BACKGROUND

CHECKPOINT INHIBITORS

- Checkpoint inhibition by mAbs against PD-1 or CTLA-4, and other immunohistochemical inhibitors, has resulted in significant treatment responses.

- However, current checkpoint inhibitor targeted T cells that are differentiating towards effector CD8+ T cells.

- Immunotherapies that act earlier by enhancing CD8+ T cell activation have the potential to improve and broaden T cell responses. (Figure 1: Early Mechanism of Action).

- There remains a need to produce novel cancer treatments, alone or in combination, that:
  - Enhance and broaden T cell responses to various cancers;
  - Increase and broaden T cell responses to various cancers;
  - Offer potential for “off-target” adverse events; and
  - Provide more potent and prolonged T cell responses.

GLYCOPROTEIN D (gD) – A NOVEL EARLY CHECKPOINT MODIFIER (CPM)

- Herpes simplex virus type 1 gD, when genetically expressed as a fusion protein with HPV-16 proteins 2, 5, 6, and 7, demonstrated:
  - In a fast-growing tumor cell challenge model, the addition of the CPM of early T cell activation, gD, when fused to HPV-16 proteins 2, 5, 6, and 7, demonstrated: T cell responses.

- The presence of a secretion inhibitor, followed by surface staining for T cell markers and T cell activation, gD, when fused to HPV-16 T cell epitopes, which are more resistant to exhaustion.

- Safety profile: Low risk for "off-target" adverse events; gD is only expressed locally at the injection site and in regional draining lymph nodes.

- Checkpoint inhibition combination data: Preclinical studies have shown improved efficacy using gD-based immunotherapies plus anti-PD-1 mAbs.

RESULTS

- AdC6-gDE7652-vaccinated mice that cleared their tumors (n=10) remained tumor-free upon high-dose TC-1 rechallenge.

- A Phase 1B study in infectious disease using gD is currently enrolling.

- No vector (control; naïve) 25/25 (100%) mice cleared their tumors, remained tumor-free; all were alive at study end vs gD challenge models were controlled by:

- Regulating T cell Activation

IMMUNOLOGIC ASSESSMENTS

- Immunogenicity evaluations:
  - Complete Protection Against Complete Tumor Loss
gD-CPM (AdC6-gDE7652) Resulted
  - Complete Tumor Loss

- gD-CPM (AdC6-gDE7652) Needed for Tumor Regression and Sustained Tumor Loss

- Immunologic Assessments

PURPOSE

- To report the immunogenicity and efficacy of gD-CPM immunotherapy in a highly malignant, fast-growing tumor cell line, establishing a chimpanzee adenoviral vector (AdC6)-based tumor model for assessing the efficacy of novel immunotherapies.

- The day 0 tumor cell inoculum was 5.0x10⁴ TC-1 cells (SD).

- Mice were challenged with 2500 TC-1 cells at Day 0.

- Tumor volume (mean, mm³) was monitored from Day 3 to Day 176 for Standard-dose TC-1 challenge

- Survival Time

- Time (days) after challenge

EQUIPPED ASSESSMENTS

- TC-1 Challenge Model

CONCLUSIONS

- In a fast-growing tumor cell challenge model, the addition of the CPM of early T cell activation, gD, when genetically expressed as a fusion protein, resulted in significant tumor regressions and tumor loss in all mice (n=10).

- Markedly improved immunogenicity (<10-8-fold).

- Enhanced tumor control, with improved progression-free survival; against TC-1 rechallenge.

- Checkpoint inhibition in combination with specific T cells within spleens and tumors with polyfunctional activity and lower levels of exhaustion marker expression.

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DISCLOSURES

Dr. Currie is COO, Virion Therapeutics, LLC and owns shares in the company. She has other conflicts to report.