

Older Women Treated With Adjuvant Chemotherapy for Breast Cancer at Increased Risk of Leukemia; Anthracyclines Increase Risk of Heart Failure

An analysis of data in the Surveillance, Epidemiology, and End Results/Medicare database showed that older women who receive adjuvant chemotherapy for breast cancer are at a small but significantly elevated risk of developing acute myeloid leukemia (AML). The findings were published by Dr. Sharon H. Giordano and colleagues in the September 1 issue of the *Journal of Clinical Oncology*. The dataset included 64,715 women diagnosed with nonmetastatic breast cancer from 1992 to 2002 (age range, 66–104 years). Of these patients, 10,130 received adjuvant chemotherapy and the mean follow-up period was 54.8 months. The absolute risk of developing AML at 10 years was 1.8% in women who had received adjuvant chemotherapy, compared to 1.2% in women who had not received adjuvant chemotherapy. On multivariate analysis, the increased risk of AML associated with adjuvant chemotherapy was 53%. The authors noted that their study may have underestimated the risk, though, because it was not possible to assess the occurrence of myelodysplastic syndromes in the cohort based on the available data. Additionally, they noted that treatment with granulocyte colony-stimulating factor within the first year after diagnosis did not increase the risk of AML, as has been reported previously. In conclusion, the authors noted that their findings may help patients evaluate short- and long-term risks of chemotherapy and make informed decisions regarding treatment.

Another analysis of the database by the same authors also published in the September 1 issue of the *Journal of Clinical Oncology* showed that older women with breast cancer who receive anthracycline-based chemotherapy in the adjuvant setting are at significantly increased risk of congestive heart failure. Although anthracyclines are quite effective for the treatment of patients with breast cancer, there was a lack of data on their long-term cardiac safety in women over 65 years of age. Women 66–80 years old, with no history of congestive heart failure, and diagnosed with stage I–III breast cancer between 1992 and 2002 were included in the analysis. The total population analyzed consisted of 43,338 women with a median age of 73.2 years; 4,712 (11%) of these women received adjuvant chemotherapy with anthracyclines and 3,921 received adjuvant chemotherapy without anthracyclines.

The median follow-up was 56 months. Overall, 10,096 (23.3%) patients subsequently developed congestive heart failure. Among those women 66–70 years old, who received anthracycline-based adjuvant chemotherapy, the risk of developing congestive heart failure was 26% higher than for those who received non-anthracycline-based chemotherapy. In women 71–80 years old, the type of adjuvant chemotherapy received was not associated with congestive heart failure. At 5 years of follow-up, the absolute difference in rates of congestive heart failure between women 66–70 years old, who received anthracyclines, and those who received other adjuvant chemotherapy or no adjuvant chemotherapy was 1% versus 4.6%. At 10 years of follow-up, the increased risk of this cardiac complication in anthracycline-treated patients was amplified. The researchers believe their findings demonstrate the need for prospective studies to elucidate the risk of congestive heart failure and the best treatment regimens in the population of older women with breast cancer.

Refractory Metastatic Melanoma May Be Treated Successfully With IL-2

Dr. Ahmad A. Tarhini and associates concluded that patients with metastatic melanoma, whose disease has progressed after biochemotherapy, achieve durable benefit from high-dose bolus administration of interleukin-2 (IL-2). Their findings were published in the September 1 issue of the *Journal of Clinical Oncology*. Twenty-six patients received second- or third-line treatment with high-dose bolus IL-2 (600,000 U/kg per dose for up to 14 doses per cycle, with 1 week of rest between cycles). All but 3 patients underwent at least two treatment cycles, comprising one course, and 10 patients received two courses of therapy. Of these patients, 5 (19%) responded, with 4 complete responses and 1 partial response. Of the complete responders, 2 patients' response was ongoing at over 26 months' follow-up. Though they eventually progressed, 5 patients had stable disease for up to 3 months. Grade 3 and 4 hyperbilirubinemia, thrombocytopenia, and neurologic toxicity were seen in 10, 6, and 2 patients, respectively. Disease progression was the most common reason for discontinuation of treatment (in 77% of patients). Previous response to biochemotherapy did not predict response to treatment with high-dose bolus IL-2. This study demonstrated that predictive biomarkers are needed to select patients who will respond to IL-2 and other forms of biotherapy.