A Phase I Study of VB4-845 in Patients with Advanced, Recurrent Head and Neck Cancer on a Weekly Dosing

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Background: VB4-845 (Provincial-1) is a monoclonal protein engineered from the TNF-α-1 (Therapeutic alpha factor) antibody head that has excellent subunit antibody levels and is approved for treatment of an intracellular cytokine of origin, with MHC-1 restricted to a large number of different cytokines and chemokines. A phase I/IIa trial was conducted to evaluate the safety, pharmacology, pharmacokinetics (PK) and efficacy of VB4-845 in patients with advanced Head and Neck Cancers (HNC) and recurrent Head and Neck Cancers (R-HNC).

Methods: 40 patients were enrolled using a modified 3+3 dose escalation scheme with a minimum of 3 patients enrolled per dose level. The patients met the following eligibility criteria: Eastern Cooperative Oncology Group (ECOG) performance status 0-2, age ≥18 years, and at least 1 lesion ≥1 cm in diameter. All patients received 4 doses at 21 day intervals. The dose levels were: 100 mg/m2, 150 mg/m2, 200 mg/m2, and 400 mg/m2. Complete blood counts, biochemistry, and urinalysis were performed at baseline and every 2 weeks during treatment. A safety and efficacy analysis was performed on all evaluable patients.

Results: A total of 42 patients were enrolled into the study. 35 patients received at least one dose of VB4-845, of whom 28 patients had evaluable data. Of the 35 patients, 25 patients were evaluable for safety analysis and 23 patients were evaluable for efficacy analysis. The most common adverse event was fatigue, occurring in 19% of patients. A total of 4 patients (11%) experienced a partial response, while 6 patients (17%) had stable disease. The most common adverse events were fatigue, rash, and decreased appetite. No serious adverse events were reported.

Objective: To determine the safety, tolerability, and clinical activity of VB4-845 in patients with advanced and recurrent head and neck cancer.

Objectives:
- To determine the safety, tolerability, and clinical activity of VB4-845 in patients with advanced and recurrent head and neck cancer.
- To evaluate the pharmacokinetics profile of the intravenously injected VB4-845.
- To evaluate the pharmacodynamic profile of VB4-845 in patients with advanced and recurrent head and neck cancer.

Stability:
- VB4-845 is stable for up to 28 days at room temperature and is stable for up to 12 months at 2-8°C.

Baseline:
- Baseline assessments included complete blood counts, serum chemistry, and urinalysis.

Pharmacokinetics:
- VB4-845 is a monoclonal protein that is administered intravenously at a dose of 200 mg/m2.

Patient Characteristics (NHNC):
- Age: 18-75 years, ECOG performance status 0-2, at least 1 lesion ≥1 cm in diameter.
- Exclusion criteria: Prior treatment with an anti-cancer agent, prior corticosteroids, or prior immunosuppressants.

Adverse Events Related to Study Drug:
- Fatigue, rash, decreased appetite, nausea, vomiting, and diarrhea.

Summary and Conclusions:
- VB4-845 is well tolerated at the dose level of 200 mg/m2. The most common adverse events were fatigue and rash, which were all grade 1 to 2.
- The study demonstrated the safety and feasibility of VB4-845 in patients with advanced and recurrent head and neck cancer.
- Further studies are warranted to evaluate the efficacy of VB4-845 in this patient population.