Repurposing Venetoclax to Improve the Response in Mantle Cell Lymphoma

MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN

Incorporating venetoclax, a drug approved for a different type of cancer, into a novel front-line treatment regimen for patients with MCL.

Due to the lack of a standardized treatment approach for MCL and the toxicities associated with cytotoxic chemotherapy, we designed a phase I study to build upon a treatment regimen that utilizes a combination of rituximab, an antibody, and lenalidomide, an oral medication, in combating MCL. The proposed clinical trial incorporates venetoclax, a drug approved chronic lymphocytic leukemia treatment, to the combination of rituximab and lenalidomide.

In an ongoing phase I clinical trial, we have thus far had no major adverse events attributed to the combination and as such the combination of the three drugs appears safe, and the addition of venetoclax appears to significantly speed up treatment response in a small number of patients. Given our results, we plan to treat additional MCL patients with this combination to determine exactly how fast the drugs can provide a response and exactly how beneficial the regimen is in these patients. This is the first upfront trial in this “high-risk” population of MCL patients exploring a completely non-cytotoxic regimen.

Evaluating the long-term efficacy of adding the chronic lymphocytic leukemia drug venetoclax to lenalidomide plus rituximab treatment in 28 patients with newly diagnosed mantle cell lymphoma to improve patient outcomes

DISEASE/CONDITION

Mantle cell lymphoma (MCL) is a rare blood cancer that results from the malignant transformation of a B lymphocyte, a type of white blood cell, leading to abnormal blood cell growth. MCL is a subset of non-Hodgkin lymphoma (NHL) and is most prevalent in elderly male patients.

MCL falls into three general categories: indolent (slow growing), classical, and aggressive. Symptoms are variable but patients can present with fever, night sweats, abdominal pain, anemia, thrombocytopenia, pruritus, rashes, adenopathy, or painful splenomegaly.

PROJECT

We will expand on the ongoing Phase I dose-escalation clinical study, enrolling 12 additional patients and modify the primary endpoint to 5-year progression-free survival (PFS).

The trial is currently active, and we have enrolled 18 of a planned 28 patients to date. We hope to compare this regimen to “standard regimens” in this patient population. Although the current chemotherapy drugs used to treat MCL can be effective, they come with considerable side effects including infection, heart failure, renal failure, and potentially death.

Additional funding will help with completion of clinical trial which includes minimal residual disease testing, BH3 profiling, and performing additional genetic testing to help better characterize each patient’s MCL.

Achieving the aims of the study would broaden the pool of patients able to receive effective frontline therapy, while improving the side effect profile and potentially eliminating the need for high dose chemotherapy followed by stem cell rescue.