Toca 511 and Toca FC selectively destroys cancer cells within the body, while leaving healthy cells unharmed.

5-FC (Toca FC) results in formation of 5-FU within infected tumor cells expressing CD2. 5-FU kills cancer cells and selectively infects and spreads in tumor cells. Subsequent oral administration of investigational extended-release 5-FU has a very short half-life so systemic toxicity is not observed

Proposed MOA: Tumor Infiltrating T Lymphocytes

- Responses occurred gradually over time ~ 6-19 months, consistent with immunologic response
- Each CR occurred in a different clinical site
- Completed Response
- Partial Response
- SD
- CR
- PR
- SD
- PR
- SD

Conclusions

- Both murine and human data support the proposed immunotherapeutic mechanism of Toca 511 and Toca FC therapy
- Potential predictive markers from both blood and tumor sampling have been identified (serum cytokine and immune cell infiltration)
- MOA is different from other immunotherapeutics like checkpoint inhibitors which appear to do better in tumor infiltrating non-T immune cells in patient tumors between complete responders and those with progressive disease. (Right) Kaplan-Meier plot. “LO” are patients whose tumors had low levels of certain non T immune cells while “H” had high levels of the non-T immune cells

References:
5.  Cloughesy TF. et. al. Phase 1 trial of vocimagene amiretrorepvec and 5-fluorocytosine for recurrent high-grade glioma. Sci Transl Med. 2016 Jun 1;8(341) p. 930-939
19(7): 918-929

RNA Sequencing was perfonned on 1 to 3 spatially distinct pieces of tumor from each patient depending on availability. Transcript profiles were analyzed using Cibersort analytical tool to quantitate frequency of 23 non-malignant cell types within each sample. (Left) Significant difference in tumor-infiltrating non-T immune cells in patient tumors between complete responders and those with progressive disease. (Right) Kaplan-Meier plot. “LO” are patients whose tumors had low levels of certain non-T immune cells while “H” had high levels of the non-T immune cells

Cytokines putatively associated with patient outcomes identified by multivariate analysis

(Wilcoxon rank sum test p-value displayed)

Toca 5 Pivotal Phase 3 Trial Ongoing

Primary Endpoints: Overall Survival
Secondary Endpoints: Include Durable Response Rate

Immune profile of tumor microenvironment helps predict response in patients treated with an investigational immunotherapeutic consisting of a retroviral replicating vector (Toca 511) and an extended-release formulation of 5-fluorocytosine (Toca FC)

Derek Ostertag, PhD, William Accomando, PhD, Leah Mitchell, PhD, Maria Rodriguez-Aguirre, Daniel Hogan, PhD, Oscar Diago, Dawn Gammon, Ali Highgahi, Harry Gruber, MD, Jolene Shorr, Asha Das, MD and Douglas Jolly, PhD

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Clinical Results

Phase 1 Ascending Dose Trial of Safety & Tolerability of Toca 511 & Toca FC in HGG: Toca 511 Administered into the Resection Cavity Wall After Tumor Removal

A Positive Association of Durable Response with Overall Survival: Best Response & Survival Post Progression

High DNA Mutation Frequency Not Associated with Response or Survival

Responders showed increased Tumor-Infiltrating T Lymphocytes in the Tumor-Pretreatment

Toca 511 & Toca FC Activates Durable Immune Response Against Tumor Only in Immune Competent Mice, Activating a Durable T Cell Mediated Immune Response

Surgery

Adjuvant Therapies

Chemotherapy (temozolomide) or bevacizumab

**Chemotherapy with or without [bevacizumab]

Conclusions

- Both murine and human data support the proposed immunotherapeutic mechanism of Toca 511 and Toca FC therapy
- Potential predictive markers from both blood and tumor sampling have been identified (serum cytokine and immune cell infiltration)
- MOA is different from other immunotherapeutics like checkpoint inhibitors which appear to do better in tumor with high mutational burden
- Immunotherapeutic mechanism of Toca 511 and Toca FC activity continues to be corroborated and is actively being investigated in an ongoing phase 3 trial (NCT02414165)

References:
6. Cloughesy, T. F. Toca 511 clinical trial of oncolytic adenovirus and 5-fluorocytosine for recurrent high-grade glioma. Sci Transl Med. 2016. 8(341)