Thalidomide-based treatment for Waldenstrom's macroglobulinemia

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We have previously reported that thalidomide had activity in Waldenstrom's macroglobulinemia (WM). In our original trial, 20 patients with WM were treated with thalidomide at a starting dose of 200 mg PO daily with dose escalation in 200 mg increments every 14 days as tolerated to a maximum of 600 mg. On an intention to treat basis, 5 of 20 patients (25%) achieved a partial response. Time to response was short ranging from 0.8 months to 2.8 months. Adverse effects were common and 7 patients interrupted thalidomide within 2 months because of intolerance. The median duration of response was 11 months.

A preliminary report has indicated that the combination of thalidomide with clarithromycin and dexamethasone (ClaTD) was associated with response in 6 of 8 evaluable patients (Coleman, et al 2001). In order to confirm this observation we initiated a prospective phase II trial of clarithromycin 500 mg PO BID continuously, thalidomide 200 mg PO QHS continuously and dexamethasone 40 mg PO Q week. Dose reduction for all agents was scheduled for pertinent side effects. Twelve patients have been enrolled so far. All have been previously treated and their median age is 70 years (range 42 to 85 years). Among the 10 patients evaluable for response so far, 2 have achieved at least 50% reduction of monoclonal protein and one is showing >25% reduction. An additional patient with 25% reduction of monoclonal protein died of acute myocardial infarction within 3 weeks of treatment. Side effects included constipation (8 patients), somnolence and/or fatigue (7 patients), tremor (4 patients), upper gastrointestinal tract symptoms (5 patients), fluid retention, edema with or without Cushing's-like signs (4), hyperglycemia (2 patients) and peripheral neuropathy (2 patients). We conclude that the ClaTD regimen has some activity in heavily pretreated patients with WM. This regimen is associated with a variety of side effects due to thalidomide and to corticosteroids. We also confirm previous reports which indicated that clarithromycin may augment the corticosteroid-induced side effects.