When Prognosis Is Poor, Does False Hope Add to Leukemia Patients’ Pain?

Although advances in chemotherapy treatments for chronic lymphocytic leukemia have increased the quality of life for many patients, few advances have had a substantial effect on survival for those in the late stages of the disease. In light of a June 3, 1998, report in the *Journal of the American Medical Association* on false hope adding to cancer patients' pain, what should doctors be telling patients about the latest advances in treatment for later stage CLL, a stage of the disease with a poor prognosis?

CLL is a disease that can remain indolent for up to a decade, but once a patient advances to its later stages, therapy often can be both intensive and unsuccessful, especially for older patients. Until recently, many patients were enrolled in one of the many autologous bone marrow transplant clinical trials, but many of those trials have proven disappointing for older people. According to the National Cancer Institute’s Wyndham Wilson, M.D., Ph.D., “researchers are now concentrating more on targeted therapies. Unfortunately, I don’t see any major clinical breakthroughs on the horizon, and the role of autologous and allogeneic bone marrow transplant therapies remains unclear at this time.”

A late stage CLL patient could expect another year or two of life if he or she withstood the rigors of aggressive chemotherapy said Gerald Marti, M.D., of the Food and Drug Administration’s Center for Biologics Evaluation and Research. But according to a recent article in *JAMA*, doctors are not communicating the fact that the disease is often terminal, nor are patients hearing that message even when their doctors actually communicate it clearly. The *JAMA* paper reported that patients are far more optimistic than their doctors, often asking for aggressive anticancer treatments even though there is little hope of remission or quality of life benefit.

More Realistic Approach

Marti said that, “for a late stage CLL patient, there may be some more realistic approaches to late stage treatment that should be discussed rationally with their oncologist. Because new purine analog drugs have given a greater quality of life to many patients and even newer derivatives show greater promise in ongoing trials, the likelihood of benefit for the individual should be thoroughly evaluated.”

As NCI’s Bruce Cheson, M.D., Clinical Investigations Branch, pointed out, “consideration of clinical trials should not be pushed aside during late stage doctor-patient discussions. There are so many high quality investigators now at work in the field of CLL, the knowledge that patients could lend to the field at this stage of our understanding could be tremendous.”

According to Marti “there is a definite and desperate need for available protocols in the area of refractory CLL. With an aging population, this need has become even more pressing. For patients and their families who are willing to take a chance on new protocols, we will continue to test and look for experimental drugs that can reduce the leukemic phase of CLL.”

In the 1980s, an alkylating agent called chlorambucil was the drug of choice for treating advanced CLL. Marti said that while chlorambucil is still a good drug for the treatment of progressive and advanced CLL in some clinical settings (a majority of patients with CLL initially respond to chlorambucil), it is no longer the first drug of choice because many patients eventually become refractory, or don’t respond readily to it.

Drugs of Choice

After many clinical trials, purine analogs such as fludarabine, which has its own toxicities, have now become the drugs of choice when patients become refractory to other drugs. Using fludarabine as a first line agent, and adding other drugs such as cytoxan to the regimen, promises to be much more effective than the often more toxic chlorambucil treatments of the 1980s. Oncologists are also administering longer doses of fludarabine and getting
better response rates. Marti cautioned that “fludarabine is not an ideal drug however, as prolonged administration of the drug results in severe T-cell depletion and suppression.”

Many leukemia researchers think 506U may be the drug of choice for treating CLL in the next decade. In Phase I trials it has shown greater efficacy than any other drug commercially available. It will be entering phase II trials this summer and researchers hope that a good sense of its possibilities will emerge sometime in 1999.

Marti believes however that “the real hope for late stage CLL patients lies in multiple therapies that combine the best of the biological approaches with new and exciting molecular treatments which are still evolving.” Scientists are also looking at new ways to modulate cells to the sensitivity of chemotherapies.

— Mike Miller

Patient Advocates Help Researchers Avoid “Bumps in the Road”

When it comes to patient advocates and medical researchers, some envision worlds colliding or impassable bridges. But a few trailblazers within the Specialized Program of Research Excellence (SPORE) are convincing skeptics that strong bonds can be forged between these diverse camps for a better research program.

Advocates have been a formal part of the breast cancer SPORE based at the University of California at San Francisco since its inception in 1992. Their example is spurring similar partnerships at other NCI-supported SPOREs and cooperative groups. The two main benefits of advocate participation mentioned by both sides are focus and a common language.

Easily Distracted

“It’s easy to become distracted when doing scientific research and follow things of scientific importance but not necessarily translational importance. Advocates bring a continual reminder that this is breast cancer we’re working on, not one’s research career. They provide a centering force all the time,” said Joe Gray, Ph.D., principal investigator for the San Francisco breast cancer SPORE.

Deborah Collyar described the challenge: “Researchers become experts in the letter Q and can tell you all about Q. But they forget that it’s only part of the alphabet.” Collyar is an advocate member of the UCSF SPORE and president of Patient Advocates in Research.

**Stat Bite**

**Age Distribution of Leukemias**

Acute lymphocytic leukemia represents about 12% of all leukemias in the United States and is predominantly found in persons younger than 20. The majority of leukemias, including chronic lymphocytic leukemia and acute and chronic myeloid leukemias, are more commonly found in people aged 65 and older.

*Percent incidence of leukemias, 1991-1995, by age*

- 65+ 13.0%
- 55-64 4.9%
- 45-54 4.5%
- 35-44 5.8%
- 20-34 11.1%
- Under 20 60.8%

Acute lymphocytic leukemia

- 65+ 15.1%
- 55-64 15.1%
- 45-54 9.5%
- 35-44 6.0%
- 20-34 4.5%
- Under 20 3.0%

All other leukemias