

Determining Optimal Antifungal Prophylaxis in Acute Myeloid Leukemia Patients Receiving Venetoclax

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Background: Venetoclax was recently approved in 2018 for initial treatment of AML in combination with hypomethylating agents or low-dose cytarabine among elderly patients. During treatment for AML, neutropenia is common and increases the risk for development of infections, including fungal infections. Specifically, treatment with venetoclax often results in profound and prolonged neutropenia. Appropriate antifungal prophylaxis has not yet been determined.

Purpose: This study looks at patients with AML that received antifungal prophylaxis to compare the effectiveness of the antifungal agent. At the University of Kansas Health System (TUKHS), antifungal prophylaxis recommendations have not yet been determined, though fluconazole or posaconazole are often prescribed. The primary outcome is to compare the rate of fungal infections in patients receiving venetoclax in combination with fluconazole or posaconazole. The secondary outcome is to compare the duration of cytopenias [specifically absolute neutrophil count (ANC) and thrombocytopenia] in patients receiving the previously mentioned treatment. It is hypothesized that patients receiving fluconazole as antifungal prophylaxis will have higher rates of invasive fungal infections compared to posaconazole as antifungal prophylaxis.

Methods: This study is a single center, retrospective cohort study looking at patients at TUKHS from November 1, 2018 through January 31, 2020. Patients 18 years and older who received treatment with venetoclax in combination with a hypomethylating agent for AML will be included. Data that will be analyzed include dosing of venetoclax, the hypomethylating agent used, dosing of the hypomethylating agent, the response seen after each cycle, and days from induction therapy until ANC and platelet recovery. If a fungal infection is present, additional data collected include treatment antifungal agent, site of fungal infection, and fungal pathogen.

Results: This study evaluated the antifungal prophylaxis regimen of 96 patients who were also being treated with venetoclax and a hypomethylating agent. Twelve of the patients developed a fungal infection while receiving prophylaxis. Of these twelve patients, 1 patient received fluconazole and 2 patients received posaconazole. Treatment with fluconazole or posaconazole showed better efficacy for preventing fungal infections compared to voriconazole or isavuconazole ($p = 0.001$). Posaconazole had an average duration of neutropenia of 61.9 days compared to fluconazole which had an average duration of 83.3 days. Of the patients who developed a fungal infection, all patients had prolonged neutropenia greater than 30 days. Fluconazole also had significantly longer duration of thrombocytopenia than posaconazole (49 days vs. 112.4 days).

Conclusion: The rates of invasive fungal infections were similar between fluconazole and posaconazole, but fluconazole had significantly longer durations of neutropenia and thrombocytopenia. Isavuconazole and voriconazole should be avoided as antifungal prophylaxis due to more frequent infections.