骨髄線維症の新規治療薬は血小板減少症を伴っていても有効である (Abstract LBA7006)

PERSIST：新規JAK阻害剤は血小板数が減少している患者であっても症状軽減に有効であることが証明された

PERSIST: Novel JAK inhibitor proves effective for easing symptoms of myelofibrosis even for patients with low platelet counts

骨髄線維症患者を対象としたPERSISTスタディの結果、pacritinibは血小板が非常に減少した患者であっても現状で利用可能な最良の治療（BAT）よりも有効であることが示唆された。このスタディにおいて、327人の患者がpacritinibまたはBATによる治療群にランダムに割り付けられた。BAT治療群患者はエリスロポエチン刺激薬、免疫調節薬（例えば、サリドマイド、レナリドミド）、およびヒドロキシウレアなどの承認適応外の骨髄線維症治療薬を定期的に投与された。このスタディは血小板数が非常に少ない患者を組み入れたため、ルキソリチニブは安全ではないと思われ、あえて除外した。Pacritinibの効果は治療開始後4週と、早い時点で認められた。24週後には、pacritinib群患者の19.1%において脾臓サイズが減少したのに対し、BAT群におけるその割合はわずか4.7%であった（p=0.003）。血小板数が最も少ない患者サブグループにおいて、脾臓縮小はpacritinib 群の33.3%に認められたのに対し、BAT群では0%であった。Pacritinib群患者は悪液質、盗汗、発熱、および骨痛などの症状の軽減が大であった。このスタディ結果は、第51回American Society of Clinical Oncology年次集会で発表された。

Full Text

Findings from the PERSIST study of patients with myelofibrosis suggest that pacritinib is significantly more effective than best available therapy (BAT), which includes a range of off-label treatments, even in patients with very low platelet counts. At 24 weeks of treatment, 19.1% of patients on the pacritinib arm experienced spleen shrinkage, compared to only 4.7% of patients on the BAT arm. The study findings were presented at the American Society of Clinical Oncology's 51st Annual Meeting.

Myelofibrosis is a rare blood cancer, and spleen enlargement is a common, debilitating symptom. Pacritinib also improved a range of additional symptoms and eliminated the need for blood transfusion in a quarter of patients who had previously been dependent on transfusions due to low blood counts.

This experimental therapy was also beneficial for a subgroup of patients with thrombocytopenia, for whom no FDA approved therapy exists.

"There is a huge unmet clinical need for patients with myelofibrosis. Only one drug is currently FDA approved for the disease, and it is not safe for patients with low platelet counts," said lead study author Ruben A. Mesa, MD, Deputy Director of the Mayo Clinic Cancer Center in Scottsdale, AZ. "We were encouraged to see that pacritinib was safe and effective in the trial, even in patients with severely low blood counts."

There is currently no cure for myelofibrosis, besides allogeneic hematopoietic stem cell transplant, which is an option that is not feasible for many, and the only FDA approved treatment is a JAK inhibitor, ruxolitinib. Several other agents targeting JAK proteins are in development.

In PERSIST, 327 patients were randomly assigned to treatment with pacritinib or BAT. Patients on the BAT arm received therapies that are routinely prescribed off-label for myelofibrosis, such as erythropoietin stimulating agents, immunomodulatory drugs (e.g., thalidomide, lenalidomide), and hydroxyurea. Ruxolitinib was intentionally excluded because this study included patients with very low platelet counts, for which this drug is not deemed to be safe.

The effects of pacritinib were seen as early as four weeks of starting treatment. At 24 weeks, 19.1% of patients in the pacritinib arm had a reduction in spleen size, compared to only 4.7% in the BAT arm (p=0.003). In the subgroup of patients with the lowest platelet counts (those who are not candidates for ruxolitinib), spleen shrinkage occurred in 33.3% of patients in the pacritinib arm and 0% in the BAT arm.

Compared to patients on the BAT arm, patients on the pacritinib arm experienced a greater degree of relief from symptoms such as cachexia, night sweats, fever, and bone pain. The vast majority (79%) of patients on the BAT arm eventually crossed over to the pacritinib arm.

Pacritinib also helped alleviate anemia in some patients; among patients who had been dependent on red blood cell transfusion, 25.7% no longer needed the procedure. In contrast, none of the patients on the BAT arm became transfusion independent.

The most common side effects of pacritinib were diarrhea, nausea, and vomiting. The symptoms typically lasted less than one week and few patients discontinued treatment due to side effects.

Longer follow up is needed to determine if pacritinib improves survival. The ongoing PERSIST-2 phase III trial is exploring pacritinib for the treatment of patients who have low blood platelet counts due to their disease, or due to their therapy. Dr. Mesa remarked that pacritinib may be an attractive agent to combine with other therapies, as it does not cause low platelet counts.

ASCO President-Elect Julie M. Vose, MD, MBA, FASCO commented on the study. "This is exciting news for patients with myelofibrosis, a blood cancer for which the discovery of new treatments has been slow. It's especially encouraging that pacritinib is effective in some patients with low blood counts, since they are not ideal candidates for the only other FDA approved therapy."

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