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Cytosine arabinoside potentiates the apoptotic effect of bendamustine on several B- and T-cell leukemia/lymphoma cells and cell lines

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Abstract

Bendamustine and cytosine arabinoside (ara-c) are commonly used cytotoxic agents with unique mechanisms of action. We have previously reported a striking additive cytotoxic effect of the consecutive combination of bendamustine and ara-c in mantle cell lymphoma (MCL) cell lines. In the present study, cell lines of follicular lymphoma (DOHH-2), chronic lymphocytic leukemia/lymphoma (EHEB), diffuse large B-cell lymphoma (SU-DHL-4), T-cell leukemia/lymphoma (JURKAT and KARPAS-299) and MCL (JEKO-1 and GRANTA-519) were exposed to the two single drugs or the drugs combined, given simultaneously and consecutively. Peripheral blood chronic lymphocytic leukemia (CLL) B-cells from five patients were also analyzed. Apoptosis, cell proliferation/metabolic activity and mitochondrial damage were evaluated. The combination index (CI) was used to assess synergy between the drugs. Bendamustine exhibited a relevant cytotoxic effect that was dose- and time-dependent, except for SU-DHL-4 and T-cell lymphoma cells. The addition of ara-c after bendamustine significantly potentiated the single-drug cytotoxic effect of bendamustine on all cell lines, including 17p - CLL B-cells, JURKAT and SU-DHL-4, the latter presenting the highest synergism (CI < 0.01). Bendamustine and ara-c are highly synergistic on T- and B-cell lymphoma cells and cell lines, similar to MCL, overcoming resistance to the single agents.