A Phase II Study of Vicinium™ Given by Intravesical Administration In Patients with Superficial Transitional of the Bladder: Phase I Final Results

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Updated Abstract

Background: Vicinium is a factory process synthesized drug conjugate targeted against E-cadherin, which is a cell-cell adhesion molecule that is overexpressed in a majority of bladder tumors. Preclinical data demonstrated that Vicinium could be delivered intravesically and that it selectively killed tumor cells in a xenograft model in nude mice. As a result, a Phase I study was designed to evaluate the maximum tolerated dose and safety profile in patients with superficial bladder tumors. Results from a Phase I trial where Vicinium was delivered intravesically to 21 patients with superficial TCC of the bladder showed the drug to be very well tolerated and provided promising clinical activity.

Methods: At patients with E-Cadherin positive superficial TCC of the bladder, T1, Ta, T1a, or T1b tumors were eligible for this study. Eligibility was determined by a negative trans-urethral resection biopsy showing invasion of the superficial TCC tumor in the absence of invasive disease. Patients received 4 intravesical instillations of Vicinium at 4-week intervals.

Results: Vicinium was very well tolerated at all doses. No dose-limiting toxicities were observed. One patient died of disease progression 7 weeks after the last treatment. The patients received a median of 5 doses (range 1-8) and a median of 2 cycles (range 1-7). The median tumor burden was 16.2 cm2 (range 0.2-326.5 cm2) and 10 patients had stage III tumors. Two patients experienced grade 3/4 adverse events, including urinary retention in one and anemia in another. No deaths were attributed to the study drug.

Objectives

Primary
- To assess the safety and maximum measured dose of Vicinium administered in adults with E-Cadherin positive superficial transitional cell carcinoma (TCC) of the bladder.

Secondary
- To determine the efficacy of Vicinium administered to patients with superficial transitional cell carcinoma of the bladder.

Methodology

Eligibility
- Patients aged ≥18 years with histologically confirmed diagnosis of superficial transitional cell carcinoma (TCC) of the bladder.

Risk Factors at Baseline
- Increased age
- Advanced stage
- Prior history of bladder carcinoma

Pharmacokinetics
- Vicinium plasma concentration was measured using an HPLC-based assay to determine drug exposure against the UCRC of 10 ng/mL.

Summary and Conclusions:
- Vicinium was well tolerated at no dose levels in the Phase I trial, and the Phase II study will be expanded to include patients with advanced stage and invasive disease.

Participating Investigators

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Baseline Histology

- Tumor: Grade 1
- Tumor: Grade 2
- Tumor: Grade 3
- Tumor: Grade 4

Adverse Events Related to Study Drug

- Urinary retention
- Hematuria
- Pain in lower abdomen
- Dysuria
- Flank pain

Patient Baseline Characteristics (N=24)

- Age: Median 65 years (range 41-80 years)
- Sex: Female: 11, Male: 13
- Tumor stage: Ta: 10, T1: 14
- E-cadherin expression: Positive: 24, Negative: 0
- Prior treatments: None: 12, Chemotherapy: 12

Summary of Efficacy by Dose (N=24)

- Complete response: 0
- Partial response: 0
- Stable disease: 12
- Progression: 12

Summary of Overall Efficacy at Final Visit (N=24)

- Complete response: 0
- Partial response: 0
- Stable disease: 9
- Progression: 15

- No serious adverse events were observed. The most common adverse events were urinary retention, hematuria, and pain in the lower abdomen.

- Adverse events were primarily grade 1 or 2 in severity.

- No deaths were attributed to study drug.

- The trial was stopped early due to lack of efficacy in the Phase II study.