Anemic patients with MDS gain long-term benefits from erythropoietin and a myeloid growth factor

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Myelodysplastic syndromes (MDS), a group of blood disorders that can lead to acute myeloid leukemia (AML) in some patients, often cause severe anemia (when the body lacks a sufficient number of functional red blood cells). While certain treatments can help manage the symptoms of anemia, some studies have suggested that they may lead to complications. A new study, however, demonstrates that MDS patients with anemia may benefit from treatment with an erythropoietin (EPO)-based regimen plus supportive care without added complications as compared with those receiving supportive care alone. The study will appear in the September 17 issue of *Blood*, the official journal of the American Society of Hematology.

The phase III prospective, randomized trial, conducted by research teams of the Eastern Cooperative Oncology Group, was designed to evaluate the efficacy and safety of EPO with or without myeloid growth factor treatment (G-CSF, or granulocyte colony-stimulating factor) and supportive care (SC) with red blood cell transfusions for patients with early-stage MDS (n=53), in comparison to supportive care alone (n=57).

For the study, the researchers followed MDS treatment and dosing guidelines recommended by the National Comprehensive Cancer Network, which include managing anemia with erythropoiesis-stimulating agents (ESAs) such as EPO. EPO is a drug that imitates the action of the hormone erythropoietin, which stimulates the body to

produce more red blood cells. Generally, therapy with G-CSF interacts with EPO treatment synergistically to improve erythroid (red blood cell) responses, especially in MDS patients that do not respond to EPO alone.

"EPO is a recommended treatment for MDS, but the combination with G-CSF and supportive care required comparative studies in this patient population," according to lead study author Peter Greenberg, MD, Professor of Medicine, Stanford University Cancer Center. "Our goal was to manage anemia while not increasing the risk of transformation to leukemia, and we undertook this study to understand if this combination might be successfully utilized in these patients."

The results of the study proved successful for this group of patients with lower-risk MDS and anemia. After the first course of therapy, 36 percent of patients in the EPO arm responded to treatment, compared with only 9.6 percent in the SC alone arm. After subsequent courses, 47 percent responded in the EPO arm. Researchers then followed both patient groups for a median of 5.8 years to determine their long-term response to treatment. Responders to EPO experienced increased survival in comparison to the non-responders (5.5 vs. 2.3 years) and significantly improved physical, emotional, and functional well-being, reduced fatigue, and improved overall quality of life. The research team otherwise found no statistically significant differences in overall survival of patients between the EPO and SC arms (3.1 vs. 2.6 years) or the incidence of transformation to AML (7.5 vs. 10.5 percent of patients, respectively), suggesting long-term safety of the EPO treatment regimen.

The study results also indicated that the combination of EPO plus G-CSF was beneficial for patients who either did not respond initially to EPO or who experienced a delayed response. Furthermore, higher doses of EPO seemed to prove valuable for a proportion of patients who initially failed to respond. Importantly, the outcomes suggested long-term tolerance to the treatment combination, with a low overall

incidence of adverse events. Specifically, the researchers found no significant treatment-related increase in incidence of either cardiovascular or thrombotic (clotting) events or transformation to AML in the patients who received EPO alone or with G-CSF, as compared with those in the SC arm.

Recently, the FDA has issued alerts regarding the use of ESAs, noting increased mortality, possible tumor promotion, and thromboembolic events that have been observed in some studies of non-MDS patients receiving ESAs. However, other studies of patients with solid tumors receiving chemotherapy did not demonstrate an adverse effect of ESAs on survival.

"We believe the data suggest that the negative effects of cytokines, like ESAs, demonstrated in some studies of other diseases may relate to biologic and clinical features or the specific treatments associated with the differing disorders studied," said Dr. Greenberg. "Findings from this study demonstrate the relative safety and efficacy of EPO plus G-CSF for treating anemic lower-risk MDS patients and may be considered as part of future treatment recommendations for the use of this class of therapies."

Source: American Society of Hematology