FDA expands ibrutinib indications to chronic GVHD

On August 2, 2017, the U.S. Food and Drug Administration approved ibrutinib (Imbruvica, Pharmacyclics LLC) for the treatment of adult patients with chronic graft versus host disease (cGVHD) after failure of one or more lines of systemic therapy. This is the first FDA-approved therapy for the treatment of cGVHD.

Approval was based on Study PCYC-1129-CA (NCT02195869), an open-label, multi-center, single-arm clinical trial enrolling 42 patients with cGVHD after failure of first-line corticosteroid therapy and requiring additional therapy. The majority of patients (88%) had at least two organs involved at baseline. The most common organs involved were mouth (86%), skin (81%), and gastrointestinal tract (33%).

Patients received ibrutinib orally at 420 mg once daily. Investigator-assessed overall response rate was 67%, or 28 patients (95% CI: 51%, 80%). The median time-to-response coinciding with the first scheduled response assessment was 12.3 weeks (range, 4.1 to 42.1 weeks). Responses were seen in all organs involved with cGVHD (skin, mouth, gastrointestinal tract, and liver). Responses lasting five months or longer were observed in 48% of the patients (n=20).

The most common adverse reactions (≥20%) were fatigue, bruising, diarrhea, thrombocytopenia, stomatitis, muscle spasms, nausea, hemorrhage, anemia, and pneumonia. Atrial fibrillation occurred in one patient (Grade 3). Treatment was discontinued due to adverse reactions in 24% of the patients. The most common adverse reactions leading to discontinuation were fatigue and pneumonia. Adverse reactions leading to dose reduction occurred in 26% of patients.

FDA previously approved ibrutinib for the treatment of chronic lymphocytic leukemia/small lymphocytic lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma with 17p deletion, Waldenström's macroglobulinemia, marginal zone lymphoma, and mantle cell lymphoma.

The recommended dose of ibrutinib for cGVHD is 420 mg taken orally once daily (three 140 mg capsules once daily).

Full prescribing information is available at:
https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/205552s017lbl.pdf
(https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/205552s017lbl.pdf)

FDA granted Breakthrough Therapy and Orphan Drug designations to ibrutinib for this indication, as well as priority review. A description of FDA expedited programs is in the Guidance for Industry: Expedited Programs for Serious Conditions-Drugs and Biologics, available at:
http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm358301.pdf
(/media/86377/download).

Healthcare professionals should report all serious adverse events suspected to be associated with the use of any medicine and device to FDA's MedWatch Reporting System by completing a form online at http://www.fda.gov/medwatch/report.htm (http://www.fda.gov/medwatch/report.htm), by faxing (1-800-FDA-0178) or mailing the postage-paid address form provided online, or by telephone (1-800-FDA-1088).

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