

## **Phase I clinical trial of the *anti*-CD-33 immunotoxin HuM195/rGel.**

**Moshe Talpaz, Hagop Kantarjian, Emil Freireich, Vilma Lopez, Wehei Zhang, Jorge Cortes-Franco, David Scheinberg, Michael G. Rosenblum. UT M. D. Anderson Cancer Center, Houston, TX; Sloan Kettering Cancer Center, New York, NY.**

The immunotoxin HuM195/rGel is composed of the humanized anti-CD-33 antibody HuM195 chemically conjugated to the recombinant plant toxin gelonin (rGel). Pre-clinical studies have demonstrated that this agent is specifically cytotoxic to CD-33 expressing human tumor cells growing both in vitro and as subcutaneous xenografts in nude mice. In addition, this agent was effective in vitro against primary tumor cells obtained from 9 AML patients. A dose-escalation Phase I study was initiated at MDACC employing a 1 hr i.v. infusion of HuM195/rGel. One course consisted of 4 infusions spaced 72 hrs apart followed by a 2-week observation period. Dose levels were 10,12,18,28 and 40 mg/m<sup>2</sup>/course. Twenty-one patients have been entered thus far completing the 28 mg/m<sup>2</sup> dose level. Two patients received 2 courses of the drug. Thus far, there were no major drug-related toxicities. Fever and chills were noted during the infusion. Six of 21 patients demonstrated a reduction in peripheral blood (PB) CD-33 count. One patient (12 mg/m<sup>2</sup>) had a complete clearance of PB CD-33 cells. Evidence for a substantial reduction in PB blasts were noted in 6/21 patients. 5/6 of these responses were noted at doses at 18 mg/m<sup>2</sup> and above. In bone marrow, there was a modest(10%) reduction in CD-33 cells noted in 3 pts at 10 mg/m<sup>2</sup> and in 2 at patients at 28 mg/m<sup>2</sup>. In two patients at 28 mg/m<sup>2</sup>, there was nearly complete clearance of CD-33 positive cells from bone marrow (94% to 1% and 85% to 15%). Pharmacokinetic analysis demonstrated that the highest achieved blood levels were 200-300 ng/ml which cleared with a half-life of ~20 hrs. Only 2/20 patients (10%) developed antibodies to the rGel portion of the drug. These studies suggest that the HuM195/rGel immunotoxin appears to be safe and well-tolerated with evidence of biological activity in some patients. Dose escalation studies are continuing. Research conducted, in part, by the Clayton Foundation for Research.

Presenter: Michael G. Rosenblum

Affiliation: UT M. D. Anderson Cancer Center, Houston, TX . Email: mrosenbl@notes.mdacc.tmc.edu

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