Gemtuzumab Ozogamicin Makes a Comeback

Seven years after it was pulled from the market, gemtuzumab ozogamicin (Mylotarg; Pfizer) has been approved anew—this time for adults newly diagnosed with acute myeloid leukemia (AML), as well as patients 2 years of age and older with relapsed/refractory disease. The CD33-targeting antibody–drug conjugate (ADC) got the nod to be given as a single agent or in combination with chemotherapy.

“I’m convinced this is a good drug, and I’m very happy that it’s back,” says Richard Stone, MD, director of the adult leukemia program at Dana-Farber Cancer Institute in Boston, MA.

Mark Litzow, MD, who heads the Mayo Clinic’s acute leukemia group in Rochester, MN, is also pleased about gemtuzumab ozogamicin’s (GO) renaissance. “I think its withdrawal at the time was unfortunate, although understandable,” he says.

In 2000, GO earned accelerated approval as monotherapy for patients with AML who were 60 years of age and older, had experienced an initial relapse, and weren’t good candidates for standard intensive chemotherapy. The drug was “going on its merry way,” Stone says, “when the required confirmatory trial [SWOG-0106] came back negative.”

However, that trial assessed the drug in a different patient population, Stone points out: Newly diagnosed patients were randomly assigned to receive GO on a fractionated schedule and at a lower dose than was originally approved. This was key in reducing the risk of hepatic veno-occlusive disease, the severe toxicity that prompted GO’s market withdrawal.

With safety issues halting Seattle Genetics’ development of vadastuximab talirine earlier this year, GO is the sole approved CD33-targeting ADC. “The challenge is this fine line between excess toxicity and therapeutic efficacy—exemplified by GO early on—because normal myeloid cells express CD33 too,” Litzow notes, adding that “there’s interest, now, in directing CAR T cells at this antigen, but a lot of concern about doing so safely.”

Overall, this is a banner year for AML. Stone and Litzow agree, with GO being the fourth approved therapy. Midostaurin (Rydapt; Novartis) and enasidenib (Idhifa; Celgene/Agios) are targeted at more specific patient subsets. CPX-351 (Vyxeos; Jazz), however, is a fixed-dose liposomal formulation of daunorubicin and cytarabine—both commonly given with GO. “We still need to hash out which [GO plus conventional chemotherapy, versus CPX-351] to use and when,” Litzow says.

GO, ultimately, “is for almost everyone, seeing as more than 90% of patients have CD33-expressing blasts,” Stone observes. “I do think it will be used a good deal in AML, now that it’s widely available again.” –Alissa Poh ©

Three trials in particular helped sway the FDA. In ALFA-0701, among 271 patients with newly diagnosed AML, those randomly assigned to receive GO alongside chemotherapy had a longer median event-free survival than those given just chemotherapy: 17.3 months versus 9.5 months. AML-19 randomized 237 elderly patients who could not tolerate other therapies to receive single-agent GO or best supportive care; the median overall survival was 4.9 months and 3.6 months, respectively. In MyloFrance-1, 57 patients with initial disease relapse received single-agent GO; 15 achieved a complete remission that lasted 11.6 months on average.

Importantly, across these trials, patients were given GO on a fractionated schedule and at a lower dose than was originally approved. This was key in reducing the risk of hepatic veno-occlusive disease, the severe toxicity that prompted GO’s market withdrawal.

The FDA launched a public dashboard to enable better access to reports of adverse drug reactions. The interactive web-based tool, available at www.fda.gov, is designed so that consumers can easily query the FDA’s Adverse Event Reporting System using various criteria, including biological product and type of adverse event. The agency hopes the tool will spur the submission of more detailed safety reports.

Three Bristol-Myers Squibb trials evaluating nivolumab (Opdivo)-based combinations in multiple myeloma were placed on partial clinical hold by the FDA. The move came a week after the agency issued a safety alert on the use of certain pembrolizumab (Keytruda; Merck) combinations to treat the disease. For now, the FDA has determined that the risks of such combination therapies for multiple myeloma outweigh the potential benefit.

Eli Lilly announced plans to cut about 3,500 jobs globally, a move expected to yield annual savings of $500 million starting in 2018. The cuts translate to a workforce reduction of roughly 8% and will mainly come from a voluntary early-retirement program offered in the United States.

The FDA granted accelerated approval to copanlisib (Aliqopa; Bayer), which inhibits PI3Ka and PI3kB, for the treatment of follicular lymphoma, an indolent form of non–Hodgkin lymphoma with few therapeutic options. In a trial of 104 patients who had relapsed after at least two prior therapies, 59% had a complete or partial response. In a trial of 104 patients who had relapsed after at least two prior therapies, 59% had a complete or partial response to copanlisib for a median of 12.2 months.

Researchers pegged the cost of developing a single cancer drug in the United States at $968 million; median revenue for the 10 drugs considered in their analysis was calculated to be $1,658.4 million for the 10 drugs considered in their analysis. The cut in subsidies is estimated to cost the U.S. government $500 million annually.