

## **A phase I/II dose escalation trial of ONCOHIST (recombinant human histone H1.3) in patients with relapsed or refractory acute myeloid leukemia**

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**Body: Background:** Histone H1.3 suppresses tumor growth of leukemic cells in vitro, ex vivo and in animal models. To evaluate toxicity and efficacy of ONCOHIST, recombinant human histone H1.3 (rhH1.3) in patients suffering from acute myelogenous leukemia, we initiated a phase-I/II dose escalation study. **Methods:** This was an open-label unicentric phase I/II study. Nine patients suffering from relapsed or refractory acute myeloid leukemia (median age: 69 years, range 49 to 83 years) with a life expectancy of at least one month who were unable or unwilling to receive curative chemotherapy without major organ dysfunction were eligible for the trial. Exclusion criteria were presence of HIV, HBV, or HBC infection, heparin treatment during the 2 weeks before enrolment, and medical conditions known to potentially interfere with rhH1.3 treatment such as rheumatoid arthritis or SLE, as well as circulating anti-histone H1.3 antibodies. One treatment course consisted of 9 applications in 3 weeks. 3 patients were treated at each dose level. Starting dose level was 60 mg/m<sup>2</sup> and in the absence of dose-limiting toxicities, the dose was increased to the next higher dose level (392 and 628 mg/m<sup>2</sup> rhH1.3) in the third week of the treatment course. Primary endpoints of the study was the definition of the maximal tolerated dose and dose-limiting toxicities of the study drug. **Results:** To date, 9 patients have been treated and all patients are evaluable for toxicity and efficacy. No side-effects were observed except for one atrial fibrillation under infusion of rhH1.3, which was considered not to be related to the study drug. All patients completed one course of therapy (9 applications), and one responding patient received a second course without side effects. No dose-limiting toxicities were observed and the maximal tolerated dose has not been reached at 628 mg/m<sup>2</sup>. With respect to efficacy, the formal criteria of response were not met in any of the 9 patients. However, two patients had a temporary increase of their platelet counts while on therapy, and in one patient platelet counts raised from 22 000/mm<sup>3</sup> to 100 000/mm<sup>3</sup>, remaining stable for 3 months. Two patients achieved a reduction of blasts upon treatment. **Conclusion:** rhH1.3 is well tolerated at the doses treated so far. While the achieved serum levels are still below the growth-inhibiting concentrations in vitro, first clinical effects have been observed. Additional patients and higher dose levels are needed to delineate the efficacy and toxicity profile of rhH1.3 for the treatment of acute myelogenous leukemias.

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