モノクローナル抗体は非ホジキンリンパ腫の寛解を2倍にする (Abstract LBA8502)

Obinutuzumabは再発性緩徐進行性非ホジキンリンパ腫の寛解期間を2倍にする

Obinutuzumab doubles remission duration in patients with relapsed, indolent non-Hodgkin lymphoma

第III相試験の中間解析の結果、緩徐進行性非ホジキンリンパ腫（NHL）に対し標準的なベンダムスチン治療にCD20モノクローナル抗体obinutuzumabを追加することによりNHLの進行が遅延するとの研究結果が、第51回American Society of Clinical Oncology年次集会で発表された。スタディでは様々なタイプのNHL患者396人を対象とし、うち最も多いのが濾胞性リンパ腫であった。この疾患の標準的な初回治療は、化学療法と分子標的治療薬リツキシマブの併用である。多くの患者が最終的にはリツキシマブ耐性となり、その後の治療選択肢は限られている。Obinutuzumabは、B細胞リンパ腫細胞を含む全てのB細胞の表面に存在するCD20蛋白を標的とする。患者はベンダムスチン単独治療群とベンダムスチンとobinutuzumabの併用後にobinutuzumab単独療法を受ける群とにランダムに割り付けられた。もはやリツキシマブ療法が有益でなくなった患者において、新たな併用療法施行後の平均寛解期間は29.2か月であったのに対し、ベンダムスチン単独群では14か月であった。これらの有望な結果に基づき、トライアルは早期に中止された。Obinutuzumabによる全生存率への有益性の可能性を確定するために長期追跡が必要である、と筆者らは述べている。

Full Text

Interim analysis of a phase III study finds that adding the new anti-CD20 monoclonal antibody obinutuzumab to standard bendamustine chemotherapy significantly delays progression of indolent non-Hodgkin lymphoma (NHL) according to researchers at the American Society of Clinical Oncology's 51st Annual Meeting. Among patients for whom rituximab therapy no longer provided benefit, the average duration of remission was 29.2 months after receiving the new combination vs. 14 months after bendamustine alone. The trial was stopped early based on these encouraging results.

"Unfortunately, there is yet no cure for indolent lymphoma, so the overall goal of treatment is to increase the amount of time patients remain symptom-free and in remission. The fact that this new approach doubled average remission time marks a major step forward for our patients," said lead study author Laurie Helen Sehn, MD, MPH, a medical oncologist at the BC Cancer Agency in Vancouver, Canada. "Obinutuzumab may offer patients the chance to stay well for a significantly longer period of time, putting off the need for additional chemotherapy."

Indolent NHL is a very common type of lymphoma. The standard initial treatment for this disease is a combination of chemotherapy and the targeted drug rituximab. The majority of patients ultimately become resistant to rituximab, and such patients have limited options for further treatment.

Obinutuzumab targets the CD20 protein, which is located on the surface of all B cells, including B-cell lymphoma cells. Previous research suggested that when monoclonal antibodies attach to this protein, some lymphoma cells die, and others appear to become more sensitive to chemotherapy.

While obinutuzumab has been tested in smaller clinical trials in various types of lymphoma, this is the first randomized phase III trial to assess the potential benefit of obinutuzumab in patients with NHL.

The study included 396 patients with various types of NHL, the most common being follicular lymphoma. The patients were randomly assigned to treatment with bendamustine alone or a combination of bendamustine and obinutuzumab followed by obinutuzumab single-agent therapy.

After an average follow-up of 21 months, the median investigator-assessed progression-free survival was 14 months for bendamustine alone vs. 29.2 months for the combination arm. The median progression-free survival by independent review has not been reached. Dr. Sehn noted that longer follow-up is needed to determine the potential overall survival benefit associated with obinutuzumab.

In general, there were no unexpected side effects or safety concerns from the combination regimen. Low white blood cell counts and infusion-related reactions were slightly more frequent in the combination arm compared to the bendamustine arm. The rates of low platelet counts, anemia and pneumonia were higher in the bendamustine alone arm.

"It's encouraging to see such impressive results for a novel anti-CD20 monoclonal antibody in a difficult-to-treat patient population such as those with rituximab-refractory indolent non-Hodgkin lymphoma," says ASCO Expert Merry-Jennifer Markham, MD. "The fact that this approach stalled cancer progression by more than a year will be good news to patients, who urgently need additional treatment options."

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