FDA Approves Venclexta for More Types of Leukemia

Approval was based on improves progression-free survival in the MURANO trial.

June 8, 2018 By Food and Drug Administration (FDA)

On June 8, 2018, the Food and Drug Administration granted regular approval to venetoclax (VENCLEXTA, AbbVie Inc. and Genentech Inc.) for patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL), with or without 17p deletion, who have received at least one prior therapy.

Approval was based on MURANO (NCT02005471), a randomized (1:1), multicenter, open-label trial of venetoclax with rituximab (VEN+R) versus bendamustine with rituximab (B+R) in 389 patients with CLL who had received at least one prior line of therapy. Patients in the VEN+R arm completed a 5-week ramp-up venetoclax scheduleand then received venetoclax 400 mg once daily for 24 months measured from the rituximab start date. Rituximab was initiated after venetoclax ramp-up and given for 6 cycles (375 mg/m^2 intravenously on cycle 1 day 1 and 500 mg/m^2 intravenously on day 1 of cycles 2-6, with a 28-day cycle length). The comparator arm received 6 cycles of B+R (bendamustine 70 mg/m2 on days 1 and 2 of each 28-day cycle and rituximab at the above described dose and schedule).

Efficacy was based on progression-free survival (PFS) as assessed by an Independent Review Committee. After a median follow-up of 23 months, the median PFS was not reached in the VEN+R arm and was 18.1 months (95% CI: 15.8, 22.3) in the B+R arm (HR 0.19; 95% CI: 0.13, 0.28; $p<0.0001$). The overall response rate was 92% in the VEN+R arm compared to 72% for those treated with B+R.

In patients treated with VEN+R, the most common adverse reactions (incidence ≥20%) were neutropenia, diarrhea, upper respiratory tract infection, fatigue, cough, and nausea. Grade 3 or 4 neutropenia developed in 64% of these patients, and grade 4 neutropenia developed in 31%. Serious adverse reactions occurred in 46% of patients. Serious infections developed in 21% of patients, most commonly pneumonia (9%).

Due to rapid reduction in tumor volume, tumor lysis syndrome (TLS) is an important identified risk with venetoclax treatment. See the prescribing information for TLS risk stratification, prophylaxis, and monitoring.

All approved venetoclax regimens begin with a 5-week ramp-up. Full prescribing information is available at: Venclexta PI.

FDA granted venetoclax in combination with rituximab Breakthrough Therapy Designation and granted this application priority review. A description of FDA expedited programs is in the Guidance for Industry: Expedited Programs for Serious Conditions-Drugs and Biologics.

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 or by calling 1-800-FDA-088.

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