中11人（79%）は治療が奏効したと見なすのに十分な腫瘍縮小を示し、残りの3人は疾患が安定していた。患者の腫瘍容積は平均61%減少し、全体的な関節機能、疼痛やこわばりの軽減などの症状改善を含む迅速で実質的な改善が認められた。この薬剤の忍容性は良好であった。最も多い治療関連副作用は髪色変化、倦怠感、嘔気、眼周囲浮腫、味覚異常、下痢、嘔吐、および食欲低下であった。

Full Text

According to early results from a phase I study presented at ASCO's 2014 Annual Meeting, a new targeted drug, PLX3397, appears remarkably active against pigmented villonodular synovitis (PVNS), a rare neoplastic joint disorder. The study evaluated patients whose disease had progressed despite all other available therapies. More than three-quarters (79 percent) of the evaluable patients responded to the treatment, having a mean 61 percent reduction in tumor volume and rapid and substantial improvements in symptoms.

"These results are a shining example of how patients can experience a meaningful clinical benefit when we are able to match the right treatment with the right target," said lead author William D. Tap, M.D., Chief of the Sarcoma Medical Oncology Service at Memorial Sloan-Kettering Cancer Center in New York, NY. "PLX3397 seemed to have a tremendous impact on the joint-destructive disease process as patients often reported a marked decrease in swelling and pain even very early in their treatment course."

PVNS is a type of rare, often locally aggressive, musculoskeletal neoplasm that arises from the soft tissues of joints and tendons. In these patients, tumors form in the joint cavity, leading to gradual destruction of the joint and debilitating symptoms. Although it is characterized by an overgrowth of abnormal cells, PVNS is not referred to as a cancer per se, because it usually does not spread to other parts of the body. PVNS typically affects the hip or knee, and tends to occur in younger persons. Symptoms include joint swelling, pain, and reduced mobility.

While most patients are well managed with surgery, in some patients the disease comes back, necessitating additional surgery often requiring a joint replacement, and eventually advances to the point where it is no longer operable. PLX3397 may be an effective new therapy option for such patients.

PLX3397 is a novel oral tyrosine kinase inhibitor that blocks several molecular targets including the colony stimulating factor 1 (CSF1) receptor. In PVNS, a genetic abnormality causes the neoplastic cells to overproduce CSF1. This recruits CSF1 receptor-bearing immune cells that fill and destroy the joint. Therefore, PLX3397 blocks molecular pathways of the genetic abnormality that drives PVNS. This may slow the destruction of the joint and also reduce the inflammation that accompanies the disease process.

Results from the first 23 patients treated on this single-arm, phase I study are being reported. The patients had advanced PVNS with tumors in the knees, ankles, feet, or elbows. Most of the patients have undergone multiple surgeries and some have received prior treatment with radiation and/or with other systemic targeted treatments such as imatinib or nilotinib. The patients remained on the study until disease progression or inability to tolerate the drug.

Eleven out of 14 (79 percent) evaluable patients had tumor shrinkage sufficient to qualify as responders, and the disease was stable in the other three patients. Patients had substantial improvements in overall joint functionality, as well as decreased pain and stiffness. The drug was well tolerated. The most common treatment-related side effects were hair color changes, fatigue, nausea, swelling around the eyes, abnormal taste, diarrhea, vomiting, and decreased appetite.

"While it's still early, this study offers an exciting glimpse of the payoff of the precision medicine era, even for rare diseases like PVNS," said Clifford A. Hudis, M.D., FACP, ASCO President. "The research shows what's possible when we unravel the molecular drivers of a disease and identify a drug that directly targets these defects."

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