

Fighting Relapsed Leukemia

by Jeff Worley

When cancer returns, it can come back with a vengeance. And older people are particularly susceptible to cancer's return because their immune systems aren't generally as strong as those of younger patients.

The University of Kentucky's Markey Cancer Center is conducting a clinical trial for elderly and relapsed Acute Myeloid Leukemia (AML) patients with the goal of helping this group of patients live longer. Dianna Howard, a physician-researcher in the Department of Internal Medicine, is leading this study.

AML is a cancer of the white blood cells, characterized by the rapid proliferation of abnormal cells that accumulate in the bone marrow and interfere with the production of normal blood cells. AML is the most common acute leukemia affecting adults,


and its incidence increases with age.

Howard and her team found that the combination of a new drug, bortezomib (Velcade), with a standard chemotherapy drug, idarubicin, rapidly kills AML cells, including AML stem cells—the cells thought to be responsible for leukemia relapse in the majority of patients. The drug combination also offers the potential for remission with fewer side effects than other traditional combinations. Bortezomib interrupts the biological signals that keep AML cells alive and makes them more likely to die when treated with idarubicin. With the same drug combination, normal stem cells, the cells responsible for producing normal blood cells, are not killed.

"We demonstrated that this novel combination of drugs could kill leukemia cells in the Petri dish, so we were eager to move into clinical trials," says Howard, who has been on the faculty at Markey since 1999.



Dianna Howard's son, Will, was diagnosed with Acute Lymphoblastic Leukemia when he was 9. The good news? He's been in remission for over four years now.

A microscopic image of Acute Myeloid Leukemia (AML) cells, showing numerous large, immature white blood cells with prominent nuclei and some with reddish granules.

Dianna Howard found that a new drug, bortezomib, in combination with a standard chemotherapy drug rapidly kills AML cells.

“We’re now heading up a Phase I trial to determine a safe dose of these drugs in our 15 patients, and once we do that we’ll look at the efficacy of the drug combination and expand the number of patients in the study.”

Howard says this clinical trial is particularly important because in the past about half of adults over age 60 that were diagnosed with leukemia were never offered therapy for their disease, since the perception of the therapy has been that an effective dose of drugs would be too toxic. “That view is changing, and we’re trying to be a part of that change,” says Howard, who has seen some encouraging signs so far in the study. “With this combination of drugs, some of our patients have gone into complete remission, which in a Phase I study is somewhat remarkable—you don’t expect remissions with such low dosages.”

Leukemia Research: Up Close and Personal

In December 2003, Howard’s research became personal, very personal: Her 9-year-old son, Will, was diagnosed with Acute Lymphoblastic Leukemia (ALL). ALL is a fast-growing type of leukemia in which too many immature white blood cells congregate in the blood and bone marrow.

“When we got the diagnosis, I was in disbelief,” Howard says. “How do you make sense out of something like this? I came around to the realization that there’s no purpose in asking why—things don’t happen for reasons, they just happen. This is something my patients through the years have taught me. Reason is what evolves as you respond to what happens. Looking ahead, we wanted Will to walk away from this experience acknowledging that it didn’t make sense but that if he could endure this, he could endure anything.”

Will’s endurance has been tested. He’s had three years and three months of chemotherapy, and physical therapy is still a part of most days. But the news is good: He has been in remission for over four years now. “Will achieved a rapid and complete remission early with therapy—the best possible outcome. The longer he stays in remission, the more likely he is cured,” says Howard.

And she feels lucky that she has had such a strong support system throughout this ordeal. “My colleagues at UK went beyond themselves to support me personally and professionally. I’m surrounded by some of the most remarkable people anyone could ask for.”

Howard also got “amazing support,” she says, from the Leukemia and Lymphoma Society. She is now a participant in a group called Team In Training (TNT), the world’s largest endurance sports training program. The program provides training to run or walk marathons and half marathons, or participate in triathlons and 100-mile bike rides. This program raises nearly half the national budget for the Leukemia and Lymphoma Society.

“TNT has given me a venue to connect to other moms, professionals and patients on a very personal level,” Howard says. “Through this small test of my endurance, I can honor my son and so many others like him—my patients—who really know what endurance means. I’d walk to the other side of the world if it moves us one step closer to a cure for leukemia.” ■