HEM/ONC News

By Devon Schuyler

Aspirin Linked to Higher Rate of Cancer-Related Mortality

Aspirin causes a slight increase in the risk of cancer-related mortality—although without an increase in cancer cases—when taken by healthy older people, according to a report from a study conducted in Australia and the United States.

Results from the study, called ASPREE, appeared online September 16 in the *New England Journal of Medicine* in 3 reports by Dr John McNeil and colleagues.

For ASPREE, researchers randomly assigned more than 19,000 people—aged 70 and older if white and aged 65 and older if black or Hispanic—to receive daily low-dose aspirin (100 mg) or placebo for a median of 4.7 years.

The risk for death from any cause was higher in the aspirin group than in the placebo group (12.7 vs 11.1 events per 1000 person-years, respectively; hazard ratio [HR], 1.14; 95% CI, 1.01-1.29), although this was not statistically significant after accounting for multiple comparisons. The majority of the excess mortality in the aspirin group was caused by cancer-related death, which occurred in 3.1% of participants in the aspirin group and 2.3% of those in the placebo group (HR, 1.31; 95% CI, 1.10-1.56).

The researchers also found that daily aspirin use in healthy elderly persons did not prolong disability-free survival or reduce the rate of cardiovascular disease compared with placebo, but led to a higher rate of major hemorrhage.

Dr McNeil and his coauthors wrote that the principal limitation of their study was the limited follow-up, "which may have ended before the possible emergence of a preventive effect on cancer."

Fatal Side Effects From Checkpoint Inhibitors Rare, Vary According to Agent

Fatal side effects with checkpoint inhibitors are rare, according to a new systematic review and meta-analysis, but usually occur soon after treatment. The review also determined the most common fatal side effects, and found that these varied according to the checkpoint inhibitor used.

For the review, which appeared online September 13 in *JAMA Oncology*, researchers led by Dr Daniel Wang collected data from the World Health Organization's pharmacovigilance database (which includes more than 16 million adverse drug reactions) and records from 7 academic medical centers. They also performed a meta-analysis of published trials of checkpoint inhibitors.

The researchers found that the rate of fatal side effects ranged from 0.3% to 1.3% in patients treated with checkpoint inhibitors. When these fatal side effects occurred, they tended to arise early in treatment—a median of 40 days after monotherapy and a median of 14.5 days after combination immunotherapy.

The most common fatal side effect with ipilimumab monotherapy was colitis/diarrhea, whereas the most common fatal side effects with anti–programmed death 1/programmed death ligand 1 monotherapy were pneumonitis, hepatitis, colitis, neurologic events, and myocarditis.

The authors noted that the risk of fatal side effects "remains very low for individual patients with advanced cancer, and should not dissuade use of these potentially curative therapies."

Moxetumomab Pasudotox Approved in Relapsed/Refractory Hairy Cell Leukemia

On September 13, the US Food and Drug Administration approved moxetumomab pasudotox (Lumoxiti, AstraZeneca) for adults with relapsed or refractory hairy cell leukemia (HCL) who have received at least 2 prior systemic therapies, including treatment with a purine nucleoside analogue (PNA). Moxetumomab pasudotox is a CD22-directed cytotoxin.

Approval was based on a single-arm phase 3 study of 80 patients (NCT01829711) with histologically confirmed HCL or HCL variant requiring treatment based on the presence of cytopenias or splenomegaly and who had received prior treatment with at least 2 systemic therapies, including one PNA. Patients received intravenous moxetumomab pasudotox over 30 minutes on days 1, 3, and 5 of each 28-day cycle for a maximum of 6 cycles or until documentation of complete response (CR), disease progression, or unacceptable toxicity.

The durable CR rate was 30% (95% CI, 20%-41%), and the CR rate was 41% (95% CI, 30%-53%). The most common non-laboratory adverse reactions of any grade were infusion-related reactions, edema, nausea, fatigue, headache, pyrexia, constipation, anemia, and diarrhea. The most common grade 3 or 4 adverse reactions were hypertension, febrile neutropenia, and hemolytic uremic syndrome. Adverse reactions resulting in permanent discontinuation of moxetumomab pasudotox occurred in 15% of patients.