Liminatus Pharma LLC

GCC Cancer Vaccine

Pre-Clinical Study

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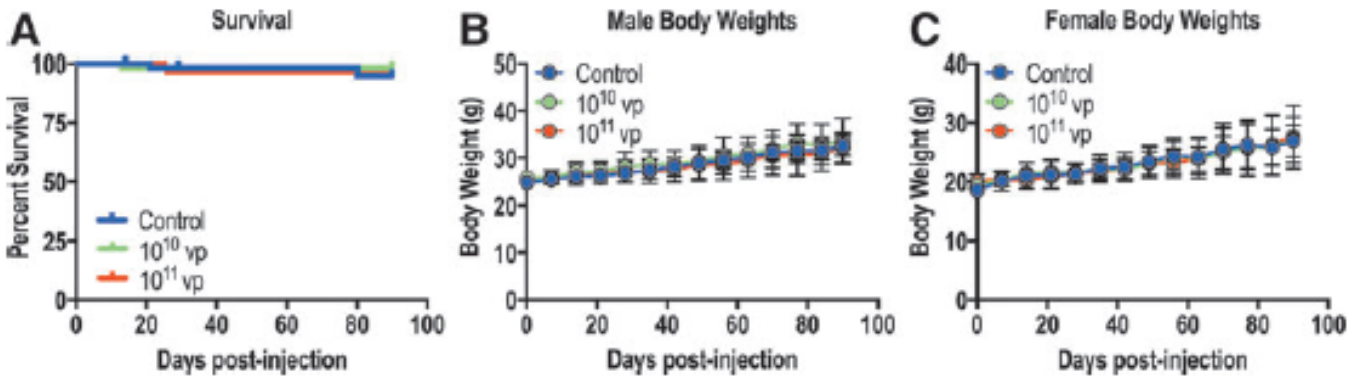
We have completed a Pre-clinical study of first-generation GCC Cancer Vaccine (adenovirus serotype 5 vaccine expressing GCC and the PADRE T-helper epitope), and below are the results that characterized the biodistribution, immunogenicity, and safety of that vector which supported advancing this vaccine into clinical trials in colorectal cancer patients.

