Background VerImmune is developing a novel immune-oncology therapeutic approach known as ‘Anti-tumor Immune Redirection’ (AIR). This approach leverages pre-existing CD8+ T-cell immune memory acquired from controlling past human cytomegalovirus (HCMV) infections. These HCMV specific memory CD8+ T-cells are re-directed by VerImmune’s lead product, VERI-101, to attack tumors for destruction. VERI-101 consists of VerImmune’s proprietary platform technology known as ViPs (Virus-inspired Particles). ViPs are based on a modified mouse papillomavirus capsid protein of which 60 copies self-assemble into a 20–30nm T=1 icosahedral structure. To utilize these ViPs for AIR, the ViPs are then conjugated on their surface with a CD8+ T cell viral peptide antigen. In the case of VERI-101, the ViP is conjugated with an HLA-A*0201 restricted peptide epitope (NLVPMVATV, [NLV]), derived from the CMV pp65 antigen with an upstream furin protease cleavage site.

Methods and Results VERI-101 has a three-step mechanism of action. Briefly, (1) VERI-101 targets the surface of the tumor cells and (2) enables the presentation of the CMV viral epitopes on their surface MHC, together (3) stimulating a recall of the pre-existing CMV memory response to attack the cancer cells. We have demonstrated each step of this MOA for VERI-101. We show that VERI-101 binds to an array of human cancer cells but not cells defective in proteoglycan synthesis, indicating a requirement for HSPGs on the tumor cell surface. For the second step, we demonstrate loading of the CMV peptide of VERI-101 on tumor cells using a soluble T-cell receptor-like antibody that specifically recognizes the NLV-CMV peptide-MHC-I complex. For the third and final step, utilizing an in vitro cytotoxicity co-culture immuno-assay system, we showed specific immune redirection of human donor CMV CD8+ T-cell cytotoxicity against several human tumor cell lines incubated with VERI-101, but not with unconjugated ViP controls. To further demonstrate the biological proof of concept for VERI-101, we showed that an MCMV AIR-ViP (VERI-003, used as a surrogate as HCMV does not infect mice) administered either as a monotherapy or in combination with anti-PD-1 to MC38 tumor bearing mice with pre-existing MCMV immunity led to statistically significant reductions in tumor growth and in certain cases, complete regression of tumors compared to untreated controls.

Conclusions In conclusion, our results demonstrate the tumor antigen-agnostic therapeutic potential of AIR and VERI-101 as novel class of immuno-therapeutic drugs known as Virus-inspired Drug Conjugates (ViDCs) that could be used either as a monotherapy or in combination with checkpoint inhibitors.

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