MedicalXpress

Drug shows positive responses, low side-effects in multiple myeloma

December 7 2009

NEW ORLEANS — The second-generation proteasome inhibitor carfilzomib is showing noteworthy response rates and low levels of adverse side effects among multiple myeloma patients in a phase II clinical trial, researchers reported today at the 51st Annual Meeting of the American Society of Hematology.

The updated data from the 17-site study focuses on patients with relapsed or resistant multiple myeloma who have received one to three prior therapies, but not the drug bortezomib, the original proteasome inhibitor.

"These findings are truly an advance for patients with multiple myeloma," said Michael Wang, M.D., associate professor, Department of Lymphoma/Myeloma at M. D. Anderson and lead author on the study. "This is an incurable, challenging disease with devastating consequences.

"While new agents are extending life expectancies, they often have adverse side effects, including severe neuropathy. Carfilzomib is showing good response rates, with an improved side effects profile," Wang said. Neuropathy is peripheral nerve pain or numbness that can become debilitating enough to halt treatment.

According to the American Cancer Society, more than 20,000 cases of multiple myeloma will be diagnosed this year in this country. More than 10,000 people will die of this disease, which is a type of blood cancer.

Better tolerated than other agents

In preclinical studies carfilzomib has been better tolerated than bortezomib, allowing consecutive day dosing and treatment over extended periods of time. Both drugs work by targeting the cell's proteasome, which destroys mutated or damaged proteins. Blocking this process causes cell death. Carfilzomib targets and binds to the proteasome differently than bortezomib.

Researchers previously observed higher response rates to carfilzomib among patients who had never been treated with bortezomib compared to those with relapsed disease following bortezomib therapy.

Fifty-seven bortezomib-naive patients have been enrolled, and 56 have received at least one dose of carfilzomib. Prior therapies included alkylators, stem cell transplant, thalidomide, lenalidimide and anthracyclines. Patients entered the trial with a variety of side effects from previous treatments including 21 patients with neuropathy (37 percent) and 12 (21 percent) with impaired renal function. The mean time from diagnosis was four years.

Response rate almost half

Carfilzomib was given intravenously on six days every 28 days for up to 12 cycles. To date, the mean number of doses administered per patient is 30. Five patients have completed the full 12-cycle protocol, and another five have completed at least nine cycles. Seventeen are continuing on in the study.

Among 51 evaluable patients, overall response rate has been 45 percent, including one complete response and 18 partial responses. An additional nine patients had minor response, and disease stabilized at least six weeks in 10 patients. This is considered noteworthy for a single-agent

drug regimen in patients with tumor progression despite previous therapy with novel combinations.

"Adverse events, most of which were minor, included fatigue, nausea and anemia," Wang said. The incidence of neuropathy dropped to seven cases (12 percent) in 51 evaluable patients. Dose modifications rarely were required. No patients who entered the trial with impaired renal function needed to have their dose reduced due to renal side effects.

Source: University of Texas M. D. Anderson Cancer Center (news : web)