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Advancing anti-ROR1 CAR-T cells employing a cirmtuzumab based T-cell CAR to eradicate lethal castration resistant ROR1^{pos} prostate cancer.

Background:
One in six men will be diagnosed with prostate cancer (PCa), making it one of the leading health problems affecting men. The main treatment for advanced prostate cancer (PCa) affecting up to one quarter of PCa patients is androgen deprivation therapy (ADT) which targets androgen receptor (AR) signaling. These patients, however, inevitably become resistant to ADT and develop lethal castration resistant prostate cancer. A particularly malignant form of CRPC called neuroendocrine prostate cancer (NEPC), is emerging with increasing frequency in patients treated with ADT.

Methods:
Cirmtuzumab-based T-cell CAR was generated to target treatment resistant ROR1^{pos} cancers. To test and demonstrate the activity of this CAR product, a series of 2nd generation T-cell CAR constructs were produced that when transduced into human T-cells demonstrated highly potent and specific anti-tumoral activity and specificity in *in vitro* and *in vivo* test systems of hematological and human solid tumor cancers. LDH cytotoxicity and Incucyte assays were performed using various effector to target ratios (E:T) of ROR1 CAR-T cells against ROR1 positive NEPC prostate cancer cell lines.

Results: Anti-ROR1 T-cell CAR is highly potent in targeting and killing ROR1 expressing NEPC cell lines even at low effector to target (E:T) ratios when compared to mock transduced control T cells in Incucyte assay and LDH release assay.

Conclusion: The highly potent, prolonged and specific activities we observe with the cirmtuzumab-based anti-ROR1 T-cell CARS encourage the advancement of this product into human clinical studies.