NEW AGENT FOR LEUKEMIA AND MDS

In patients with acute myeloid leukemia (AML) or acute lymphoblastic leukemia (ALL) the overall survival and event-free survival rates are poor, despite advances in modern combination chemotherapy regimens. The use of nucleoside analogs such as azacitidine, decitabine, and cytarabine in patients with myelodysplastic syndromes (MDS) has demonstrated promising results; however, new and effective therapies are needed for patients with high-risk MDS who have a median survival of <2 years. A recent study by Kantarjian *et al*. demonstrated that the deoxycytidine analog sapacitabine is well tolerated and has antileukemic activity in patients with leukemia and MDS.

Sapacitabine is an oral prodrug of the compound CNDAC, which is an analog of decitabine that has a unique mechanism of action. The researchers carried out a phase I study to determine the dose-limiting toxic effects of sapacitabine in 47 adults with relapsed or refractory AML, ALL or MDS. Sapacitabine was given orally twice daily for 7 days or twice daily for 3 days in 2 week intervals; both regimens were repeated every 3–4 weeks. The maximum tolerated doses were 375 mg twice daily for 7 days and 425 mg twice daily for 3 days (days 1–3 and days 8–10). The recommended phase II dose was established as 425 mg orally twice daily on days 1–3 for 2 weeks or 325 mg orally twice daily on days 1, 2, 3 each weekly for 2 weeks every 3–4 weeks. The dose-limiting toxic effects were gastrointestinal.

In total, 13 of the 47 patients achieved an objective response, and four of these were complete responses. An additional 20 patients had considerable reductions in their bone marrow blasts. The researchers conclude that "The drug was well tolerated and showed encouraging antileukemic activity in the setting of poor prognosis AML and MDS."

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Original article Kantarjian, H. *et al*. Phase I clinical and pharmacokinetic study of oral sapacitabine in patients with acute leukemia and myelodysplastic syndrome. *J. Clin. Oncol.* **28**, 285–291 (2010)