Drugs are safe, active in patients normally ineligible for clinical trial

December 10 2010

A two-drug combination is safe and active in newly diagnosed acute myeloid leukemia and myelodysplastic syndrome patients who are usually excluded from clinical trials because they have other illnesses or poor performance status - a measure of disease progression - researchers reported this week at the 52nd American Society of Hematology Annual Meeting.

"Our findings suggest current eligibility standards that prevent participation by these patients in phase I and phase II clinical trials might be inadequate," said Guillermo Garcia-Manero, M.D., professor in The University of Texas MD Anderson Cancer Center Department of Leukemia, who presented early results of an ongoing phase II clinical trial. Such patients also are not eligible for standard therapies.

Newly diagnosed patients with AML or MDS who have an additional disease, including a second cancer, or lack good performance status, survive for less than 60 days without treatment, Garcia-Manero said. Performance status is measured by Eastern Cooperative Oncology Group criteria, which score patients from 0 (fully active) to 4 (completely disabled).

The phase II clinical trial accepts only those with ECOG performance status higher than 2 (capable of self care, unable to work, up more than half of waking hours) and those with other diseases.

The drug combination of 5-azacitidine and vorinostat is known to be safe

and active against AML and MDS among patients without the complications that participants in this trial have, Garcia-Manero said.

So far, 27 patients have been treated, nine with AML, 18 with MDS. Their median age is 69, ranging from 44 to 83. At a median follow up of 3.6 months, 20 of 24 survived past 60 days (83 percent). One patient died during therapy, two died of disease progression after going off the study.

Fifteen could be evaluated for response to the combination, seven (46 percent) had complete responses. Stable disease was noted in two patients - one with metastatic sarcoma and one with breast cancer.

Benchmarks of survival and response that would require stopping the trial have not been met and Garcia-Manero said indications are that the study will continue and not hit either measure.

"This combination is safe and active for these poor-prognosis patients at similar levels of safety and activity seen among patients who are eligible for clinical trials," Garcia-Manero said.

Garcia-Manero and colleagues also have developed a prognostic model for MDS patients that takes into account additional diseases or conditions, called co-morbidities, to help predict survival in those patients.

Azacitidine, known commercially as Vidaza, activates genes that have been silenced by stripping them of methyl groups, which protrude like bookmarks from a gene's promoter region. Vorinostat, known commercially as Zolzinza, activates genes by protecting acetyl groups that adhere to histones - proteins connected to DNA like beads on a string.

Both drugs reactivate enough tumor-suppressing genes to have an effect on AML and MDS.

Provided by University of Texas M. D. Anderson Cancer Center