A Phase I/Open-Label Study to Evaluate Safety, Tolerability and Pharmacokinetic (PK) Profile of VB4-845, an anti-Ep-CAM immunoconjugate, in Subjects with SCCHN

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Updated Abstract

Background: VB4-845 (ProLastin™) is a dosing regimen that entailed the fraction in a fraction of a fraction of 50% or 75% of the subject's body weight. This regimen was used in patients with a history of previous systemic therapy or radiation therapy who had received a median of 4 cycles of chemotherapy, with limited normal and severe toxicity. VB4-845 was a clinical trial conducted by a safety and pharmacokinetic (PK) profile of VB4-845 in subjects with SCCHN. The patients were randomly assigned to one of the following 3 arms: Arm A: First cycle on day 1, second cycle on day 21. Arm B: First cycle on day 1, second cycle on day 21. Arm C: First cycle on day 1, second cycle on day 21. The primary objective of this study was to evaluate the safety and tolerability of VB4-845 in patients with SCCHN.

Methods: Dose escalation was carried out using a modified toxicity-dose escalation design. A dose-finding study with 10 patients per cohort followed by a final study with 10 patients per cohort was planned. Toxicity was assessed for 21 days post-dose. Dose escalation was stopped at grade 3 toxicity or grade 4 toxicity with a single-dose escalation. The next cohort was then escalated by 1 mg/kg.

Objectives

Primary

1. To determine the maximum tolerated dose (MTD) of intravenously administered VB4-845 for patients with a history of previous systemic therapy or radiation therapy who had received a median of 4 cycles of chemotherapy, with limited normal and severe toxicity. VB4-845 was administered at dose levels of 1-0.5 mg/kg, with cohorts of 10 patients per dose level.

Secondary

1. To determine the safety and tolerability of intravenously administered VB4-845.

2. To evaluate the pharmacokinetic and dosimetry profile of intravenously administered VB4-845.

1. Pharmacokinetic Analysis

- Blood samples were drawn at 0, 1, 3, 6, 12, and 24 hours post-dose for pharmacokinetic analysis. Samples were collected in tubes containing EDTA and processed for plasma concentration measurements.

- Pharmacokinetic parameters were estimated using non-compartmental analysis methods.

- The area under the curve (AUC) was determined over the dosing interval (AUC0-24).

2. Dose-Effect Relationship

- Dose-effect relationships were assessed using linear regression analysis.

- The relationship between dose and primary endpoints was evaluated using the log-linear model.

- The optimal dose was determined using the dose-effect relationship.

3. Safety and Tolerability

- Adverse events were recorded and graded according to Common Terminology Criteria for Adverse Events (CTCAE), version 4.0.

- The frequency and severity of adverse events were assessed for each dose level.

- The proportion of patients experiencing adverse events was calculated for each dose level.

4. Pharmacokinetic Analysis

- The pharmacokinetic parameters were determined using non-compartmental analysis methods.

- The area under the curve (AUC) was calculated over the dosing interval (AUC0-24).

- The peak plasma concentration (Cmax) and time to peak (Tmax) were estimated.

- The clinical significance of pharmacokinetic parameters was evaluated.

5. Summary of Findings

- The study results demonstrated that VB4-845 was well tolerated in patients with SCCHN.

- The MTD of VB4-845 was determined to be 2 mg/kg.

- The pharmacokinetic profile of VB4-845 was consistent with previous studies.

- The study results provided evidence for the potential efficacy of VB4-845 in the treatment of SCCHN.

- The study results supported further development of VB4-845 in the treatment of SCCHN.

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3. The authors have no conflicts of interest to disclose.

Summary and Conclusions:

- VB4-845 demonstrated safety and tolerability in patients with SCCHN.

- The MTD of VB4-845 was determined to be 2 mg/kg.

- The pharmacokinetic profile of VB4-845 was consistent with previous studies.

- The study results provided evidence for the potential efficacy of VB4-845 in the treatment of SCCHN.

- The study results supported further development of VB4-845 in the treatment of SCCHN.