Toca 511 (oxecamine amiretrorepvec) is an investigational, conditionally lytic, retroviral replicon that activates the immune system selectively against the tumor.* Produces CD to convert 5-FC (5-fluorocytosine) into the anticancer drug 5-FU (5-fluorouracil) Buds off from but does not lyse infected cells directly Toca 511 infection was sufficient to increase survival. This model, Toca 511 infection was sufficient to increase survival. Toca 511 and 5-FC treatment activated anti-tumor immune response. The tumor rejection responses were against endogenous tumor antigens released by Toca 511 and 5-FC. Induced cell killing, not the virus, as the long-term survivors were re-challenged with non-infected, parental Toca511 cells (Yagi et al., 2017). Animals that survived for 60 days without further treatment beyond the 4th 5-FU cycle (from Fig. 4B) were re-challenged with non-infected, parental Toca511 cells (Yagi et al., 2017). Value symbols were used as a control to monitor tumor growth and survival.

**Conclusions**

**In vivo:**
- Toca 511 presence followed by four courses of 5-FU significantly reduced tumor burden and prolonged survival compared to PBS treatment in a Toca 511 dose-dependent manner.
- In this model, 10% Toca 511 infection was sufficient to increase survival.

**Toca 511 and 5-FC treatment activated anti-tumor immune response.** The tumor rejection responses were against endogenous tumor antigens released by Toca 511 and 5-FC. Induced cell killing, not the virus, as the long-term survivors were re-challenged with non-infected, parental Toca511 cells (Yagi et al., 2017). Animals that survived for 60 days without further treatment beyond the 4th 5-FU cycle (from Fig. 4B) were re-challenged with non-infected, parental Toca511 cells (Yagi et al., 2017). Animals that survived for 60 days without further treatment beyond the 4th 5-FU cycle (from Fig. 4B) were re-challenged with non-infected, parental Toca511 cells (Yagi et al., 2017). Value symbols were used as a control to monitor tumor growth and survival.

**In vitro:**
- Reduction in myeloid-suppressor cells (MDSCs)
- Increase in CD4 T helper cells in a dose-dependent manner
- In this model, GFP expressing cells which cannot be infected, still get kill after Toca511 cells are killed

**Toca 511 & S-FC: ANTI-TUMOR ACTIVITY, IMMUNE MEMORY AND PROLONGED SURVIVAL EVEN AT LOW INFECTION LEVELS**

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**Abstract #123**

**Toca 511 (oxecamine amiretrorepvec) is an investigational, conditionally lytic, retroviral replicating vector (RRV). The vector selectively infects cancer cells because productive infection is dependent on cell division, and viral replication is enabled in tumors by the immune suppressed microenvironment.** A recent study has been published after treatment of High Grade Glioma patients with Toca 511 and Toca FC, supporting an immune mechanism; and 2) it is currently uncertain what percent of, or total number of cancer cells infections leads to benefit. To understand better how much transduction is sufficient to generate a useful anti-tumor response, we have developed a novel animal model. To avoid the use of exogenous drugs which could distort outcomes, we biologically blocked the infectious spread of Toca 511 in tumors at various defined levels, then evaluated survival and generation of anti-tumor immunity. Data suggest that even a small percent of infection shows meaningful and durable benefit.

**Introduction**

**Background: Toca 511 & Toca FC**

Toca 511 is a retroviral replicating vector (RRV) expressing a cytomegalovirus (CMV) gene which:
- Selectively infects cancer cells
- Buds off from but does not lyse infected cells directly
- Produces CMV to convert S-FC (5-fluorocytosine) to the anticancer drug S-FC (5-fluorouracil) or
- Activates the immune system selectively against the tumor

* (Ostertag et al., 2012; Yagiz et al., 2016; Mitchell et al., 2017)

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**Methods and Results**

**Maintenance of Superinfection to Superinfection**

**Bystander Effect of S-FC Following Toca 511 and S-FC Treatment**

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**Results**

**Glioma Cells by Toca 511 and 5-FC**

**Anti-tumor Immune Response Following Toca 511 and 5-FC Treatment**

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**Conclusions**

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