HEM/ONC News

By Devon Schuyler

PALOMA-3 Stopped Early Based on Efficacy of Palbociclib

A trial of palbociclib (Ibrance, Pfizer) in metastatic breast cancer was stopped early after an improvement in progression-free survival was found for those taking palbociclib plus fulvestrant vs those taking fulvestrant (Faslodex, AstraZeneca) alone, according to the drug's manufacturer. Palbociclib is an inhibitor of cyclin-dependent kinase 4/6. It was approved in February 2015 as a first-line treatment for women with advanced estrogen receptor–positive, human epidermal growth factor receptor 2 (HER2)–negative metastatic breast cancer.

The multicenter phase 3 trial, called PALOMA-3, enrolled 521 women with hormone receptor–positive, HER2–negative metastatic breast cancer that had progressed despite endocrine therapy. Women were randomly assigned 2 to 1 to either palbociclib plus fulvestrant or placebo plus fulvestrant. The study was stopped early based on an assessment by an independent Data Monitoring Committee.

Adverse effects of palbociclib included neutropenia, leukopenia, fatigue, anemia, upper respiratory infection, nausea, stomatitis, alopecia, diarrhea, thrombocytopenia, decreased appetite, vomiting, asthenia, peripheral neuropathy, epistaxis, and pulmonary embolism.

Detailed efficacy and safety results from PALOMA-3 will be submitted for presentation at the 2015 annual meeting of the American Society of Clinical Oncology.

Extra-Fresh Blood Does Not Benefit Transfusion Patients

Extra-fresh blood is no more effective than standard blood at reducing mortality in critically ill adults who require transfusion, according to a study published by Lacroix and colleagues in the April 9 issue of the *New England Journal of Medicine.* Previous observational studies had found an association between older blood and an increased risk of death.

For the ABLE (Age of Blood Evaluation) trial, researchers randomly assigned 2430 critically ill adults to receive transfusions of either extra-fresh red blood cells, which had been stored for less than 8 days, or standard red blood cells, which had been stored for up to 42 days. The average duration of storage was 6.1 days in the extra-fresh blood group vs 22.0 days in the standard-blood group.

At 90 days after transfusion, the hazard ratio for death was 1.1 in the extra-fresh blood group compared with the standard-blood group (95% CI, 0.9-1.2; P=0.38). No significant differences between the 2 groups were found in any of the secondary outcomes, which included length of stay in the hospital and transfusion reactions.

Although it is possible that some groups of critically ill patients might be especially vulnerable to the adverse effects of red blood cell storage, the authors concluded that preferential use of extra-fresh blood "is not justified at this time."

Type and Location of BRCA1/2 Mutations Affect Breast and Ovarian Cancer Risk

The type and location of mutations in *BRCA1* and *BRCA2* affect the risk of breast and ovarian cancer, according to a large observational study published by Rebbeck and colleagues in the April 7 issue of the *Journal of the American Medical Association*.

The study, called the CIMBA (Consortium of Investigators of Modifiers of BRCA) initiative, included data on 19,581 carriers of *BRCA1* mutations and 11,900 carriers of *BRCA2* mutations from 55 centers in 33 countries. The women were first seen in the clinic between 1937 and 2011, although research participation may have occurred many years later. Women who carried a mutation in both *BRCA1* and *BRCA2* were excluded from this study.

Among the carriers of *BRCA1* and *BRCA2* mutations, respectively, the rates of breast cancer were 46% and 52%, the rates of ovarian cancer were 12% and 6%, and the rates of both breast and ovarian cancer were 5% and 2%. In the *BRCA1* gene, the researchers identified 3 regions that increased the risk of breast cancer by 34% to 46% and 1 region that increased the risk of ovarian cancer by 38%. In the *BRCA2* gene, the researchers identified 3 regions that increased the risk of breast cancer by 63% to 131% and 2 regions that increased the risk of ovarian cancer by 43% to 49%. For both *BRCA1* and *BRCA2* mutation carriers, mutations leading to nonsense-mediated decay were linked to an increased risk of breast and ovarian cancer and an earlier age of breast cancer diagnosis.

The researchers concluded that with appropriate validation, these data "may have implications for risk assessment and cancer prevention decision making among carriers of *BRCA1* and *BRCA2* mutations."