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In vitro correlates of low dose ara-C efficacy: clinical, cytogenetic, and bone marrow culture analysis

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Abstract

Low-dose Ara-C (10 mg/m2 subcutaneously bid) has been used as an alternative therapy for acute nonlymphocytic leukemia (ANLL) and myelodysplastic syndromes. We sought to define its therapeutic mechanism by assessing clinical and cytogenetic responses to treatment in conjunction with careful in vitro study of both morphologic and functional characteristics of bone marrow cells cultured with Ara-C. Sixteen patients (12 ANLL, four myelodysplastic syndrome) were treated. All developed pancytopenia and 11 of 12 had bone marrow hypoplasia during treatment. Four had a meaningful clinical response while five more showed in vivo leukemic cell sensitivity to low-dose Ara-C. Seven showed no response. Cells with cytogenetic abnormalities were either decreased in number or eradicated during clinical improvement. Liquid culture of marrow mononuclear cells with Ara-C (.033-.333 micrograms/ml X 7 days) produced little evidence of morphologic or functional differentiation (ten of 11 studied). No functional maturation was observed in cells from clinically responding patients. We conclude that low-dose Ara-C is modestly effective for some patients with ANLL or myelodysplasia. However, no evidence for in vivo leukemic differentiation is suggested by either in vitro culture studies or cytogenetic correlates of clinical response. In vitro marrow culture studies failed to predict clinical response to Ara-C.

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