Venetoclax

Management and care for patients with relapsed or refractory chronic lymphocytic leukemia

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BACKGROUND: Venetoclax (Venclexta™) is a potent, selective, orally available, small-molecule B-cell lymphoma 2 inhibitor that achieves response rates of about 80% and has an acceptable safety profile for patients with relapsed or refractory chronic lymphocytic leukemia (CLL).

OBJECTIVES: The aim was to describe treatment management considerations when caring for patients using venetoclax.

METHODS: A review was done of safety and management considerations based on current clinical practice and 240 patients with CLL who received venetoclax monotherapy on clinical trials from 2011–2016.

FINDINGS: Common adverse events were neutropenia, diarrhea, nausea, anemia, upper respiratory tract infection, thrombocytopenia, and fatigue. Because of rapid tumor reduction with venetoclax, nurses should be aware of the potential for tumor lysis syndrome (TLS) and the need to educate patients on steps to minimize risks, including gradual dose ramp-up, adequate hydration, and use of prophylactic antihyperuricemia agents. Following implementation of these risk-reducing measures, no clinical TLS events were reported in ongoing trials.

KEYWORDS
BCL-2 inhibitor; safety; dosing; venetoclax; chronic lymphocytic leukemia

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CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) IS THE MOST COMMON SUBTYPE of adult leukemia in Western countries (National Cancer Institute [NCI], 2017). Until 2013, standard treatment for CLL was limited to aggressive cytotoxic chemotherapy regimens not easily tolerated by older or frailer individuals (Stilgenbauer, Furman, & Zent, 2015). CLL is still considered incurable, although the approvals of novel therapeutic agents, particularly those that inhibit the B-cell receptor signaling pathway, have shown promising outcomes for patients with CLL (Jain & O'Brien, 2016). Ibrutinib (Imbruvica®) is an orally available small-molecule Bruton's tyrosine kinase inhibitor that inhibits B-cell proliferation and survival (Pharmacyclics, 2017). Idelalisib (Zydelig®) is an oral inhibitor of the delta isoform of phosphatidylinositol 3-kinase, which induces apoptosis and inhibits cell-signaling pathways, including the B-cell receptor (Gilead Sciences, 2014). Approval of idelalisib and ibrutinib by the U.S. Food and Drug Administration (FDA) in 2014 greatly changed the treatment landscape. Obinutuzumab (Gazyva®), a CD20-directed antibody, in combination with chlorambucil was also approved for patients with previously untreated CLL.

In April 2016, accelerated approval of venetoclax (Venclexta™) by the FDA provided another novel therapeutic alternative (AbbVie, 2016). Venetoclax is a potent, selective, orally available small-molecule B-cell lymphoma 2 (BCL-2) inhibitor that achieves high response rates and has an acceptable safety profile for patients with relapsed or refractory CLL (Roberts et al., 2016; Stilgenbauer et al., 2016). This article provides an overview of the CLL disease state, as well as details on the pharmacokinetics, mechanism of action, efficacy, and safety profile of venetoclax.

Chronic Lymphocytic Leukemia

CLL is a lymphoproliferative disorder characterized by a progressive accumulation of monoclonal, small, mature-appearing CD5+ B cells within the blood, bone marrow, lymph nodes, and secondary lymphoid organs. CLL primarily affects older adults, with a median age of 71 years at diagnosis (NCI, 2017).

The five-year survival rate for patients with CLL is about 80%, but the clinical course is extremely variable (Stilgenbauer et al., 2015). About one-third of patients have indolent disease that does not require treatment at any point. Another third have an initial indolent phase that is followed by steady progression of the disease requiring therapy. The remaining patients have aggressive disease and require treatment at the time of diagnosis. Of patients