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-inspiredParticles). 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.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.1349