Prevention Elusive With Iplimumab Diarrhea

BY SHERRY BOSCHERT

Prophylactic budesonide did not significantly decrease the risk of grade 2 or higher diarrhea that is common in patients who have unresectable melanoma treated with the investigational drug ipilimumab, a phase II trial found.

Iplimumab is a human monoclonal antibody directed against CTL antigen-4, which is a key negative regulator of the T-cell immune response. In clinical studies, immune-related adverse events associated with ipilimumab most commonly have involved the gastrointestinal tract or the skin.

Dr. Jeffrey Weber and his associates hypothesized that oral budesonide, which is used to treat grade 2 diarrhea when it accompanies ipilimumab therapy, might work as prophylaxis to prevent diarrhea without affecting any antimicrobial activity from ipilimumab.

They randomized 115 patients with unresectable stage III or IV melanoma to treatment with open-label IV iplimumab (10 mg/kg every 3 weeks for four dos-es), plus blinded oral budesonide or placebo. The once-daily budesonide dose was 9 mg through week 12, then tapered until discontinuation at week 16.

Grade 2 or higher diarrhea occurred in 19 (33%) of the 58 patients in the budesonide group and 20 (35%) of the 57 patients in the placebo group, Dr. Weber and colleagues reported in an online article to appear in the Sept. 1, 2009, issue of Clinical Cancer Research (doi:10.1158/1078-0432.CCR-09-1024).

Patients who developed grade 2 or higher diarrhea or other immune-related adverse events discontinued the budesonide and started open-label treatment with budesonide or other steroids. If the diarrhea lasted 2 weeks or there was grade 3 or 4 diarrhea, they stopped ipilimumab. None of the patients developed gastrointestinal or colonic perforations.

Bristol-Myers Squibb, which is developing ipilimumab with Medarex, sponsored the study and funded editorial and writing assistance for the investigators. Dr. Weber and three of his associates have received funds for speaking, advising, and research for Bristol-Myers Squibb. Dr. Weber owns a patent with Medarex on CT2A-4 antibodies. The budesonide was donated without charge by Boehringer-Ingelheim. A previous article has been an advertisement because page charges were levied to defray the costs of publication.