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Researchers study use of dasatinib for patients with high-risk MDS

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Researchers at Moffitt Cancer Center have completed a phase II clinical trial to determine the safety and efficacy of dasatinib for patients with higher-risk myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia, or acute myeloid leukemia resulting from MDS and have failed treatment with azanucleosides. The therapy may not be effective for all patients, but those with trisomy 8 chromosomal disorder have higher rates of stable disease and respond better to treatment with dasatinib, the study shows.

Results of this study appear in the March issue of *Leukemia Research*.

Myelodysplastic syndromes are disorders of the stem cell in bone marrow. The marrow does not produce enough normal blood cells for the body. As the number of quality blood-forming cells declines, blood production is impaired.

According to the researchers, stem cell transplantation is the only potentially curative option for MDS but also has risks of morbidity and mortality. A class of medication called azanucleosides is the only approved medication for patients with an advanced stage of this disease. The outcome after failure of azanucleosides is poor. Therefore, new therapies for MDS are needed, said the study authors.

Dasatinib, a multikinase inhibitor, has been approved by the Food and Drug Administration for patients with chronic myelogenous leukemia. The drug has promising potential because of its activity against a broad

spectrum of tyrosine kinases, which are enzymes that function as an 'on' or 'off' switch for many cellular functions, such as increased activation of cell migration, proliferation, survival, invasion and angiogenesis (tumor blood vessel growth).

"This phase II trial was to assess whether dasatinib would be beneficial for patient with higher risk MDS whose previous treatments had failed," said study corresponding author Rami S. Komrokji, M.D., clinical director of Hematologic Malignancies and member of the Chemical Biology and Molecular Medicine Program at Moffitt. "We found that while dasatinib was well-tolerated with limited toxicities, it only had modest activity."

Among 18 patients treated, three patients responded, four had stable disease, and 10 experienced disease progression. They also noted that four of the five participants with trisomy 8, a disorder caused by having three copies of chromosome 8, had stable disease. An observation, they concluded, warrants further investigation.

More information: www.lrjournal.com/article/S0145-2126%2812%2900437-7/abstract

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