Written By: Seema Patel, PharmD
Institution: The Cleveland Clinic

Optimizing Venetoclax Treatment for Acute Myeloid Leukemia

Description:

- The purpose of this document is to highlight processes for minimizing treatment delays for patients with acute myeloid leukemia (AML) on venetoclax and hypomethylating agent (HMA) therapy including optimization of venetoclax initiation and continued patient management.

Background:

- AML is a hematologic malignancy resulting from inappropriate expansion of leukemic myeloid precursor cells in the bone marrow, peripheral blood, and/or other tissues and is the leading cause of adult leukemia deaths in the United States1-4
    - Novel therapies such as the oral B-cell lymphoma 2 (BCL-2) inhibitor venetoclax in combination with a hypomethylating agent such as azacitidine or decitabine are considered standard of care for those that are intensive induction ineligible per the National Comprehensive Cancer Network (NCCN®) guidelines
- Patients initiated on oral oncolytics such as venetoclax may encounter barriers such as distribution access necessitating sending prescriptions to an outside pharmacy, insurance approval, and costs
- While many AML patients can initiate venetoclax therapy as an outpatient, some patient-specific factors, including risk of tumor lysis syndrome (TLS), severity of baseline disease, and need for frequent transfusions, may necessitate an inpatient admission for observation
- Creating a reliable framework to minimize delays in venetoclax treatment initiation can aid in expediting patient care and maximizing clinical outcomes while on treatment
    - Necessary considerations include assessment of treatment response, ongoing monitoring for myelosuppression, and preventing infection with antibiotic/antifungal prophylaxis bearing in mind possible CYP3A4 mediated drug-drug interactions[6]

PQI Process:

- Initial patient assessment and treatment considerations
    - Upon AML diagnosis and decision to initiate venetoclax therapy, all new venetoclax prescriptions will trigger a pharmacy consult
    - The pharmacist will collaborate with the provider to:
        - Manage the risks of TLS and infection by recommending appropriate prophylaxis (e.g., antihyperuricemics, antiemetics, antimicrobials, and other supportive care)
        - Determine whether the patient should start treatment as an inpatient or outpatient according to TLS risk and necessary monitoring, transfusion threshold, ease of hospital access, etc.
        - Establish a dosing schedule and recommend dose adjustments to account for potential drug interactions
        - Review the monitoring requirements, including the timing of bone marrow biopsy (BMB) and various laboratory tests such as complete blood cell count (CBC), blood chemistry, etc.

- Medication dispensing and coordination of care
    - Pharmacist or pharmacy technician will obtain the patient's insurance information, identify the dispensing specialty pharmacy, and initiate a search for any potential patient assistance programs if needed
    - The pharmacist will assist the provider in sending the prescription to the specialty pharmacy and outreach to the pharmacy to request expedited processing of the prescription
    - Pharmacist and pharmacy technician will work together to:
        - Follow up with any materials necessary for prior authorization (PA; i.e. clinical notes, test results)
            - If patient to be hospitalized for treatment initiation, coordinate with submission of necessary PA documentation if required for inpatient admission
        - Follow up with the patient to acquire information for patient assistance programs if needed
    - Provider will reach out to the insurance company for an urgent peer-to-peer should the medication be denied
    - Once the medication is acquired
        - If patient will be admitted inpatient for venetoclax ramp up dosing, pharmacist and/or nurse navigator to advise patient to bring their home medication to the hospital to be utilized for treatment
        - Pharmacist and/or nurse navigator to coordinate concomitant initiation of venetoclax and HMA
- Remission assessment and on-going patient management
    - A bone marrow biopsy to evaluate for remission of disease is recommended between days 21 and 28 of cycle 1 (remission defined as less than 5% leukemia blasts with cytopenias)[7]. For patients with resistant disease after cycle 1, repeat BMB evaluations in cycle 2 and beyond should be performed as clinically indicated.
- See Table 1 for recommended venetoclax dosage modifications for hematologic adverse reactions
    - In clinical practice, adjustments of venetoclax cycle length may be instituted once remission is achieved and prior to occurrence of hematologic adverse events
- Cytopenias are common and recommended management is dependent on remission status (see Table 1 for management of hematologic adverse reactions based on remission status)
- Designated clinical team member will reach out to patient to encourage continued adherence to venetoclax dosing schedule or to inform patient if BMB results and/or blood cell counts necessitate treatment hold and/or initiation of supportive care measures

Table 1. Venetoclax dosage modification for hematologic adverse reactions[7]

Adverse Reaction	Occurrence	Dosage Modification
Grade 4 neutropenia with or without fever or infection; or Grade 4 thrombocytopenia	Occurrence prior to achieving remission	In most cases, do not interrupt venetoclax due to cytopenias prior to achieving remission
	First occurrence after achieving remission and lasting at least 7 days	Delay subsequent cycle of venetoclax and monitor blood counts

		Upon resolution to Grade 1 or 2, resume venetoclax at the same dose in combination with HMA
	Subsequent occurrences in cycles after achieving remission and lasting 7 days or longer	Delay subsequent cycle of venetoclax and monitor blood counts Upon resolution to Grade 1 or 2, resume venetoclax at the same dose in combination with HMA, and reduce venetoclax duration by 7 days during each of the subsequent cycles, such as 21 days instead of 28 days

Patient-Centered Activities:

- Ensure the patient is informed about the prescription status and availability for pick-up, involving the patient or a family member if needed for communication with the specialty pharmacy
- Provide the Patient Education Sheet
- Review common adverse events including neutropenia, infection, fever, chills, sore throat, burning with urination, unusual tiredness, etc. and who to contact if side effects occur
- If hospitalization recommended for treatment initiation, review steps in preparation for hospital admission with patient and caregiver
- Regularly follow up with the patient to assess adherence to treatment regimen, confirm and reinforce venetoclax dosage and schedule, and address how to manage missed doses
- Consider utilizing a daily dose tracker or calendar for assistance
- Reinforce importance of concomitant administration of venetoclax and HMA and coordination with infusion staff to ensure patient is aware of HMA administration appointments/schedule
- For more detailed information regarding risk of TLS, ramp up dosing schedule, dose adjustments for drug interactions, patient counseling etc., refer to Venetoclax (Venclexta®) for the Treatment of Acute Myeloid Leukemia PQI
- Also refer to TLS Risk Assessment Tool
- Neutropenia, including febrile neutropenia, is common due to both the nature of AML disease and treatment regimen
- Consider use of granulocyte colony stimulating factor (G-CSF) depending on remission status[8]

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