Ask ACCC's Community Resource Centers

Acute promyelocytic leukemia (APL) is a rare hematologic malignancy with less than 1,000 newly diagnosed cases annually. When existing protocols are followed, the success rate of treatment for this disease is very high—up to 97 percent. But what happens when a patient's treatment regimen goes awry or the schedule goes off-course? And what happens when patients are treated outside tertiary treatment centers where treatment regimens were developed? Are the same high cure results achieved? *Oncology Issues* asked Elihu Estey, MD, professor of hematology at the University of Washington, for answers.

"APPROPRIATE MANAGEMENT of APL can literally be the difference between life and death," said Dr. Estey, who provides care for APL patients at Seattle Cancer Care Alliance. "Prior to treatment there is a high risk of life-threatening complications, such as bleeding in the brain and lung. Platelet counts must be kept above 20,000, generally between 20,000 and 30,000, and coagulation factors must also be kept above certain threshold levels."

Current treatment for APL is well established: all-*trans* retinoic acid (ATRA; tretinoin) in combination with arsenic trioxide (ATO), often without traditional chemotherapy. Largely developed by Dr. Estey and colleagues at MD Anderson Cancer Center in Houston, the ATRA and arsenic combination treatment regimen is responsible for excellent therapeutic results—as high as 97 percent in multicenter clinical trials.[1] A study presented at the 2012 Annual Meeting of the American Society of Hematology compared standard treatment for newly diagnosed non-high-risk APL—simultaneous ATRA and chemotherapy (idarubicin)—to the combination ATRA and ATO, but without chemotherapy.[2] While complete responses were observed in 97 percent of each arm, the two-year event-free survival was higher in the arm without additional chemotherapy (97 percent) versus the controls (87 percent).[2] Based on that data, the National Comprehensive Cancer Network (NCCN) changed its treatment guidelines for APL (www.nccn.org/ordertemplates/default.asp?did=9).

Despite these studies and the changes made to the NCCN treatment guidelines for APL, an issue that has come to the forefront recently is the discrepancy between the greater than 90 percent cure rates reported from tertiary centers and the 65 percent cure rates found in population-based studies, which include many patients treated in community centers.[3] Reasons behind this discrepancy are not clear. One possible factor could be that patients being treated in the community are "sicker" than those being treated in a tertiary center. In other words, patients are presenting with more advanced disease and complicating co-morbidities. Another factor is likely to be that tertiary centers have more experience managing complex and rare diseases such as APL.

Indeed efforts to disseminate knowledge about management of APL to the broader community are in progress.[3] A key component in ACCC's education project, *Improving Quality of Care in APL*, is the identification of Community Resources Centers,

such as the Seattle Cancer Care Alliance, which are available to answer questions and provide guidance to community-based cancer programs with less experience treating patients with APL. The underlying goal behind ACCC's education program: to help ensure that APL patients who choose to be treated in their community receive the same quality of care they would receive in an academic setting. OI

References

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4. Estey E, Guillermo GM, Manero AF, Faderl S, et al. Use of all-*trans* retinoic acid plus arsenic trioxide as an alternative to chemotherapy in untreated acute promyelocytic leukemia. *Blood*. 2006;107(9):3469-3473.

ACCC's Community Resource Centers for APL

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Learn more at: www.accc-cancer.org/education/APL.

CASE STUDY

In February 2013, Dr. Estey saw a 33-year-old woman diagnosed with low-risk APL with no bleeding complications at the Seattle Cancer Care Clinic. The patient was initiated on ATRA at 45 mg/m2 divided into two doses, and arsenic (ATO) at 0.15 mg/kg daily.[4] The patient received prednisone as prophylaxis for ATRA differentiation syndrome, but had no tumor lysis, worsening DIC, or ATRA differentiation syndrome. In March 2013, this patient followed up with her medical oncologist in Tacoma. After achieving complete response, she was continued inadvertently on ATRA and ATO continuously, with ATO given five days a week, weekly, and ATRA daily, interruptedly.

"This patient had 60 days of treatment with both medications. There is no data on how to proceed in this case," Estey said. "Patients are usually treated for three to four weeks and then left to let their counts recover. The process then starts again until about 6 months of ATRA and ATO have been given."

Though his patient's counts were fine after the extended treatment period, Estey warns that patients on arsenic require checking of serum potassium and magnesium levels in the blood as low levels in combination with ATO may cause heart arrhythmias. In this example, the patient's white count was less than 10,000.

"Patients with low-risk disease like this patient can be successfully treated with ATRA and arsenic, therefore avoiding chemotherapy," Estey said. For the patient in this case study, he recommended resuming the post-remission protocol of ATO daily for five days, four weeks on and four weeks off, and ATRA daily, for two weeks on and two weeks off, to complete the total number of 80 doses. ATRA and ATO were discontinued at the same time.

Given that relapses are extremely rare in patients who begin ATO + ATRA with white counts < 10,000, experts now agree there is no need to monitor for recurrence. That said, patients often feel more comfortable if routine blood counts are checked every six months.

To talk to Dr. Estey about this case study or any questions you may have related to treating patients with APL, providers can email him directly at: *eestey@seattlecca.org*.