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Letter to Editor

Sodium-glucose transport 2 inhibitors: Practical management of the venetoclax-induced adverse events

Dear Editor

Venetoclax as a selective B-cell lymphoma 2 (BCL-2) inhibitor is approved for hematologic malignancies treatment. Beyond its established efficacy in lymphoid cancers, it exhibits strong anti-leukemic function against chronic lymphocytic leukemia (CLL) and acute myeloid leukemia (AML) (1). In clinical practice, Venetoclax has been associated with several common and serious adverse effects including tumor lysis syndrome (TLS), myelosuppression, hyperglycemia, infection, febrile neutropenia, autoimmune hemolytic anemia, cardiac toxicity, etc (1, 2). Effective management of these adverse events is critical to increase the quality of life in Venetoclax-treatment patients. Respectfully, we want to offer the concurrent use of Sodium-Glucose Cotransporter-2 Inhibitors (SGLT2Is) and Venetoclax. This appears to be an innovative approach. In addition to highlighting the beneficial supportive effects of SGLT2Is through mechanisms that might still be unclear, these medications show promise as adjunctive therapies for intractable hematological malignancies treatment (3).

SGLT2Is, initially developed as antidiabetic medications, are standard care for heart failure (HF) and chronic kidney disease (CKD) (4). These medications are generally well tolerated. The most frequent side effects observed are urogenital infections and more frequent urination. To date, no significant safety concerns have been identified (5). We are profoundly intrigued by the underexplored therapeutic effects of SGLT2 inhibitors and are committed to elucidating their novel repurposing. There is considerable evidence that SGLT2Is elevate hemoglobin and hematocrit by stimulating erythropoietin synthesis and erythropoiesis and restoring iron homeostasis. Thus, their effects on anemia improvement cannot be ignored (6, 7). Favorably, SGLT2Is are a good manager for medication-induced hyperglycemia among antidiabetic medications (8). The positive impact of SGLT2Is, in terms of lower mortality rate as well as lower incidence of sepsis and neutropenic fever in cancer patients with life-threatening consequences, should be taken seriously (9). Also, we intend to emphasize the potential influences of SGLT2Is in hyperuricemia due to tumor lysis syndrome. SGLT2Is reduce serum uric acid through two mechanisms, including decreased uric acid synthesis by downregulating the pentose phosphate pathway and increased renal excretion of urate (10).

In listing the various effects of SGLT2Is, we point out their cardio-protective effects, which notably diminished the risk of HF incidence and hospitalization among hematologic and solid tumor cancer patients, especially those treated with cardio-toxic chemotherapy agents (11, 12). Furthermore, research in cardio-oncology has demonstrated the anticancer potential of SGLT2 inhibitors, which likely operate through mechanisms such as adenosine monophosphate–activated protein kinase (AMPK) pathway stimulation, mitochondrial complex I inhibition, decreased glucose absorption, and enhanced immune responses (13). The broad therapeutic scope of SGLT2Is-spanning anemia correction, drug-induced hyperglycemia optimization, sepsis and neutropenic fever reduction, hyperuricemia mitigation, cardioprotection, and anticancer activity, makes the assertion highly convincing, that SGLT2Is can be effective in Venetoclax-induced adverse events management through a “multi-bird, one stone” mechanism. Your journal is pioneering innovative research strategies that develop valuable clinical protocols incorporating SGLT2Is, potentially enhancing patients' outcomes and quality of life.

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