Leukemia insights

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Making Cancer History®

In this month's Leukemia Insights newsletter, written by Abhishek Maiti, M.D., and Farhad Ravandi, M.D., and sponsored in part by the Charif Souki Cancer Research Fund, we discuss some of these novel oral regimens for acute myeloid leukemia (AML) being investigated at MD Anderson Cancer Center. Learn more about our Leukemia program.

Oral Therapies for Acute Myeloid Leukemia (AML)

The median age of patients with acute myeloid leukemia (AML) is 68 years, and the median life expectancy is three to ten months with best supportive care and standard therapies such as low-dose cytarabine or hypomethylating agents. In addition, chemotherapy-based regimens in older patients can have substantial toxicities and high risks of mortality within the first month of therapy. Consequently, lower-intensity regimens with better toxicity profiles are attractive options for such patients. Recently, the VIALE-A trial showed that treatment with the combination of azacitidine and venetoclax resulted in an improvement of overall survival to nearly 15 months compared with azacitidine alone in patients older than 75 years or those with comorbidities precluding standard therapy.

Current standard therapies involve intravenous or subcutaneous chemotherapy treatments that necessitate frequent travel to infusion centers and/or physicians' offices. For older or frail patients, this can be challenging from physical, logistical and financial standpoints and can cause substantial distress in addition to the anxiety and emotional burden of the disease itself. Hence, researchers have long focused on developing oral therapies for AML, and recent advances have led to the development of novel regimens that make it feasible for patients to receive treatment at home. In this issue, we discuss some of these novel oral regimens for AML being investigated at MD Anderson.

ABOUT MyMDAnderson

myMDAnderson is a secure, personalized web site helping community physicians expedite patient referrals, as well as improve continuity of care through information access and streamlined communications.

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It's the easiest way to stay current with information on the latest leukemia news, research, and resources. View archived issues.

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Population	Age (yrs)	Eligibility requirement	Regimen
Newly diagnosed AML	> 75		Venetoclax with oral decitabine (INQOVI)
	>18	With comorbidities precluding intensive therapy	
Newly diagnosed	>60		
Secondary AML	>18	With or without prior HMA for MDS	
Newly diagnosed AML	>60	IDH1 or IDH2 mutation	Venetoclax, oral decitabine and ivosidenib or enasidenib
R/R AML	>18		
R/R AML	>18		Venetoclax with oral decitabine
R/R AML	>18		ASTX660 with oral decitabine
Newly diagnosed	>75	FLT3 mutated	Venetoclax, gilteritinib, oral decitabine
	>18	With comorbidities	
R/R AML	>18	FLT3 mutated	
			Quizartinib venetoclax
			Gilteritinib venetoclax

NEWLY DIAGNOSED AML

Venetoclax and oral decitabine with cedazuridine

At MD Anderson, we have two single-arm studies evaluating the combination of venetoclax and the oral formulation of decitabine that is combined with cedazuridine. Oral decitabine is approved by the Food and Drug Administration (FDA) for the treatment of myelodysplastic syndrome and is being evaluated in multiple clinical trials in AML. One of these studies is available for patients with newly diagnosed AML who are unfit or ineligible for intensive induction chemotherapy, either due to age (75 years or older), or comorbidities (heart failure or coronary artery disease; lung disease including COPD or asthma; chronic kidney disease; or liver disease) (NCT04657081). Another study is available for patients older than 60 years who are ineligible for intensive chemotherapy, patients who progress to AML after therapy for MDS with hypomethylating agents, or patients older than 18 years with relapsed/refractory AML (NCT04746235).

Triplet therapy with oral decitabine, venetoclax, IDH inhibitor (enasidenib or ivosidenib)

This is a Phase I/II study for patients with newly diagnosed or R/R AML with *IDH1/2* mutations. Patients with R/R AML are eligible if older than 18 years, and newly diagnosed patients are eligible if older than 60 and unfit for intensive chemotherapy. Patients must have a mutation in *IDH1* or *IDH2* (NCT04774393).

RELAPSED OR REFRACTORY AML

Outcomes after failure of frontline therapy in AML are dismal, with median overall survival of six to eighteen weeks. The best treatment of such patients is on novel clinical trials.

ASTX660 with or without oral decitabine

This is a Phase I study of ASTX660 (a novel oral drug that acts as a dual antagonist of inhibitors of apoptosis proteins [IAPs]) as single agent or in combination with oral decitabine. Eligible patients include adults with primary refractory disease or relapse after intensive therapy, lower intensity therapy, or stem cell transplantation. All patients will receive one or both of these oral medications (NCT04155580).

Oral doublet combinations for *FLT3*-mutated R/R AML

For patients with relapsed/refractory AML harboring a *FLT3*-mutation we have two trials with oral doublet therapy. One ongoing Phase I trial combining venetoclax and and the FLT3 inhibitor gilteritinib (NCT03625505) has shown high efficacy in R/R *FLT3*-mutated AML, with composite complete remission rates of 84% (Daver et al. 2020 ASH annual meeting). Another is a Phase Ib/II trial combining venetoclax with the FLT3 inhibitor quizartinib (NCT03735875).

UPCOMING CLINICAL TRIALS

Venetoclax with gilteritinib and oral decitabine

This will be a single-arm study for patients with newly diagnosed or R/R *FLT3*-mutated AML. Patients with both type I and type II *FLT3* mutations will be eligible.

Announcements

Leukemia Insights Newsletter

Our Leukemia Insights e-newsletter is now available online. Started in 2007 by Hagop Kantarjian, M.D., Leukemia Insights focuses on our various therapy options at MD Anderson Cancer Center. Click here to visit our new website.

Emil J Freireich Hematology Grand Rounds

The MD Anderson Cancer Center Emil J Freireich Hematology Grand Rounds now has a virtual format. This series highlights the incredible research taking place at MD Anderson Cancer Center while showcasing leaders from our research community, in an effort to remain engaged and inspired during the COVID-19 pandemic. Hosted by the Department of Leukemia in collaboration with the Department of Lymphoma/Myeloma, and Department of Stem Cell Transplantation and Cellular Therapy, we aim to strengthen the connections between the scientific and medical community at MD Anderson Cancer Center, our colleagues, patients and friends from around the world. Click here to visit our new website.

Leukemia Faculty Contacts

Completing these studies in a timely manner will allow us to move quickly on positive leads. We appreciate referrals and will make every effort, once a patient is enrolled on a study, to continue as much of the care as possible through the referring oncologist. We also will keep you apprised of the patient's progress. View our faculty roster.

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