

A PHASE I/II STUDY OF VICINIUM™ GIVEN BY INTRAVESICAL ADMINISTRATION IN PATIENTS WITH SUPERFICIAL TRANSITIONAL CELL CARCINOMA OF THE BLADDER: PHASE I FINAL RESULTS

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ABSTRACT

Introduction: Vicinium™ is a fusion protein comprised of a humanized scFv, specific for Ep-CAM (epithelial cell adhesion molecule), and a truncated fragment of *Pseudomonas* exotoxin A. Ep-CAM is highly expressed on carcinoma cells including superficial transitional cell carcinomas (TCC) of the bladder. Vicinium specifically targets and kills Ep-CAM positive tumors. Results from a Phase I/II trial where Vicinium was instilled into the bladders of patients with superficial TCC of the bladder showed the drug to be very well tolerated and showed promising clinical results.

Methods: 64 patients with Ep-CAM positive superficial TCC of the bladder, Ta, Tis or T1 Grade 2 or Grade 3, who were refractory or intolerant to BCG therapy, were entered into the study. Dosing comprised a minimum of 3 subjects per dose level through 12 escalating doses. Vicinium was given once/week for 6 consecutive weeks by intravesical administration into the bladder via a catheter at escalating dose levels of 0.1, 0.2, 0.33, 0.66, 1.32, 2.64, 5.28, 10.56, 13.73, 17.85, 23.2 and 30.16 mg/week. All toxicities were assessed according to the NCI CTC AE v3. Blood samples were collected at different times in the study to determine systemic drug exposure and to assess immunogenicity. Efficacy was explored via biopsy, cystoscopy, urine cytology and FISH.

Results: Vicinium was very well tolerated at all doses. No maximum tolerated dose (MTD) was reached. Almost all (>98%) of the patients screened were positive for the Ep-CAM antigen. Pharmacokinetic analysis showed no evidence of Vicinium in the circulation of any of the patients. Most patients, in particular at the higher doses, demonstrated a positive clinical benefit following treatment.

Conclusions: Vicinium dosed on a weekly basis for 6 weeks was very well tolerated at all dose levels. Moreover, although this study was primarily designed to evaluate safety and tolerability, Vicinium showed promising efficacy results. The early clinical benefit observed with Vicinium strongly supports its development as a promising therapy for superficial transitional cell carcinoma of the bladder.