進行性小児がん治療に関する有望な結果（Abstract＃9500）

早期スタディにおいてcrizotinibはALK遺伝子異常により引き起こされる3つの小児がんに対し強力で長期持続する奏効を示した

In early study, crizotinib induces strong, long-lasting responses in three pediatric cancers driven by ALK gene abnormality

第48回American Society of Clinical Oncology学会で発表された第1相試験の結果、分子標的薬crizotinibは腫瘍の成長を停止させ、一部の症例では、進行性神経芽腫、未分化大細胞型リンパ腫（ALCL）または炎症性筋線維芽細胞性腫瘍（IMT）を有する選択された小児において全ての徴候を根絶することが示された。Crizotinibはこれらの小児がん患者において一般的に認められるALK遺伝子異常を標的とする。患者は6つの用量のcrizotinibのうちいずれかの用量を投与され、忍容性が良好な限りは同用量を継続した。その結果、ALCL患者の88%（7/8）において病変が検出されず完全寛解が認められた。奏効の持続は長期間認められ、治療を継続した患者は18か月間疾患の増悪を認めなかった。7人のIMT患者がこのトライアルに登録された。その多くが腫瘍の縮小から完全な腫瘍退縮に至るまでの実質的な有益性を最長2年間得た。神経芽腫患者27人中2人は完全寛解し、8人においては疾患が安定した。ALK異常が証明されている患者8人中2人が完全寛解した。治療が奏効したこれらの患者は疾患が増悪することなく9か月から2年以上にわたり治療を継続した。

Full Text

A Phase I study presented at the American Society of Clinical Oncology's 48th Annual Meeting has shown that the targeted drug crizotinib stalled tumor growth and, in some cases, eradicated all signs of cancer in select children with aggressive forms of neuroblastoma, anaplastic large cell lymphoma (ALCL) or inflammatory myofibroblastic tumors (IMT).

Crizotinib targets genetic abnormalities in the ALK gene, which are common in these pediatric cancers. If these promising early-phase findings are borne out in larger trials, crizotinib could become only the second effective molecularly targeted therapy for pediatric cancers. ALK abnormalities are present in 80 to 95 percent of ALCL cases, half of IMTs and 10 to 15 percent of aggressive neuroblastomas. Crizotinib was recently approved in the United States to treat adult ALK-driven lung cancers, about 5 percent of cases.

"It's remarkable that this targeted oral medication provided such a substantial benefit in these children with highly aggressive cancers, most of whom had already undergone every available therapy," said Yael Mosse, MD, assistant professor of pediatrics at the Children's Hospital of Philadelphia and the University of Pennsylvania. "Now that we know more about the drivers of some pediatric cancers, we can target those changes and treat patients in a much smarter, and potentially safer, way."

The study included 70 children whose cancer had progressed despite all standard therapies. When possible, patients' cancers were tested for ALK abnormalities, though this was not required for enrollment. Patients received one of six different doses of crizotinib – administered orally, twice a day – and remained on the drug as long as it was well-tolerated, which was the case in the vast majority of patients. By disease, researchers found:

- ALCL: 88 percent (7/8) of patients experienced a complete response, having no detectable disease. Responses have been long lasting, with patients remaining on treatment with no progression for as long as 18 months.
- IMTs: Seven patients with this rare disease were enrolled onto this trial. The majority have experienced substantial benefit, ranging from tumor shrinkage to complete tumor regression. Such responses have lasted for up to two years, with all patients still receiving therapy; these findings are important because no other available anticancer therapies are effective in this disease.
- Neuroblastoma: Overall, two of 27 patients had a complete response, and eight have had no disease progression (stable disease). Of patients with a proven ALK abnormality, two of eight patients experienced a complete response. These responders have remained on therapy for between 9 months to more than two years without progression – a notable finding given that most heavily pre-treated neuroblastoma patients on a Phase I trial experience cancer progression in 1 to 2 months.

Researchers also observed that neuroblastoma patients treated with higher doses of crizotinib – which in some cases were twice the approved adult dose – experienced demonstrable responses. This may explain why some neuroblastoma patients with proven ALK abnormalities did not respond to crizotinib, since they had received lower doses of the drug than the responders.

Dr. Mosse is the recipient of this year's James B. Nachman ASCO Junior Faculty Award in Pediatric Oncology.

ASCO2012特集

[News 01] 進行性小児がん治療に関する有望な結果
[News 02] メラノーマに対する有望な新併用療法
[News 03] オランザピンは化学療法の副作用をコントロールする
[News 04] 限局性高リスク前立腺がんの有望な治療
[News 05] 卵巣がんにおける無増悪生存期間の倍加
[News 06] リンパ腫の新たな治療法はCHOPよりも有効性が高い
[News 07] 進行肺がんの進行抑制
[News 08] Trametinibは進行メラノーマの生存期間を改善する
[News 09] スタディにより前立腺がんに関する論争が決着した
[News 10] 新たな分子標的薬はGIST患者の予後を改善する
[News 11] 進行乳がんに関する新たな治療法は有望である
[News 12] 進行大腸がん患者の生存期間延長
[News 13] 新たな微小管阻害薬は週1回のパクリタキセルと変わりない
[News 14] 若年の白血病患者は成人よりも予後が良好である
[News 15] 化学療法と放射線療法の併用は一部の脳腫瘍患者の寿命を延長する
[News 16] 小児がんに対する放射線治療は乳がんリスクを上昇させる
[News 17] 化学療法誘発性末梢神経障害に有効な治療
[News 18] 新たなPD-1標的免疫療法の有望な作用