

Cancer-related Mortality Down in United States

Death rates from cancer were reported to have fallen by more than 2% annually from 2002 through 2004, based on results from a study conducted by the National Cancer Institute, Centers for Disease Control, American Cancer Society, and North American Association of Central Cancer Registries. The rate of cancer deaths declined by 1.1% annually from 1993 through 2002. The recent improved rate was attributed to effective tobacco control, screening, early detection, and appropriate treatment. The American Cancer Society estimates that 1.4 million people will be diagnosed with cancer in the United States in 2007, with 560,000 deaths resulting from the disease. Specifically, the incidence of breast cancer notably declined from 2001 through 2004, which was likely based on declining use of hormone-replacement therapy, but it was also hypothesized that a decrease in screening mammography during the same period led to fewer cancer diagnoses. Additionally, the rates of colorectal cancer in both men and women decreased by more than 2%, likely as a result of preventive removal of precancerous polyps. Furthermore, the reduction in the rate of lung cancer was directly attributed to reduced use of tobacco; however, rates of lung cancer are still rising in women, who historically began smoking in large numbers after men did and did not stop smoking until later. Dr. Nancy Davidson, president of the American Society of Clinical Oncology noted that the gains in the fight against cancer are impressive but noted that a reduction in funding for cancer research during the same period could cause a delay in further advances.

Early Inhibition of BCR-ABL Linked to Long-term Response to Imatinib

Australian researchers documented the first indication that assessment of early *BCR-ABL* kinase inhibition in response to therapy with imatinib (Gleevec, Novartis) for chronic myelogenous leukemia (CML) could predict long-term molecular response. Dr. Deborah White and colleagues reported in the October 1 issue of the *Journal of Clinical Oncology* that intrinsic sensitivity to imatinib varies from patient to patient and could be used, if assessed early, to tailor dosing for a given patient. The researchers

studied 49 patients who received weekly treatment with imatinib. Molecular response was gauged by assessing the reduction in levels of Crkl, a downstream substrate of *BCR-ABL*. After 7–10 days of treatment, 21% of patients achieved inhibition of *BCR-ABL* greater than 50%; an additional 24% of patients achieved this level by days 21–28. By 24 months, all of the patients who achieved at least 50% inhibition of *BCR-ABL* experienced major molecular responses, whereas only 56% of those who did not achieve this level of inhibition experienced such a response. Furthermore, those who achieved less than 50% inhibition of *BCR-ABL* were more likely to experience suboptimal responses than those with better initial inhibition of the fusion gene. Future research may indicate whether these findings could lead to dose-adjusted therapy based on in vivo measurement of target inhibition.

Burden of Residual Breast Cancer Linked to Survival

After neoadjuvant chemotherapy for breast cancer, the degree of residual disease is an independent predictor of relapse-free survival, according to a report by Dr. W. Fraser Symmans and colleagues published in the October 1 issue of the *Journal of Clinical Oncology*. Based on the hypothesis that classification of patients into either partial remission or residual disease is insufficient because the latter comprises patients who range from near-partial remission to frank resistance, the researchers assessed the utility of residual breast cancer burden (RCB) as a continuous variable or index. The qualities of RCB were derived from the primary tumor dimensions, cellularity of the tumor bed, and axillary nodal burden. Their research included 241 patients who were divided into three classes: minimal, moderate, and extensive residual disease. It was observed that increasing residual disease was associated with increasingly poor prognosis. The overall adjusted probability of relapse within 5 years ranged from 2.4% for those with minimal residual disease to 53.6% for those with extensive residual disease. The RCB index was further validated as a prognostic measure by predicting distant relapse in 141 patients with breast cancer. The authors remarked, “Although RCB could supplement existing methods to define pathologic response, independent validation of RCB is needed before it can be broadly used as a surrogate endpoint for patient survival.”