The Role of the Advanced Practitioner in Enhancing Outcomes

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Authors' disclosures of conflicts of interest are found at the end of this article.

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Abstract

Advanced practitioners (nurse practitioners, physician assistants, pharmacists, and other health-care providers) have become increasingly integral members of the oncology care team. The accelerated rate of approvals for new therapies in acute myeloid leukemia highlights the imperative of timely collaboration between the entire team.

The employment of advanced practitioners (APs) in oncology has been shown to contribute greatly to cancer care, and APs have increasingly become integral members of the oncology care team (Bruinooge et al., 2018). Most US oncology practices that responded to the American Society of Clinical Oncology (ASCO) Oncology Practice Census reported employment of APs (81% in 2017, up from 75% in 2016; Kirkwood et al., 2018). Oncology APs spend a median of 85% of their time in direct patient care; their top four patient care activities are patient counseling, prescribing, treatment management, and follow-up visits. They conduct 51 to 78 patient visits each week, and some APs also provide specialized services, such as genetic counseling, surgery first assists, and procedures. This highlights the importance of APs in the oncology setting and importance of clinicians staying up to date

with new FDA approved therapies and indications, appropriate dosing and monitoring, and prognostic value for patients.

A NEW PARADIGM

The amount of new data generated in the oncology setting from emerging research and changing guidelines is challenging for clinicians to keep up with in order to optimize best practice for patients. With eight agents approved by the U.S. Food and Drug Administration (FDA) between April 2017 and May 2019, one new agent has been added quarterly (FDA, 2019). With these medication approvals comes changes in treatment plans and management in drug toxicities, highlighting the need for summary documents to facilitate quick adoption of new therapies and to ensure the appropriate placement in therapeutic succession. (For detailed information about the indications and clinical implications of these novel agents, see Appendix A; for dosing information,

see Appendix B; and for adverse events and drug-drug interactions, see Appendix C.) The National Comprehensive Cancer Network (NCCN) has included in its Version 1.2020 Guideline these eight FDA approvals in the following settings, listed in order of descending approval date (note ivosidenib received two indications, the first on July 20, 2018, and the second May 2, 2019; NCCN, 2019):

- **Ivosidenib:** Newly diagnosed AML with a susceptible *IDH1* mutation, as detected by an FDA-approved test, in patients who are at least 75 years old or who have comorbidities that preclude the use of intensive induction chemotherapy. Patients to receive 500 mg orally once daily with or without food until disease progression or unacceptable toxicity. For patients without disease progression or unacceptable toxicity, treatment is recommended for a minimum of 6 months to allow time for clinical response.
- **Gilteritinib:** Adult patients who have relapsed or refractory AML and, as detected by an FDA-approved test, the presence of *FLT3* ITD, D835, or I836 mutation. Gilteritinib was given orally at a dose of 120 mg daily until unacceptable toxicity or lack of clinical benefit.
- **Venetoclax:** Accelerated approval in combination with azacitidine or decitabine or low-dose cytarabine for the treatment of newly diagnosed adults with AML who are age 75 older, or who have comorbidities that preclude the use of intensive induction chemotherapy.
- **Glasdegib:** Adults age 60 or older who have been newly diagnosed with AML without actionable mutations and who are not candidates for intensive induction. Glasdegib is given as 100 mg daily without regard to food on cycle days 1 to 28 combined with low-dose cytarabine subcutaneously every 12 hours on days 1 to 10. Cytarabine dosing and disposal may complicate the practicality or the regimen.
- **Ivosidenib:** Adult patients age 60 or older with relapsed or refractory AML with a susceptible *IDH1* mutation, as detected by an FDA-approved test.
- **Gemtuzumab ozogamicin:** Adult and pediatric patients age 2 or older with newly diagnosed or relapsed or refractory CD33-positive AML in adults. Gemtuzumab ozogamicin may be

used in combination with daunorubicin and cytarabine for adults with newly diagnosed AML, or as a stand-alone treatment for certain adult and pediatric patients.

- **Liposome-encapsulated combination of daunorubicin and cytarabine (CPX-351):** Adults with newly-diagnosed therapy-related AML (t-AML) or AML with myelodysplasia-related changes (AML-MRC).
- **Enasidenib:** Adult patients with relapsed or refractory AML with an *IDH2* mutation, as detected by an FDA-approved test.
- **Midostaurin:** Patients younger than age 60 with newly diagnosed AML with intermediate-risk cytogenetics, and *FLT3*-mutated (ITD or TKD) as part of treatment induction. It is given as part of the standard 7+3 regimen: standard dose cytarabine 200 mg/m² continuous infusion for 7 days with daunorubicin 60 mg/m² for 3 days followed by midostaurin 50 mg orally every 12 hours with food given 30 minutes following antiemetic prophylaxis cycle days 8 to 21.

