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Bortezomib Therapy in Relapsed/Refractory Multiple Myeloma

DR. TOM MYERS, MD

Dr. Myers summarized the mechanism of action of proteasome inhibition in the treatment of multiple myeloma. He described the data supporting proteasome inhibition in the treatment of multiple myeloma. Dr. Myers also covered the topic of managing the side effects associated with proteasome inhibitors in the treatment of multiple myeloma.

Colorectal Cancer: Emerging Data and New Treatment Options

BILL OUTMAN, PHARMD

Xeloda in Adjuvant Colon Cancer

In June of 2005, the FDA approved Xeloda as a single agent for adjuvant treatment in patients with Dukes' C colon cancer who have undergone complete resection of the primary tumor when treatment with fluoropyrimidine therapy alone is preferred (1). This was based on an open-label, multinational, randomized, parallel group Phase III study where patients received either Xeloda 1250 mg/m² twice daily, Days 1-14 followed by 1 week rest or LV 20 mg/m²/day followed by 5-FU 425 mg/m²/day Days 1-5 with rest on Days 6-28. The primary endpoint was non-inferiority in disease-free survival (DFS).

The median follow-up at the time of the most recent analysis was 53 months. The hazard ratio for DFS for Xeloda compared to 5-FU/LV was 0.87 (95% C.I. 0.76 – 1.00). Because the upper 2-sided 95% confidence limit of hazard ratio was less than 1.20, Xeloda was non-inferior to 5-FU/LV. Survival data were not mature at the time of the analysis with a median follow-up of 53 months. The comparison of overall survival did not reach statistical significance for the test of difference (HR 0.88, 95% C.I. 0.74 – 1.05; p = 0.169).

A safety analysis of this trial conducted 19 months after enrollment of the last patient showed that patients treated with Xeloda had an improved safety profile

compared to the Mayo 5-FU/LV regimen with significantly less diarrhea, nausea and vomiting, stomatitis (including Grade 3/4), alopecia, neutropenia (including Grade 3/4) and febrile neutropenia/sepsis (2). Grade 3 hand-foot syndrome and Grade 3/4 hyperbilirubinemia were more common in the XELODA group as compared to the IV 5-FU/LV arm.

Xeloda plus Oxaliplatin in Metastatic Colorectal Cancer

Results of a Phase III study evaluating Xeloda in combination with oxaliplatin (XELOX) vs 5-fluorouracil in combination with oxaliplatin (FUFOX) presented at the 2005 ASCO meeting showed a similar safety profile for XELOX and FUFOX with significantly higher grade 2/3 hand-foot syndrome in the XELOX arm (3). In this phase III study, XELOX showed no inferiority with respect to overall response rates (47% vs 49%), time to disease progression (7 months vs 8 months) and overall survival (16.3 months vs 17.2 months) as compared with FUFOX within the study's statistical assumptions.

An ongoing phase II study, also updated at the 2005 ASCO meeting, evaluated the safety and tolerability of 3 fluoropyrimidine plus oxaliplatin based regimens alone (TREE-1) and in combination with bevacizumab (TREE-2) as first-line treatment in patients with metastatic colorectal cancer (4). In the TREE-2 study, 223 patients were randomized to receive either mFOLFOX-B (oxaliplatin 85 mg/m², leucovorin (LV) 350 mg, 5-FU bolus 400 mg/m² and infusional 2400 mg/m² over 46 hours, and bevacizumab 5 mg/kg every 2 weeks), bFOL-B (oxaliplatin 85 mg/m² Days 1 and 15, LV 20 mg/m² and bolus 5-FU 500 mg/m² Days 1, 8, 15, every 4 weeks, and bevacizumab 5mg/kg every 2 weeks), or XELOX-B (oxaliplatin 130 mg/m² Day 1 and Xeloda 1000 mg/m² orally twice daily for 14 days, and bevacizumab 7.5 mg/kg every 3 weeks). The primary endpoint was the overall incidence of Grade 3/4 toxicities during the first 12 weeks of study therapy for each of the study regimens. Secondary