

Azacitidine Prolongs Survival in Higher-risk MDS

At the annual meeting of the American Society of Hematology, Dr. Pierre Fenaux presented phase III results from the International Vidaza High-Risk MDS Survival Study Group's AZA-001 study demonstrating that azacitidine (Vidaza, Pharmion) prolongs overall survival in patients with higher-risk myelodysplastic syndromes (MDS) as compared with conventional-care regimens. The present research enrolled 358 patients with higher-risk French-American-British (FAB) MDS, as defined by refractory anemia with excess blasts (RAEB), RAEB with blasts in transformation (RAEB-T), or chronic myelomonocytic leukemia (CMML) as characterized by 10–29% marrow blasts, with an International Prognostic Symptom Score (IPSS) of int-2 or high based on pathology/cytogenetics. Conventional care regimens were either best supportive care only, low-dose cytarabine, or standard chemotherapy. Patients (median age 69 years) were stratified by FAB/IPSS and assigned to one of the three conventional-care regimens or azacitidine 75 mg/m²/day for 7 days every 4 weeks. At baseline, 95% of patients were higher-risk, with 58% RAEB, 34% RAEB-T/acute myeloid leukemia by the World Health Organization definition, and 3% CMML. By IPSS, 40% of patients were int-2–risk, 47% high-risk, and 13% indeterminate or other risk. Azacitidine was administered for a median of nine cycles. Low-dose cytarabine was administered to 49 patients (27%) for a median of four cycles. The median follow-up for the analysis of overall survival was 21.1 months. Azacitidine demonstrated statistically superior overall survival as compared to conventional-care regimens (stratified log-rank $P=.0001$). The median Kaplan-Meier overall survival time was 24.4 months for azacitidine, compared to 15 months for conventional-care regimens. The hazard ratio (HR; Cox Model) was 0.58 (95% confidence interval [CI], 0.43–0.77), for a 74% improvement in overall survival. At 2 years, there was a 2-fold overall-survival advantage observed with azacitidine (51%) versus conventional-care regimens (26%; 95% CI, 13–36%; $P<.0001$). The observed differences in median Kaplan-Meier overall survival between azacitidine and best supportive care, low-dose cytarabine, and standard chemotherapy were, in months, 12.9 (HR=0.55; $P=.0003$), 9.1 (HR=0.60; $P=.016$), and 8.7 (HR=0.69; $P=.19$), respectively. The safety profile of azacitidine did not differ from that in previously published reports. Standard care, the authors note, should change as a result of these findings of a significant advantage in overall survival, with azacitidine as frontline therapy for patients with higher-risk MDS.

Capecitabine and Oxaliplatin Effective for Advanced Esophagogastric Cancer

In a two-by-two design reported in the January 3 issue of the *New England Journal of Medicine*, Dr. David Cunningham and colleagues compared capecitabine (Xeloda, Roche) and oxaliplatin (Eloxatin, Sanofi-Aventis) to infused fluorouracil and cisplatin, respectively, for untreated advanced esophagogastric cancer. The researchers randomly assigned 1,002 patients to receive triplet therapy with epirubicin and cisplatin plus either fluorouracil (ECF) or capecitabine (ECX) or triplet therapy with epirubicin and oxaliplatin plus either fluorouracil (EOF) or capecitabine (EOX). The study's primary endpoint was noninferiority in overall survival for the triplet therapies containing capecitabine as compared with fluorouracil and for those containing oxaliplatin as compared with cisplatin. The researchers found that median survival times in the ECF, ECX, EOF, and EOX groups were 9.9 months, 9.9 months, 9.3 months, and 11.2 months, respectively; survival rates at 1 year were observed to be 37.7%, 40.8%, 40.4%, and 46.8%, respectively. Progression-free survival and response rates did not differ significantly among the regimens, and the toxicity profiles of capecitabine and fluorouracil were similar. In comparison to cisplatin, oxaliplatin was associated with lower rates of grade 3 or 4 neutropenia, alopecia, renal toxicity, and thromboembolism but with slightly higher rates of grade 3 or 4 diarrhea and neuropathy. Capecitabine and oxaliplatin are considered as effective as fluorouracil and cisplatin, respectively, in patients with previously untreated esophagogastric cancer.

In Brief

Rates of morphologic abnormalities are elevated in patients with pediatric cancers, suggesting that constitutional gene defects predispose some children to cancer. Furthermore, such tumor predisposition syndromes can be recognized by specific patterns of morphologic abnormalities. (*JAMA*. 2008;299:61-69.)

Patients with multiple myeloma treated with a combination of plerixafor (Mozobil, Genzyme) and G-CSF are able to mobilize a sufficient number of bone marrow stem cells for autologous transplant procedures in a shorter period of time than patients treated with G-CSF and placebo. (*Blood*. 2007;110(11):Abstract 445.)

In patients with non-Hodgkin lymphoma, in vivo persistence of anti-CD20 circulating antibodies after treatment with rituximab (Rituxan, Genentech/Biogen Idec) blocks subsequently administered anti-CD20 radiolabeled antibodies. (*Blood*. 2007;110(11):Abstract 525.)