This list highlights the imperative of timely collaboration between the entire collaborative team to disseminate new data as only a matter of months can dramatically impact the available options for patients.

Future Directions

As of October 2019, ClinicalTrials.gov listed 363 actively recruiting studies for AML in the US and an additional 178 international trials. Of the US trials, 26 are phase III studies, evaluating novel agents as monotherapy or in combination with existing agents. Examples of just some of the ongoing trials that include FDA-approved agents or experimental agents are shown in Table 1.

HOW ADVANCED PRACTITIONERS CAN ENHANCE OUTCOMES

Hematologic oncology is an exciting subspecialty that is developing at a rapid pace. Subscription to the FDA Hematology/Oncology (Cancer) Approvals and Safety notifications page allows for APs to receive alerts with the most current approvals. Identification of a clinic champion who will disseminate approvals to the entire collaborative team is essential. This may include the creation of

Table 1. Examples of Ongoing Phase III Trials for Novel Agents for the Treatment of AML

Agent	NCT identifier	Study name
FDA-Approved agents	Ivosidenib	Study of AG-120 (Ivosidenib) vs. Placebo in Combination With Azacitidine in Patients With Previously Untreated AML With an <i>IDH1</i> Mutation
	Gilteritinib	A Trial of the FMS-like Tyrosine Kinase 3 (FLT3) Inhibitor Gilteritinib Administered as Maintenance Therapy Following Allogeneic Transplant for Patients With FLT3/Internal Tandem Duplication (ITD) AML
	Gilteritinib	A Study of ASP2215 (Gilteritinib) by Itself, ASP2215 Combined With Azacitidine or Azacitidine by Itself to Treat Adult Patients Who Have Recently Been Diagnosed With Acute Myeloid Leukemia With a <i>FLT3</i> Gene Mutation and Who Cannot Receive Standard Chemotherapy
	Midostaurin	A Global Study of the Efficacy and Safety of Midostaurin + Chemotherapy in Newly Diagnosed Patients With <i>FLT3</i> Mutation Negative (FLT3-MN) AML
	Crenolanib, Midostaurin	ARO-021 Study of Crenolanib vs Midostaurin Following Induction Chemotherapy and Consolidation Therapy in Newly Diagnosed <i>FLT3</i> Mutated AML
	Glasdegib	BRIGHT AML1019: A Study Evaluating Intensive Chemotherapy With or Without Glasdegib or Azacitidine With or Without Glasdegib In Patients With Previously Untreated AML
Experimental agents	Uproleselan	Study to Determine the Efficacy of Uproleselan (GMI-1271) in Combination With Chemotherapy to Treat Relapsed/Refractory Acute Myeloid Leukemia
	Pracinostat	An Efficacy and Safety Study of Pracinostat In Combination With Azacitidine In Adults With Acute Myeloid Leukemia
	Devimistat	A Study Evaluating Efficacy and Safety of CPI-613 (devimistat) in Combination With HD Cytarabine and Mitoxantrone vs HD Cytarabine and Mitoxantrone in Older Patients With R/R AML
	Crenolanib	Study Investigating the Efficacy of Crenolanib With Chemotherapy vs Chemotherapy Alone in R/R <i>FLT3</i> Mutated AML
	Idasanutlin	A Study of Idasanutlin With Cytarabine Versus Cytarabine Plus Placebo in Participants With Relapsed or Refractory Acute Myeloid Leukemia (AML)
	Pevonedistat	Pevonedistat Plus Azacitidine Versus Single-Agent Azacitidine as First-Line Treatment for Participants With Higher-Risk Myelodysplastic Syndromes (HR MDS), Chronic Myelomonocytic Leukemia (CMML), or Low-Blast Acute Myelogenous Leukemia (AML)

a drug monograph for consideration by the pharmacy and therapeutics committee or assignment to a fellow team member dependent upon subspecialty. These efforts will ensure the most current data is available to practitioners as the landscape for AML management continues to grow. Implementation of these therapies relies upon understanding next-generation sequencing as well as the appropriate integration of new therapies into the management of each unique AML patient. ●

Disclosure

Dr. Nix has served on the speakers bureau for Cohrus BioSciences and advisory boards for Bristol-Myers Squibb, Genentech, Puma, Sandoz, and Teva. Ms. Price has served as a consultant for Agios and on an advisory board for Daiichi Sankyo.

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