Efficacy and safety of imatinib in adult patients with c-kit-positive acute myeloid leukemia.

This phase 2 pilot study was conducted to determine the efficacy and safety of imatinib mesylate in patients with c-kit-positive acute myeloid leukemia (AML) refractory to or not eligible for chemotherapy. Twenty-one patients were enrolled and received imatinib 600 mg orally once daily. Five responses were seen primarily in patients, starting with relatively low blast counts in bone marrow (BM) and peripheral blood (PB): 2 patients who were considered refractory on chemotherapy on the basis of persistence of blasts in PB and BM met the criteria for complete hematologic remission, 1 patient had no evidence of leukemia, and 2 patients achieved a minor response. Treatment with imatinib demonstrated a good safety profile and was well tolerated. Western blot analysis and immunohistochemistry demonstrated c-Kit activation in primary AML cells. Further, imatinib treatment of primary AML cells inhibited c-Kit tyrosine-phosphorylation. Genomic DNA-sequencing of c-KIT showed no mutations in exons 2, 8, 10, 11, 12, and 17. Although some of the responses derived from relatively small reductions in leukemic blasts and may be attributable, in part, to prior chemotherapy, these cases suggest that imatinib has interesting clinical activity in a subset of patients with c-kit-positive AML. Further clinical trials are warranted to explore the
clinical potential of imatinib in AML and to identify the underlying molecular mechanism.