Results of a phase III, randomized, placebo-controlled study of sorafenib in combination with carboplatin and paclitaxel as second-line treatment in patients with unresectable stage III or stage IV melanoma.

Abstract:

PURPOSE: This phase III, randomized, double-blind, placebo-controlled study was conducted to evaluate the efficacy and safety of sorafenib with carboplatin and paclitaxel (CP) in patients with advanced melanoma who had progressed on a dacarbazine- or temozolomide-containing regimen. PATIENTS AND METHODS: A total of 270 patients were randomly assigned to receive intravenous paclitaxel 225 mg/m² plus intravenous carboplatin at area under curve 6 (AUC 6) on day 1 of a 21-day cycle followed by either placebo (n = 135) or oral sorafenib 400 mg (n = 135) twice daily on days 2 to 19. The primary efficacy end point was progression-free survival (PFS); secondary and tertiary end points included overall survival and incidence of best response, respectively. RESULTS: The median PFS was 17.9 weeks for the placebo plus CP arm and 17.4 weeks for the sorafenib plus CP arm (hazard ratio, 0.91; 99% CI, 0.63 to 1.31; two-sided log-rank test P = .49). Response rate was 11% with placebo versus 12% with sorafenib. Dermatologic events, grade 3 thrombocytopenia, diarrhea, and fatigue were more common in patients treated with sorafenib plus CP versus...
placebo plus CP. CONCLUSION: In this study, the addition of sorafenib to CP did not improve any of the end points over placebo plus CP and cannot be recommended in the second-line setting for patients with advanced melanoma. Both regimens had clinically acceptable toxicity profiles with no unexpected adverse events. A trial of similar design for the first-line treatment of patients with advanced melanoma (intergroup trial E2603) is currently ongoing.