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Bortezomib Added to Melphalan Improves Myeloma Response

New York, August 27, 2008 (Reuters Health)

In patients with multiple myeloma who are ineligible for high-dose therapy, addition of the proteasome inhibitor bortezomib (brandname - Velcade) to melphalan plus prednisone improves response rate and survival, according to a multinational, phase III trial reported in the New England Journal of Medicine for August 28.

The VISTA trial, conducted by Dr. Jesus F. San Miguel, at Hospital Universitario de Salamanca in Spain, and colleagues, included 682 patients who were not candidates for high-dose therapy plus stem-cell transplantation because of age (65 years or older) or comorbidities.

Planned treatment for all patients comprised nine 6-week cycles of melphalan (9 mg/m²) and prednisone (60 mg/m²) on days 1 to 4. Patients were randomly assigned to no additional treatment (n = 338) or to bortezomib (1.3 mg/m², n = 344), to be administered 8 times during each of the first four cycles, then on 4 days during each of the remaining 5 cycles.

"The response was more rapid and durable in the bortezomib group than in the control group," Dr. San Miguel's group reports.

According to the article, the time to disease progression was 24.0 months in the bortezomib group vs 16.6 months in the control group (hazard ratio 0.48, p < 0.001). The authors note that "the time-to-progression benefit in the bortezomib group was independent of age, sex, race, baseline beta-2 microglobulin level, baseline albumin level, geographic region, clinical stage...or creatinine clearance."

The proportions of patients with at least a partial response were 71% in the bortezomib group and 35% in the control group. After a median follow-up of 16.3 months, 13% of bortezomib-treated patients and 22% of placebo patients had died (hazard ratio 0.61, p = 0.008).

There were substantially more cases of peripheral sensory neuropathy associated with bortezomib (151 vs 16), but "after only 16.3 months of follow-up, peripheral neuropathy improved or resolved in most patients, confirming that prompt modification of the bortezomib dose... avoids severe neurotoxicity and ensures reversibility."

In a Journal editorial, Dr. Brian G. M. Durie, at the Cedars-Sinai Outpatient Cancer Center in Los Angeles, points out that two other agents - thalidomide and lenalidomide - and other drug combinations have also shown promising results in recent trials.

"We are fortunate to have so many options, both in the clinic and in development," Dr. Durie writes. "Our challenge will be to assess each patient on an individual basis and to identify and customize therapy for maximum long-term benefit."

SOURCE: N Engl J Med 2008;359:906-917,964-966.