

## Overview of Acute Myeloid Leukemia

Acute myeloid leukemia (AML) is characterized by accumulation of immature myeloid cells in bone marrow, resulting in hematopoietic insufficiency (granulocytopenia, thrombocytopenia, and anemia). As the disease progresses, life-threatening hemorrhage or infections may result.<sup>1</sup> AML is a virulent, often fatal form of cancer, is one of the most serious forms of leukemia, and has a relatively high fatality rate.<sup>2</sup> If left untreated, death usually occurs within a few months of diagnosis. While this disease is not common, it is the second most frequent type of leukemia in adults and is more common in adults older than 60 years of age than in younger individuals. The annual incidence of AML is approximately 2.3 per 100,000 individuals; in those younger than 65 years of age, the incidence is 1.3, and in those older than 65 years of age, 12.2.<sup>3</sup>

Current treatment for AML is usually divided into 2 phases: induction chemotherapy and postremission management, both of which involve chemotherapeutic agents. The goals of treatment are to eradicate the disease as quickly as possible and induce complete remission, often at the cost of other aspects of the patient's health.<sup>3</sup> The traditional chemotherapeutic regimen is associated with a number of side effects that range from unpleasant to life threatening, including alopecia (hair loss), mucositis (sores in the mouth and intestines), organ damage, and myelosuppression, which may lead to deadly infections.

Patients who receive conventional chemotherapy tend to become very sick as a result of their treatment.<sup>2</sup>

This supplement discusses gemtuzumab ozogamicin (Mylotarg™), a drug recently approved by the Food and Drug Administration for the treatment of CD33+ AML in patients who are 60 years of age and older, are in their first relapse, and are not considered candidates for cytotoxic chemotherapy.<sup>4</sup> Patients older than 60 years of age at first diagnosis or who have relapsed are more likely than younger patients to fail conventional chemotherapy and not achieve complete remission. They may have treatment-specific problems, such as inability to tolerate aggressive chemotherapy, or disease-specific problems, such as multidrug resistance or chromosomal abnormalities.

Gemtuzumab ozogamicin is an antibody-targeted chemotherapy (ATC), combining an antibody that is highly specific to malignant cells with a potent antineoplastic drug, which allows the drug to be delivered to malignant cells but not to most normal ones. The antibody involved is specific to CD33, an antigen expressed on the surface of AML cells, but not most other cell types, in more than 80% of patients with AML. Compared with conventional chemotherapy, treatment with gemtuzumab ozogamicin is associated with a much lower incidence of certain side effects, such as severe mucositis, and does not cause alopecia.<sup>2</sup> Because most healthy cells are

not destroyed, patients do not become as sick from their treatment as they do with conventional chemotherapy. Gemtuzumab ozogamicin has the potential to be as effective as conventional chemotherapy while being better tolerated and having an improved safety profile. For patients treated with this drug, remission and survival rates are comparable to those of conventional chemotherapy.

Gemtuzumab ozogamicin was approved as an orphan drug, intended for treatment of rare diseases or conditions. This is the first ATC drug approved for the treatment of AML patients. Given in intravenous form as a 2-hour infusion in 2 doses 14 days apart, this drug contrasts with conventional chemotherapy, which is given for a 7-day course and requires patients to be hospitalized for extended periods of time.<sup>4</sup> This drug can be given in an outpatient setting, result-

ing in higher patient satisfaction and lower overall costs. However, some side effects have been noted (See Commentary).

---

... REFERENCES ...

1. Lowenberg B, Downing JR, Burnett A. Acute myeloid leukemia. *N Engl J Med* 1999;341:1051-1062.
2. Doctor's Guide [resource page]. ASCO: Mylotarg (gemtuzumab ozogamicin) promising for adults with acute myeloid leukemia. Available at: <http://www.pslgroup.com/dg/ld313a.htm>. Accessed August 9, 2000.
3. Wetzler M, Bloomfeld CD. Acute and chronic myeloid leukemia. *Harrison's Online* [text online]. Available at: <http://www.harrisonsonline.com>. Accessed August 9, 2000.
4. FDA Talk Paper. FDA Approves Chemotherapy Agent Mylotarg for Leukemia. Reuters. May 18, 2000. Available at: <http://www.fda.gov/bbs/topics/ANSWERS/ANS01016.html>. Accessed August 9, 2000.