HEM/ONC News

By Devon Schuyler

Anastrozole Reduces Breast Cancer in Postmenopausal Women at High Risk

The aromatase inhibitor anastrozole (Arimidex, AstraZeneca) reduced the 5-year risk of breast cancer in high-risk postmenopausal women from 4% to 2%, according to the first results of a study that was presented at the 2013 San Antonio Breast Cancer Symposium (Abstract S3-01) and also published online in the *Lancet* on December 12.

IBIS-II (the International Breast Cancer Intervention Study II) included 3864 women aged 40 to 70 years who were at elevated risk for breast cancer because of family history or a previous diagnosis of a noninvasive lesion. The women were randomly assigned to receive either 1 mg of anastrozole or a placebo daily for 5 years.

After a median follow-up of 5 years, the rate of breast cancer was significantly lower among women taking anastrozole than among those taking placebo (hazard ratio [HR], 0.47; 95% CI, 0.32-0.68; *P*<.0001). Dr Jack Cuzick and coauthors calculated that after 7 years, the cumulative incidence of breast cancer would be 2.8% in the anastrozole group and 5.6% in the placebo group. The number of reported deaths was 18 in the anastrozole group and 17 in the placebo group, a statistically nonsignificant difference. Women who took anastrozole were more likely to experience musculoskeletal and vasomotor symptoms.

In a commentary that accompanied the article, Dr David Cameron said that widespread use of anastrozole for breast cancer prevention was unlikely at this time given the drug's toxicity and the absence of a survival benefit.

Idelalisib Boosts Survival in Chronic Lymphocytic Leukemia

Combination treatment with idelalisib and rituximab (Rituxan, Genentech/Biogen Idec) improved progression-free survival (PFS) in patients with heavily relapsed or refractory chronic lymphocytic leukemia (CLL) by 85% compared with rituximab alone, according to the results of a study presented at the 2013 meeting of the American Society of Hematology (ASH; abstract LBA-6). Idelalisib is an investigational PI3-kinase δ inhibitor.

For the phase 3 study, Dr Richard Furman and colleagues randomly assigned 220 patients with heavily pretreated, relapsed CLL to receive rituximab plus either 150 mg of idelalisib or a placebo twice daily for 6 months. The trial was halted early after the data monitoring committee found a positive risk-benefit ratio with combination therapy.

Median PFS had not been reached for patients in the combination group when the study stopped, and was 5.5 months for those in the control group. This difference represented an 85% higher PFS in the combination group than in the control group (HR, 0.15; 95% CI, 0.08-0.28; *P*<.001). At 24 weeks, the PFS was significantly higher in the combination group than in the control group (93% vs 46%). Overall survival also was significantly higher in the combination group than in the control group (HR, 0.28; 95% CI, 0.09-0.86; *P*=.018)

The most common adverse events in both groups were pyrexia, fatigue, nausea, chills, infusion-related reactions, and cough.

Mutations in CALR Linked to Myeloproliferative Neoplasms

Two new studies have identified *CALR*, a gene that encodes calreticulin, as a major underlying driver of myeloproliferative neoplasms (MPNs) in patients with wild-type *JAK2* and *MPL*. Both studies were presented at the 2013 ASH annual meeting and also published in the December 19 issue of the *New England Journal of Medicine*.

In the first study, led by Dr Thorsten Klampfl, researchers used exome sequencing on samples from 6 patients with primary myelofibrosis who had nonmutated *JAK2* and *MPL*. All 6 samples were found to have acquired insertion and deletion mutations in *CALR*; the researchers found 36 types of mutations. Patients with mutated *CALR* had a better survival rate than those with mutations in *JAK2,* as well as a lower risk for thrombosis.

The second study, led by Dr Jyoti Nangalia, involved exome sequencing on samples from 151 patients with MPNs who had nonmutated *JAK2* and *MPL*. The researchers identified a total of 148 *CALR* mutations with 19 distinct variants. They found that *CALR* was mutated in 70% to 84% of patients with essential thrombocytopenia or myelofibrosis.

In an editorial that accompanied the articles, Dr Ross Levine wrote that the results of the 2 studies suggested that *CALR* mutations represent a novel driver event that occurs early in pathogenesis and has a functional role similar to that of *JAK2* and *MPL* mutations during the development of MPNs.