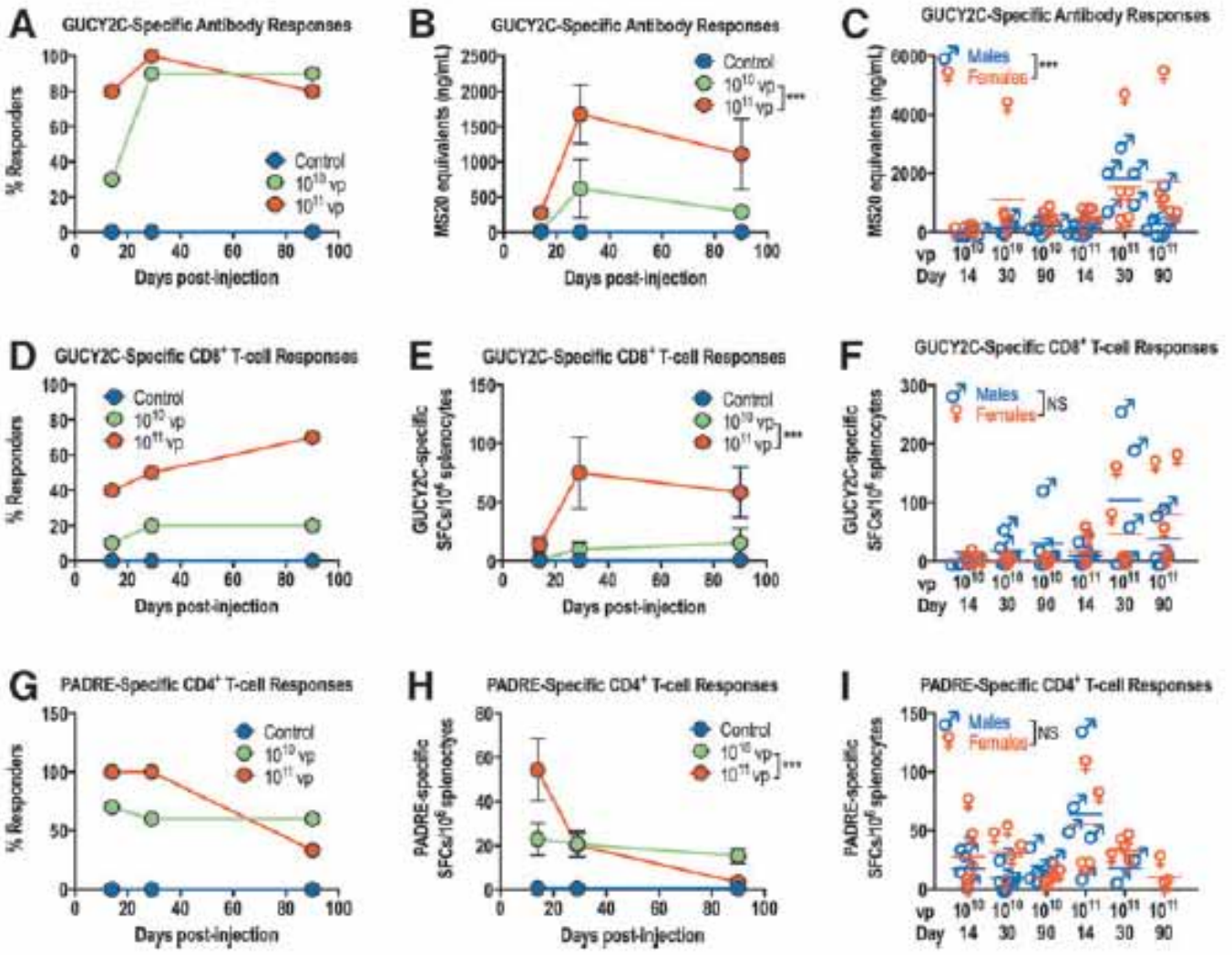
Ad5-GUCY2C-PADRE levels were highest in the injection site and distributed in vivo primarily to draining lymph nodes, the liver, spleen and, unexpectedly, to the bone marrow. Immune responses following Ad5-GUCY2C-PADRE administration were characterized by PADRE-specific CD4+ T-cell and GUCY2C-specific B-cell and CD8+ T-cell responses, producing antitumor immunity targeting GUCY2C expressing colorectal cancer metastases in the lungs, without acute or chronic autoimmune or other toxicities. Collectively, these data support Ad5-GUCY2C-PADRE as a safe and effective vaccination strategy in preclinical models and positioned Ad5-GUCY2C-PADRE for Phase I clinical testing in colorectal cancer patients.



Ad5-GUCY2C-PADRE Toxicity

C57BL/6 mice received vehicle control or a single intramuscular injection of Ad5-GUCY2C-PADRE at 10^{10} or 10^{11} vp. In the absence of any Ad5-GUCY2C-PADRE toxicity in C57BL/6 animal models, including the bone marrow, spleen, liver, and injection site, the extensive body of animal and human experience with adenovirus as a vector for vaccine delivery, and the 3,600 × lower dose to be applied to humans, Ad5-GUCY2C-PADRE is expected to have no toxicity in humans (Hum Gene Ther Methods. 2016 Dec; 27 (6):238-250).

