再発CLLの予後改善 (Abstract LBA7005)

新たなibrutinib併用療法は再発慢性リンパ性白血病においてかなりの恩恵をもたらす

New ibrutinib combination regimen shows substantial benefits in relapsed chronic lymphocytic leukemia

Ibrutinibとベンダムスチン+リツキシマブ（BR）の併用は過去の治療にもかかわらず悪化した慢性リンパ性白血病（CLL）患者の予後を改善するとの大規模第III相試験の中間解析結果が第51回American Society of Clinical Oncology年次集会で発表された。このスタディにおいて治療歴のあるCLL患者578人がibrutinibとBRまたはプラセボとBRで治療される群にランダムに割り付けられた。平均17.2か月の追跡期間の後、無増悪期間中央値はプラセボ群で13.3か月でありibrutinib群では期間中央値には達しなかった。進行または死亡のリスクはibrutinib投与群で80%低下した。奏効率はibrutinib群においてプラセボ群より有意に高かった（82.7%対67.8%）。疾患関連の倦怠感はibrutinib群で改善し、患者はその効果を早期に報告した（6か月後対14か月後）。副作用発現率と種類は2群間で同等であった。今回の顕著な結果に基づき、プラセボ群患者はibrutinib投与群にクロスオーバーすることが許可された。中間解析の時点で、プラセボ群患者の90人（31%）の患者がibrutinib群にクロスオーバーした。

Full Text

The combination of ibrutinib and bendamustine/rituximab (BR) improves outcomes for patients with chronic-lymphocytic leukemia (CLL) that worsened despite prior therapy according to an interim analysis of a large phase III study presented at the American Society of Clinical Oncology's 51st Annual Meeting.

At a median follow-up of 17 months, patients who received ibrutinib and BR had an 80% lower risk of disease progression or death than those who received placebo and BR. Based on this striking benefit, patients were permitted to cross over from the placebo group to receive ibrutinib.

For years, the standard treatment for CLL has been a combination of chemotherapy and targeted therapy (e.g., rituximab). Although these treatments help control the disease for many years, they cannot cure it, and all patients ultimately become resistant to therapy.

Until recently, patients whose disease worsened or came back despite treatment have had limited options. Last year, however, the FDA approved two new targeted drugs for such patients ─ ibrutinib and idelalisib in combination with rituximab. Ibrutinib is a first-in-class oral once-daily targeted treatment that blocks Bruton's tyrosine kinase (BTK). This protein fuels the growth of lymphocytes, the type of white blood cells that are affected by CLL.

"This was one of the most rigorous clinical trials ever conducted in CLL and it truly validates ibrutinib as an important drug for this cancer," said lead study author Asher Chanan-Khan, M.D., a professor of medicine at Mayo Clinic in Jacksonville, FL. "We found that ibrutinib can be safely paired with existing therapy to powerfully prolong remissions and improve patients' well-being."

In the study, 578 patients with previously treated CLL were randomly assigned to treatment with ibrutinib and BR or placebo and BR. After an average follow-up of 17.2 months, the median progression-free survival was 13.3 months in the placebo group and was not reached in the ibrutinib group. The risk of progression or death was decreased by 80% in those who received ibrutinib.

Response rates were significantly higher in the ibrutinib group than in the placebo group (82.7% vs. 67.8%). Disease-related fatigue improved in the ibrutinib group, and patients reported benefit sooner (at six months vs. 14 months).

At the time of the interim analysis, 90 (31%) patients from the placebo group had already crossed over to the ibrutinib group. The rates and types of side effects were comparable between the two treatment groups. The most frequent side effects were low blood cell counts and nausea.

The next steps for this area of research include evaluating ibrutinib as a single agent and in combination with drugs targeting the CD20 protein in patients with newly diagnosed, symptomatic, and asymptomatic CLL.

"Progress against chronic lymphocytic leukemia was one of the most important themes of the last two years, and now we have yet another potent treatment approach for patients who have exhausted other options," said ASCO Expert Merry-Jennifer Markham, M.D.. "These results suggest that we can achieve better outcomes for patients by pairing novel therapies with established treatments."

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