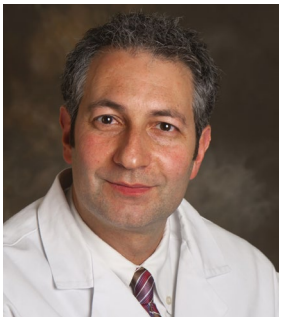
Ask ACCC's Community Resource Centers

Chronic myeloid leukemia (CML) is a rare, slow-growing hematologic malignancy affecting mostly older adults and accounting for a little over 10 percent of all new cases of leukemia. (The American Cancer Society estimated 5,920 new cases for 2013.)[1] In CML, leukemia cells can build up in the body over a number of years, often without causing symptoms. Targeted therapy drugs have revolutionized the treatment of CML, allowing many patients to live normal life spans, but successful treatment depends on consistent monitoring and management of the disease and side effects. Winship Cancer Institute of Emory University has established an outpatient coordinated team approach that has proven successful with CML patients. H. Jean Khoury, MD, Director of the Division of Hematology at Winship, and the R. Randal Rollins Chair in the Emory University School of Medicine, explains.



CHRONIC MYELOID LEUKEMIA, also known as chronic myelogenous leukemia, is most often diagnosed in the early, indolent, and asymptomatic phase called the chronic phase (CP-CML). Untreated or with ineffective therapy, CP-CML progresses within three to five years to the advanced phases of the disease called accelerated phase and blast phase.

A change within the chromosomes of the marrow stem cells leads to the formation of the BCR-ABL oncogene that is the driver of this disease. BCR-ABL can be detected by analyzing marrow cells for the presence of the Philadelphia chromosome, or by analyzing the blood using molecular methods: FISH and PCR. Targeting BCR-ABL with tyrosine kinase inhibitors (TKIs) has revolutionized outcomes in patients with CML, and has practically replaced allogeneic hematopoietic stem cell transplantation (HSCT) as first-line therapy.[2,3] Four TKIs are commercially available in the U.S. for the treatment of patients with CML: imatinib, dasatinib, nilotinib, and bosutinib. These oral agents have remarkable activity and are overall well tolerated by patients.

Indeed, the longest available follow-up of patients treated with imatinib shows that responders enjoy a lifespan that is comparable to the general population, and more importantly, no new or chronic toxicities were observed with prolonged exposure to this agent.[4] Recent studies have shown that approximately 50 percent of patients with prolonged and sustained molecular remission have discontinued imatinib, and have so far maintained these remissions, suggesting that cure with TKIs may not be a far fetched reality.[5]

There is also good news for patients for whom first-line TKIs have failed. CP-CML patients with low Sokal risk scores who have tolerated imatinib, achieved a cytogenetic response, and have subsequently failed this first-line agent, can be very effectively rescued by second-line TKIs, and have so far had very encouraging outcomes.

Given the excellent activity of dasatinib, nilotinib, and bosutinib, any of these agents is an excellent second-line therapy. To take maximum advantage of therapy with TKIs, compliance and good understanding of monitoring response to therapy are essential. And given that these pills are taken daily for years, patient monitoring and compliance issues are very important.

Therefore, in 2005, Winship Cancer Institute of Emory University established a coordinated team care approach for patients with CML.[6] The goal of this team approach is to maximize the benefits of TKI therapy through education and by engaging patients, their caretakers, and the referring oncologist in disease management. The team consists of a dedicated hematologist, physician assistant (PA), nurse coordinator, social worker, pharmacist, and research coordinator who comprehensively address patient issues—including psychosocial, financial, insurance coverage, and transportation—from the first visit through the long course of the disease, and provide a good understanding of monitoring results.

In our team model, the patient's understanding of response monitoring results is used to tailor additional education at each subsequent clinic visit. Through frequent communication between the leukemia specialist and the referring physician oncologist, knowledge about the disease and monitoring is relayed beyond the academic medical center to community providers.

This team approach is effective for early detection and management of side effects, which improves patient compliance. Team members deliver a consistent message throughout the course of the disease, using simple graphics and a disease-monitoring flow chart that allows patients to visualize their progress with therapy, which in turn increases the chances of adherence to treatment with TKIs. (Winship's disease-monitoring flow chart is available online at www.accc-cancer.org/oncology_issues/MA2014.asp.)

CASE STUDY

After being diagnosed in November 2003 with chronic phase CML, a 71-year-old woman transformed to lymphoid blast phase (LBP) CML six months after an excellent response and complete cytogenetic remission (CCyR), with imatinib 400 mg/day.

She achieved remission with chemotherapy (HCVAD) that was given for five cycles, but relapsed while on maintenance therapy in November 2005, and was resistant to additional chemotherapy.

Patient was offered to enroll on a clinical trial (protocol CA180015) and started dasatinib 70 mg twice daily in December 2005. Due to gastrointestinal side effects, the dose was reduced to 50 mg twice daily. Patient achieved an excellent response (CCyR) and complete molecular remission (CMR) in April 2006, but due to unexplained and persistent twitching that did not resolve with interruption of dasatinib, patient decided to come off the clinical trial in February 2007.

In March 2007, while in CMR, patient was offered to enroll on another clinical trial (protocol 3160A4-200-WW) and started bosutinib 500 mg/day. Due to gastrointestinal side effects, the dose was reduced to 400 mg/day in July 2007. The patient maintained CMR, but after a diagnosis of pulmonary fibrosis not related to bosutinib, patient decided to come off the clinical trial in December 2011, and no further therapy for CML was started. Patient remained in sustained CMR, now 25 months after bosutinib discontinuation, and perhaps cured from her blast phase CML.

This very unusual case shows that enrollment on clinical trials—and a close monitoring of disease and side effects—can provide patients with opportunities otherwise not readily available for the management of their disease.

To contact Dr. Khoury about treating patients with CML, providers can call him at: 404.778.3932.

In summary, a coordinated team care approach is essential for the management of CML. This approach coaches patients through their cancer journey. Providing patients with education enables them to better understand their disease and put in perspective the results of the monitoring tests. It improves compliance and engages patients as active team members. Additionally, incorporating the referring community oncologist improves alliances between the healthcare team members and extends the tracking of monitoring results to the community practice. In our experience, and based on our very low rates of "clinic no shows," lapses in TKI refills, and "lost to follow-up," we are confident that this coordinated team approach is highly effective for the management of CML patients. OI

References

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