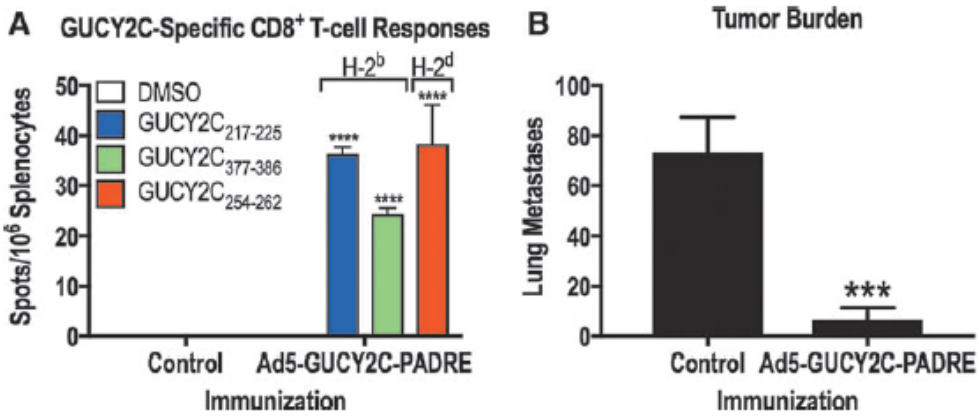
GCC Cancer Vaccine
Pre-Clinical Study



Ad5-GUCY2C-PADRE Immunogenicity

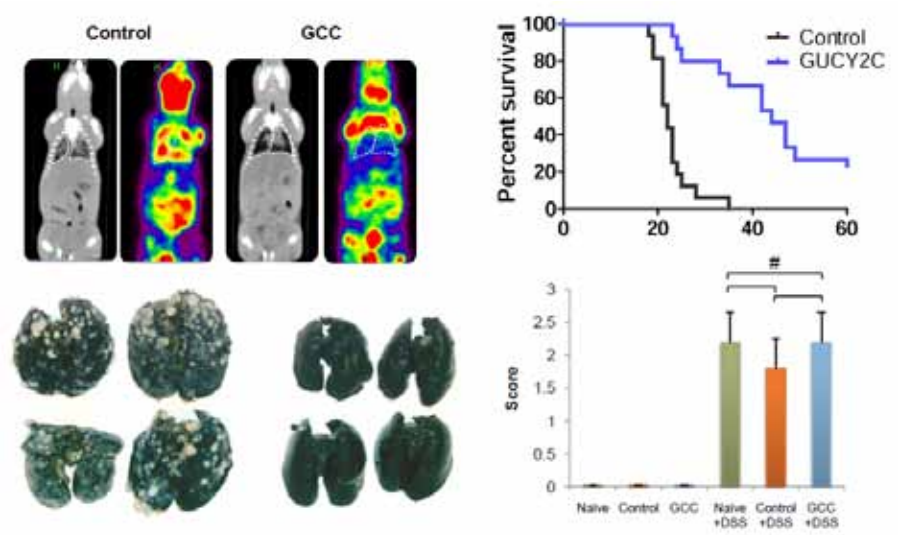
C57BL/6 mice were immunized intramuscularly with 10^{10} or 10^{11} vp Ad5-GUCY2C-PADRE or vehicle control. Serum and spleens were collected 14, 30, or 90 days later and subjected to GUCY2C enzyme-linked immune sorbent assay (ELISA) and IFN-γ ELISpot, respectively. Immune responses following Ad5-GUCY2C-PADRE administration were characterized by PADRE-specific CD4+ T-cell, GUCY2C-specific B-cell and CD8+ T-cell responses; and comparison of the three immune responses measured in each mouse revealed that GUCY2C-specific T-cell responses were slightly better predictor of GUCY2C-specific antibody responses than PADRE specific T-cell responses (Hum Gene Ther Methods. 2016 Dec; 27 (6):238-250).

GCC Cancer Vaccine
Pre-Clinical Study



Ad5-GUCY2C-PADRE Antitumor Efficacy

CB6F1/J mice were immunized with 10^{11} vp of Ad5-GUCY2C-PADRE intramuscularly or with Ad5-Control-PADRE. T-cell responses were quantified 14 days later by interferon gamma (IFN-γ) enzyme-linked immunospot (ELISpot). Importantly, these mice produced antitumor immunity against GUCY2C-expressing CT26 cells following Ad5-GUCY2C-PADRE immunization, confirming the antitumor efficacy of the Ad5-GUCY2C-PADRE vector (Hum Gene Ther Methods. 2016 Dec; 27 (6):238-250).



GCC Vaccine Has Therapeutic Efficacy without Toxicities

The preclinical study results revealed that the first-generation GCC Cancer Vaccine-administered group (GCC) prevented the development of metastatic colorectal tumors in lungs, compared to control group. The cohort receiving the GCC Cancer Vaccine (GUCY2C) exhibited a higher survival rate compared to control group, and as high as 30% of the group were cured of metastatic cancer. In addition, neither inflammatory bowel disease nor intestinal disorder occurred in cohorts receiving the GCC Cancer Vaccine.