# 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（Abstract No.3）

## メトトレキサート大量療法はB前駆細胞性急性リンパ性白血病の小児および若年成人の無イベント生存率を上昇させる

High-dose methotrexate boosts event-free survival for children and young adults with B-precursor acute lymphoblastic leukemia

高リスクB前駆細胞性急性リンパ性白血病（ALL）の小児および若年成人においてメトトレキサート大量療法は標準的なメトトレキサート 漸増療法よりも優れているとのスタディ結果が第47回ASCOで発表された。このPhase IIIスタディは高リスクB前駆細胞性ALLと新たに診断された1～30歳の患者2,426人を、標準的な導入化学療法および地固め化学療法後の2ヵ月の中間維持治療期間中にメトトレキサート大量療法群またはメトトレキサート漸増とアスパラギナーゼの併用群に無作為に割り付けた。計画されていた中間解析における5年間の無イベント生存率は、メトトレキサート大量療法群で**82%**でありメトトレキサート漸増療法群においては75%であった。骨髄およびCNS再発もまた大量療法群において有意に少なかった（それぞれ42対68および22対32）。発熱性好中球減少症発現率は大量療法群で低かった（5.2%対8.2%；P=.005）。その他の有意な毒性に関して差はなかった。登録は早期に中止され、メトトレキサート大量療法の適応である患者はその後、大量療法レジメンを受けることができた。

## Full Text

A randomized Phase III Children's Oncology Group study shows that a high-dose methotrexate regimen is superior to the standard regimen of escalating methotrexate for children and young adults with high risk B-precursor acute lymphoblastic leukemia. This regimen improved five-year event-free survival and had no greater significant side effects compared to the standard regimen. The trial establishes a new standard treatment for these patients.

"Pediatric ALL was once a deadly form of leukemia, and now it's one of the most curable. This trial helps us address an important need for patients with this disease. With these results, we now have an approach that will raise cure rates even higher," said Eric C. Larsen, M.D., principal investigator of the study and director of the Maine Children's Cancer Program and the Division of Pediatric Hematology/Oncology at the Barbara Bush Children's Hospital at Maine Medical Center. "Based on the findings from this trial all current and upcoming treatment protocols for children with newly diagnosed high risk B-precursor ALL will use this regimen."

Methotrexate has been an essential component in the treatment of children with ALL for more than 50 years, but the optimal dose and schedule has been a matter of debate and clinical research. Escalating intravenous methotrexate followed by a second chemotherapy drug called asparaginase (together known as the Capizzi regimen) has been an effective standard treatment for ALL for approximately two decades. This approach involves starting at a low dose of methotrexate and gradually increasing the dose depending on a patient's tolerance.

The escalating methotrexate regimen has led to improved cure rates for ALL, by decreasing relapses in the bone marrow, where the disease initially occurs. Relapse rates in the central nervous system (CNS) have not declined as significantly, representing an ongoing need for better treatment options. To reduce these CNS relapses, this study tested a methotrexate regimen, which delivers a dose 50 times the starting dose of the escalating regimen. The high-dose regimen has a greater potential to reach tumor cells in the central nervous system.

The Phase III study randomized 2,426 patients ages 1 to 30 with newly diagnosed high-risk B-precursor ALL to high-dose methotrexate versus escalating methotrexate plus asparaginase during a two-month interim maintenance phase of therapy following standard induction and consolidation chemotherapy. At a planned interim analysis, the five-year, event-free survival for patients who received high-dose methotrexate was 82 percent, compared to 75 percent for patients on the escalating methotrexate regimen.

There were also significantly fewer bone marrow and CNS relapses in the high-dose group. Enrollment was halted early as a result, and certain patients were eligible to then receive the high dose methotrexate regimen.

The investigators were initially concerned that there might be more side effects in the group receiving high-dose methotrexate, however these patients actually had a lower incidence of febrile neutropenia than those on the standard regimen. There were no differences in other significant toxicities.

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## ASCO2011特集