Second-line CML drugs evoke faster response than front-line therapy

December 7 2009

Two medications approved as treatment for drug-resistant chronic myeloid leukemia continue to provide patients with quicker, better responses as a first treatment than the existing front-line drug, researchers at The University of Texas M. D. Anderson Cancer Center reported at the 51st Annual Meeting of the American Society of Hematology.

Initial therapy for CML remains imatinib, a Novartis drug known as Gleevec®, which has increased the five-year survival rate for the disease from 50 percent to 90 percent of patients. In separate clinical trials, M. D. Anderson researchers are comparing nilotinib, a Novartis drug known as Tasigna®, and dasatinib, a Bristol-Myers Squibb drug known as Sprycel®, to historical results from earlier trials of imatinib.

"More patients taking nilotinib or dasatinib are achieving complete responses more quickly than they do on either of two daily doses of imatinib," said Jorge Cortes, M.D., professor in M. D. Anderson's Leukemia Department and leader of both studies.

For example, 96 percent of those taking nilotinib and 94 percent of those on dasatinib reached a complete cytogenetic response at six months, compared with 54 percent of those taking 400 mg a day of imatinib and 85 percent of those taking 800 mg. Over the longer term up to 30 months, complete cytogenetic response induced by the two drugs is comparable to that of the higher-dose imatinib.

Complete cytogenetic response is the absence of the defective chromosome that causes the disease.

CML is caused by an abnormality known as the Philadelphia chromosome that produces an aberrant protein, Bcr-Abl, which causes the overproduction of one type of white blood cell that drives the disease. All three drugs are tyrosine kinase inhibitors, which block the action of Bcr-Abl. Nilotinib and dasatinib target more variations of the protein and often work after imatinib has failed. Both are approved by the U.S. Food and Drug Administration for patients who can't tolerate imatinib or whose CML resists the drug.

The dasatinib trial has enrolled 62 patients with previously untreated early stage CML taking either 50 mg twice daily or 100 mg once a day. Among 50 patients followed for at least three months, 49 (98 percent) achieved complete cytogenetic response. Major molecular response, a more stringent measure of remission, was reached in 35 patients (70 percent) with five (10 percent) achieving complete molecular response.

The researchers have dropped the twice daily arm of the trial, keeping the 100 mg once a day arm open because it has produced higher rates of major molecular response with fewer side effects.

The nilotinib trial has enrolled 65 patients with the 400mg twice daily dose producing complete cytogenetic responses in 50 of 51 patients (98 percent) followed for at least three months. Major molecular response has been achieved in 32 patients (63 percent) with 12 (24 percent) achieving complete molecular response.

All patients in both trials are alive, and enrollment continues. Side effects are being closely monitored and some patients in each trial had their treatment reduced or temporarily interrupted because of toxicities. Side effects are manageable and similar to those seen for imatinib,

Cortes said.

Early results for both comparisons

Months on therapy Percent of patients with Complete Cytogenetic Response

Dasatinib Imatinib 400mg Imatinib 800mg
3 82 37 63
6 94 54 85
12 98 65 89
18 89 67 89
24 84 67 88
30 83 67 89

Months on therapy Percent of patients with Complete Cytogenetic Response (Number of valuable patients)
Nilotinib Imatinib 400mg Imatinib 800mg
3 90 37 63
6 96 54 85
12 97 65 89
18 93 67 89
24 93 67 88
30 92 67 89

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