Tocagen, Inc.

A Phase 1b Study of Toca 511, a Retroviral Replicating Vector, Followed by Toca FC in Patients With Advanced Cancer

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BACKGROUND

Toca 511 (bosonavir amagertropism) is an investigational, conditionally lytic, retroviral replicating vector (RRV). With selectively infecting cancer cells due to the presence of defects in innate and adaptive immune responses that support viral replication, and the RRV's requirement for cell division for virus integration into the genome.

Based on preclinical data, S-Tau kills infected dividing cancer cells and diffuses and kills surrounding cancer cells, myeloid derived suppressor cells (MDSCs), and tumor associated macrophages. Thus, treatment with Toca 511 & Toca FC activates the immune system against cancer with treatment cell killing in S-Tau, which promotes local immunostimulation, and by killing immunosuppressive myeloid cells in the tumor microenvironment. Together, these events promote T-cell infiltration into the tumor microenvironment and prime an antitumor immune response (Figure 2).1,2

CLINICAL STUDIES IN RECURRENT HIGH GRADE GLIOMA

Toca 511 & Toca FC treatment has been evaluated in three Phase 1, ascending dose studies in 127 patients with recurrent high grade glioma (HGG). Each evaluating a different method of delivery of Toca 511. Data from a study in which Toca 511 was injected into resection cavity with following injection of 1 (E) durable complete responses, with a median followup of 30 months.2 (3) responses were observed in both HGG (1) and multiform tumors (although there may be an enrichment of responses in HGG 1st mutated tumors), and 1 prolonged survival relative to historic benchmarks. A randomized Phase 3 trial of Toca 511 & Toca FC (NCT01434160) in patients with recurrent HGG currently is underway.

In a study in which Toca 511 was injected intravascularly (IV) to patients with recurrent HGG for 1, 3, or 5 consecutive days, CD protein was expressed in tumors that were subsequently resected. The highest level of CD protein expression was observed following 3 days of IV injection.

PRECLINICAL MODELS OF METASTATIC COLORECTAL CANCER

Extending development beyond HGG, we first showed the RVG-FIT (green fluorescent protein) can reach, productively infect, and spread in tumor in a mouse colorectal liver metastasis model, while no off-target infection was observed (Figure 3).4

STUDY OBJECTIVES

Primary

- To evaluate changes in immune activity following treatment with Toca 511 & Toca FC in patients with solid tumors

Secondary

- Safety and tolerability
- Vector deposition in tumor specimens following IV Toca 511
- Clinical activity of Toca 511 & Toca FC, alone or in combination with standard of care therapies

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RESULTS

Enrollment into the study is ongoing. As of the cut-off date for analysis (27 March 2018), 7 patients were enrolled into the study across 3 study sites:
- University of Miami
- MD Anderson Cancer Center
- Sarah Cannon Research Institute

Analyses include vector deposition in tumor tissues, viral clearance from plasma, and adverse events; immune activity and response data are not yet available for this study. Demographic and baseline characteristics data are summarized in Table 2.

CONCLUSIONS

Based on limited experience to date in this ongoing study of patients with advanced solid tumors, treatment-related adverse events were reported for 4 (57%) patients (Table 3). Although not considered related to treatment, treatment-related adverse events were reported for 4 (57%) patients (Table 3). Treatment-related adverse events limited to 1007 days following IV delivery of Toca 511 & Toca FC in patients with advanced solid tumors. IV administration of Toca 511 was associated with expression of viral protein in metastatic sites of disease in 5 of 5 patients, including liver metastases from 4 of 4 patients with colorectal cancer.

REFERENCES