Ibrutinib Approval Expanded to Include Chronic GVHD

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Ibrutinib is the first FDA-approved drug for treating GVHD.

The US Food and Drug Administration (FDA) has approved the tyrosine kinase inhibitor ibrutinib (Imbruvica, Pharmacyclics) for adult patients with chronic graft vs host disease (GVHD) who have failed on one or more lines of prior systemic therapy. Ibrutinib is the first drug to be approved by the FDA for the treatment of GVHD.

"Unfortunately for patients who fail frontline corticosteroid therapy there are no approved or effective therapies," Lori Styles, MD, medical director of Pharmacyclics in Sunnyvale, California, told *Cancer Network* last year at the 58th Annual Meeting of the American Society of Hematology (ASH), where results of a phase I/II study of ibrutinib in patients with chronic GVHD were presented. The FDA's approval was based on these results.

VIDEO: Lori Styles, MD, on Ibrutinib in Patients With Chronic GVHD

The open-label, multicenter trial included 42 patients with chronic GVHD who had failed on corticosteroid therapy and required additional treatment. The majority of patients (88%) had at least two organs involved at baseline, most commonly the mouth (86%), skin (81%), and gastrointestinal tract (33%).

Patients were treated with oral ibrutinib 420 mg once daily. About two-third of patients (67%) responded to the drug. The median time to response coinciding with the first scheduled response assessment was 12.3 weeks and responses were seen in all organs involved. About one-half of patients (48%) had responses lasting 5 months or longer.

"That is significant because [these patients] are also on corticosteroids, and those are effective but have a large associated morbidity and cause a lot of side effects," Styles said. "Patients were able to sustain the response; they also showed a decrease in the use of corticosteroids."

The most common adverse reactions were fatigue, bruising, diarrhea, thrombocytopenia, stomatitis, muscle spasms, nausea, hemorrhage, anemia, and pneumonia. About one-quarter of patients had to discontinue treatment due to adverse reactions to the drug.

Commenting on this approval, James L. M. Ferrara, MD, DSc, the Ward–Coleman Chair in Cancer Medicine and Director of the Hematologic Malignancies Translational Research Center at the Tisch Cancer Institute at Mount Sinai in New York said, "This is an important advance and great news for our patients, because it is the first drug to be approved for this difficult condition. Chronic GVHD is a major complication of bone marrow and stem cell transplants that can be fatal when it does not respond to therapy, and a number of trials have failed in the past. The response rate here is very high and extremely encouraging. Further trials will test whether ibrutinib can be used as primary therapy at the onset of disease, perhaps providing even better responses."

The FDA previously approved ibrutinib for the treatment of chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), CLL/SLL with 17p deletion, Waldenström macroglobulinemia, marginal zone lymphoma, and mantle cell lymphoma.

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