

Hematopoietic Cell Transplants Increase Survival Odds for a New Subgroup of Hutch AML Patients

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Acute myeloid leukemia (AML) is the most common adult leukemia, with incidence increasing with age. AML is characterized by rapid growth of abnormal immature white blood cells of the myeloid line, which accumulate in the bone marrow and interfere with the development of normal blood cells. AML progresses rapidly and, if untreated, is typically lethal within months. Initial treatment of AML aims to induce remission by eliminating leukemic cells. Post-remission therapy is designed to eradicate any remaining undetectable cells, and can be implemented as either chemotherapy or hematopoietic cell transplantation (HCT). Based on the differentiation state and cytogenetic abnormalities of the leukemic cells, AML is broken into several subtypes, each with unique prognoses and treatment options. A subgroup of AML patients recently defined by [Medeiros et al.](#) (2010) has an extremely unfavorable prognosis. This subgroup, termed monosomal karyotype (MK), is characterized by at least two autosomal monosomies, or a single autosomal monosomy in the presence of other genomic structural abnormalities. Less than 4 percent of MK+ patients are projected to live beyond 4 years from diagnosis; surviving MK+ patients had undergone HCT during remission, suggesting that HCT may be a favorable treatment for MK+ AML. To determine the efficacy of HCT in this poor prognosis subgroup of AML patients, Dr. Min Fang and co-authors in the Clinical Research Division examined the remission and survival of 432 AML patients treated at Fred Hutchinson Cancer Research Center and Seattle Cancer Care Alliance since 2006.

Similar to previous reports, frequency of MK among AML patients increased with age and was only seen in patients with other poor-prognosis cytogenetic factors. MK status further divided poor-prognosis patients into two subgroups: MK- patients who had a better outcome, and MK+ patients with a very poor outcome. However, HCT improved the outcomes of both MK-, and particularly, MK+ patients. MK+ AML patients receiving HCT at the Center had a 25 percent 4-year survival rate, compared to similar patients in another study receiving only chemotherapy with a 3 percent 4-year survival rate. Furthermore, MK+ patients with a complex karyotype, defined by three or more chromosomal abnormalities, had a much poorer outcome relative to MK+ patients without a complex karyotype. Specifically, monosomy of chromosome 5 showed a significant effect on prognosis, with a 0 percent 4-year survival rate compared to a 4-year survival ranging from 13 percent to 39 percent

for other monosomies. Overall, this study suggests that HCT is likely a beneficial treatment for poor-risk MK+ AML patients, particularly those under age 60 and without complex karyotypes. However, the poor survival rate for those older than 60 or those with complex karyotypes stresses the need for new approaches for these patients.

[Fang M, Storer B, Estey E, Othus M, Zhang L, Sandmaier BM, Appelbaum FR. 2011.](#) Outcome of patients with acute myeloid leukemia with monosomal karyotype who undergo hematopoietic cell transplantation. *Blood* 118:1490-4.

Also see: [Medeiros BC, Othus M, Fang M, Roulston D, Appelbaum FR. 2010.](#) Prognostic impact of monosomal karyotype in young adult and elderly acute myeloid leukemia: the Southwest Oncology Group (SWOG) experience. *Blood* 116:2224-8.