What are the current treatment options for older secondary acute myeloid leukemia (sAML) patients with myelodysplasia (MDS)-related changes?

Jeffrey E. Lancet, MD
Department Chair
Malignant Hematology
Moffitt Cancer Center
Tampa, Florida

In a patient who can tolerate intensive therapy with potential candidacy for bone marrow transplant, induction chemotherapy would be very reasonable. What often works in these cases is CPX-351. CPX-351 is a liposomal encapsulated formulation of both cytarabine and daunorubicin in a fixed molar concentration ratio of 5:1. CPX-351 has been studied over the past several years, and findings have indicated that CPX-351 is an effective therapy that is better than traditional induction chemotherapy for older patients with newly diagnosed secondary or therapy-related acute myeloid leukemia (AML).

It is important to recognize that CPX-351 is, of course, considered intensive induction chemotherapy and should be managed as such. The main toxicities that we think about with such a regimen would mainly be related to neutropenia and infection.[1] These are not unique to CPX-351 but are something we must need to pay close attention to in our patients on this particular therapy.

In addition, it is important to recognize that the hematologic toxicities of CPX-351 are more pronounced than traditional induction chemotherapy with 7+3; specifically, the duration of neutropenia and thrombocytopenia is approximately 7 to 10 days longer with CPX-351 compared with 7+3.[2] This is important because it can potentially leave patients at higher risk for infection over a longer period of time, and it is therefore important to be very judicious about when to begin to back off antibiotics and to monitor infections very closely.

Alternately, an older, frail patient who is not considered a transplant candidate should preferentially receive a combination of hypomethylating agent (HMA) and venetoclax. The combination of HMA therapy, namely azacitidine, plus the BCL2 inhibitor venetoclax, was recently demonstrated in a phase 3 randomized trial to have significant superiority in terms of overall survival compared with the use of single HMA therapy, indicating that the combination of HMA plus venetoclax is also an appropriate therapy for older patients with newly diagnosed AML.[3]

However, we have to recognize that these two strategies, CPX-351 and HMA/venetoclax, have not been compared head-to-head. Thus, we cannot speak to the superiority of one regimen versus the other. I think this is going to be one of the most important debates or dilemmas that we have over the next few years with respect to initial therapy for sAML.

For more information on intensive therapy, please view the full newsletter by clicking here. (https://managingaml.com/treatment/90-a-case-study-in-secondary-aml-best-practice-for-treatment-selection)

References

1. Lancet JE, Uy GL, Cortes JE, et al. CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed acute myeloid leukemia. *J Clin Oncol.* 2018;36(26):2684-2692.
2. VYXEOS™ (daunorubicin and cytarabine injection), solution for intravenous use [package insert]. Palo Alto, CA; Jazz Pharmaceuticals, Inc.; 2019.
3. DiNardo CD, Jonas BA, Pullarkat V, et al. Azacitidine and venetoclax in previously untreated acute myeloid leukemia. *N Engl J Med.* 2020;383:617-629.