High activity of sorafenib in FLT3-ITD-positive acute myeloid leukemia synergizes with allo-immune effects to induce sustained responses.

Preliminary evidence suggests that the multikinase inhibitor sorafenib has clinical activity in FLT3-ITD-positive (FLT3-ITD) acute myeloid leukemia (AML). However, the quality and sustainability of achievable remissions and clinical variables that influence the outcome of sorafenib monotherapy are largely undefined. To address these questions, we evaluated sorafenib monotherapy in 65 FLT3-ITD AML patients treated at 23 centers. All but two patients had relapsed or were chemotherapy-refractory after a median of three prior chemotherapy cycles. Twenty-nine patients (45%) had undergone prior allogeneic stem cell transplantation (allo-SCT). The documented best responses were: hematological remission in 24 patients (37%), bone marrow remission in 5 patients (8%), complete remission (with and without normalization of peripheral blood counts) in 15 patients (23%) and molecular remission with undetectable FLT3-ITD mRNA in 10 patients (15%), respectively. Seventeen of the patients without prior allo-SCT (47%) developed sorafenib resistance after a median treatment duration of 136 days (range, 56-270 days). In contrast, allo-SCT patients...
developed sorafenib resistance less frequently (38%) and significantly later (197 days, range 38-225 days; P=0.03). Sustained remissions were seen exclusively in the allo-SCT cohort. Thus, sorafenib monotherapy has significant activity in FLT3-ITD AML and may synergize with allogeneic immune effects to induce durable remissions.