Journal of Leukemia
ISSN: 2329-6917
OPEN ACCESS Freely available online
Opinion Article

A Comprehensive Overview on the Effectiveness of Venetoclax used in Treatment of Acute Myeloid Leukemia

Santorsola Mariachiara*

Department of Pathology, University Hospitals Cleveland Medical Center, Cleveland, USA

DESCRIPTION

The most prevalent form of adult leukemia is Acute Myeloid Leukemia (AML), a hematological cancer. High genetic diversity and heterogeneity with gene mutations are features of AML. AML has a significant death rate, with less than 50% of patients surviving for five years overall. Furthermore, the majorities of AML patients frequently develop resistance to chemotherapy and relapse. Therefore, novel approaches to treating AML are required. Chemotherapy-induced cell death is a promising technique for treating malignant tumors, and numerous anti-tumor medicines have been developed to target molecules involved in cell death. Apoptosis (type I), autophagic (type II), and necrotic (type III) cell death are the three main forms of cell death. Other forms of cell death that have been documented include necroptosis, ferroptosis, and pyroptosis. The mechanism of apoptosis has been well studied among the several types of cell death. An increase in the permeability of the mitochondrial outer membrane causes apoptosis. A shift in Mitochondrial Outer Membrane Permeabilization (MOMP) causes the release of cytochrome C from the mitochondria into the cytoplasm, which in turn causes the activation of proteases specialized to cysteine aspartate, which cleaves a variety of substrates and causes apoptosis.

The B Cell Leukemia gene-2 (*Bcl-2*) family negatively regulates the rise in MOMP during the execution of apoptosis. Pro-apoptotic proteins including *Bcl-2* homologous antagonist/killer and *Bcl-2*-associated X protein (Bax) are thought to multimerize in response to apoptotic stimuli and create pore on mitochondria, which raises MOMP. Conversely, *Bcl-2* and Bcl-XL function as anti-apoptotic agents by blocking multimerization through their interactions with Bak or Bax via the BH3-domain. Thus, *Bcl-2* and Bcl-XL suppression can encourage malignant tumor cells to undergo apoptosis. Navitoclax (ABT-263) is a tiny chemical mimicking the BH3 domain that was initially created as an anti-tumor drug to cause the malignant tumor cells to undergo apoptosis. In general, nibolax binds to members of the anti-apoptotic *Bcl-2* family, including *Bcl-2*, Bcl-XL, and Bcl-w. In clinical trials, navigoclax demonstrated positive effects on small-cell lung cancer and Chronic Lymphocytic Leukemia (CLL); however, because to the platelet-producing function of Bcl-XL, it also demonstrated dose-limiting thrombocytopenia. As a result, the *Bcl-2* specific inhibitor venetoclax (ABT-199) was created to lessen the thrombocytopenic impact. In phase III clinical trials, venetoclax was tested in combination with rituximab for CLL.

After 4 years, the overall survival increased to 85.3% in venetoclax + rituximab *vs* 66.8% in rituximab alone, and the progression-free period increased to 57.3% in venetoclax + rituximab *vs* 4.6% in rituximab alone.

Venetoclax was licensed by the U.S. Food and Drug Administration (FDA) in 2016 for patients with relapsed or refractory Chronic Lymphocytic Leukemia (CLL). Phase III trials combining azacitidine or low-dose cytarabine have been carried out in the clinical research of AML, and in both instances, the median overall survival has been extended. In 2018, the FDA additionally approved venetoclax for patients 75 years of age and older who had recently been diagnosed with AML or had problems that precluded them from receiving intense induction chemotherapy. A short chain fatty acid called Sodium Butyrate (NaB) is created when dietary fibers are broken down. NaB is known to have the ability to stop the proliferation of cells in malignant tumors, and this action is thought to be mediated *via* its HDAC inhibitory function.

Previously it was demonstrated that through the overexpression of its receptor, NaB sensitized a variety of human malignant tumors to the anti-tumor cytokine, Tumor-Necrosis Factor Related Apoptosis Ligand (TRAIL). Furthermore, t (8;21) AML cells, in which TRAIL was downregulated by an RUNX1-ETO fusion protein, were efficiently destroyed by the combination of NaB and TRAIL. Given that NaB has a tumoricidal impact, we postulated that NaB could compensate for venetoclax's limited effectiveness in the treatment of acute myeloid leukemia.

Correspondence to: Santorsola Mariachiara, Department of Pathology, University Hospitals Cleveland Medical Center, Cleveland, USA, E-mail: mariachiara@gmail.com

Received: 05-Feb-2024, Manuscript No. JLU-24-30060; **Editor assigned:** 07-Feb-2024, PreQC No. JLU-24-30060 (PQ); **Reviewed:** 28-Feb-2024, QC No. JLU-24-30060; **Revised:** 06-Mar-2024, Manuscript No. JLU-24-30060 (R); **Published:** 13-Mar-2024, DOI: 10.35248/2329-6917.24.12.374

Citation: Mariachiara S (2024) A Comprehensive Overview on the Effectiveness of Venetoclax used in Treatment of Acute Myeloid Leukemia. J Leuk. 12:374.