



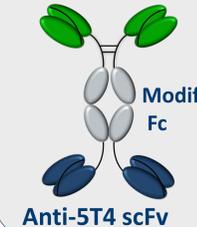
Introduction

- 4-1BB (CD137) is an activation-induced costimulatory immune receptor expressed on tumor-infiltrating T cells and NK cells
- Stimulation of 4-1BB leads to enhanced proliferation, increased survival, intensified cytolytic activity, and induced IFN- γ production of T and NK cells
- 4-1BB-targeting immunotherapies have shown promising anti-tumor effects clinically however, a monospecific 4-1BB agonist (urelumab) induced dose-limiting hepatic toxicities
- 5T4 is a tumor-associated antigen expressed in a variety of malignancies, including NSCLC, head and neck, mesothelioma, renal, pancreas, bladder, breast, colorectal, gastric, ovarian and cervical cancers

About ALG.APV-527

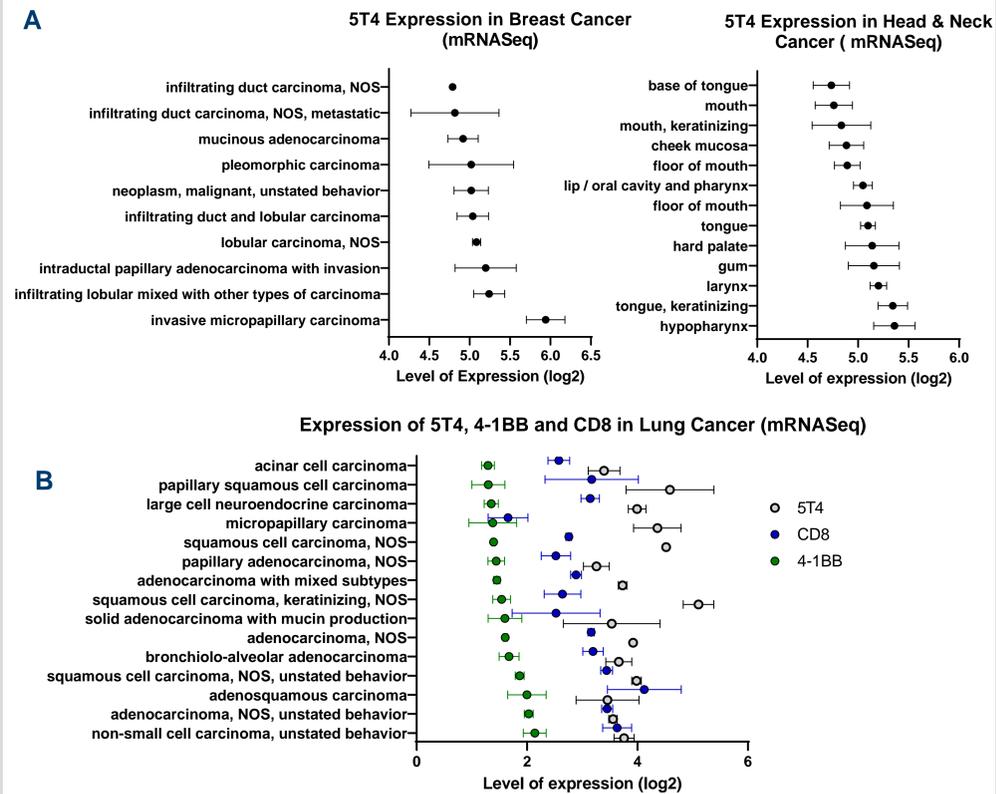
- ALG.APV-527 is a bispecific antibody therapeutic containing two sets of scFv binding domains targeting 5T4 and 4-1BB which are linked to an effector-null Ig Fc domain, providing an antibody-like *in vivo* half-life
- The scFvs originate from the Alligator Gold® human scFv library
- Each scFv has been optimized for use in the bispecific ADAPTIR™ format
- ALG.APV-527 features target-driven T cell stimulation, optimized stability, good manufacturing properties with potential for better risk-benefit in humans than monospecific 4-1BB antibodies
- ALG.APV-527 is cross-reactive to 4-1BB and 5T4 from cynomolgus monkey and can enhance stimulation of CD3-activated human and cynomolgus T cells *in vitro*

Anti-4-1BB scFv



Anti-5T4 scFv

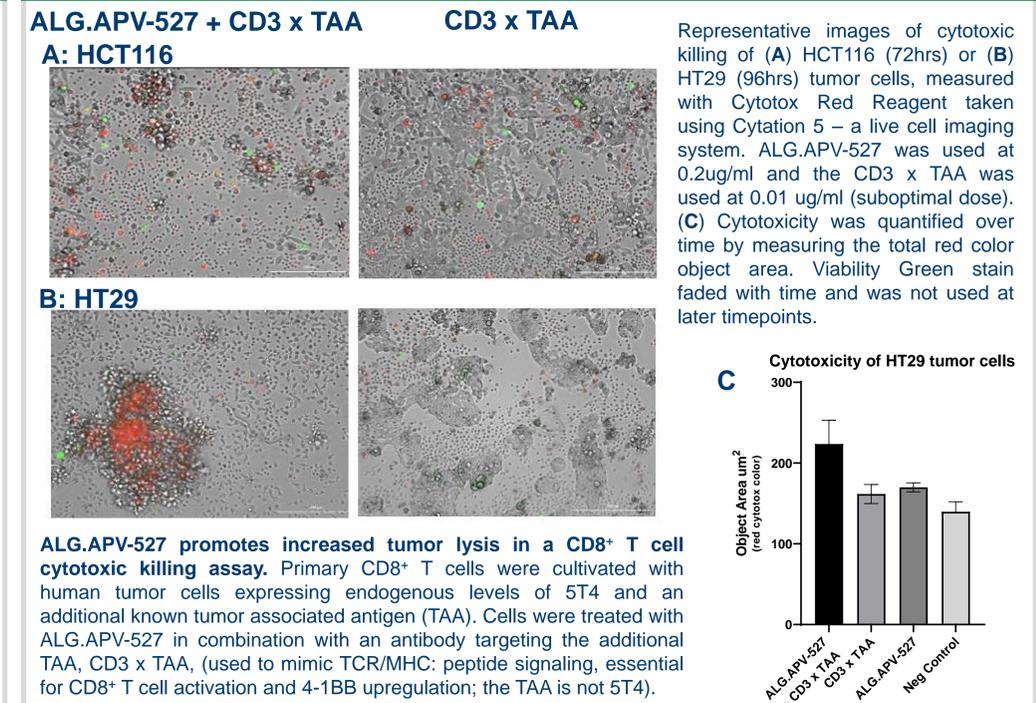
Evaluation of 5T4, 4-1BB & CD8 co-expression



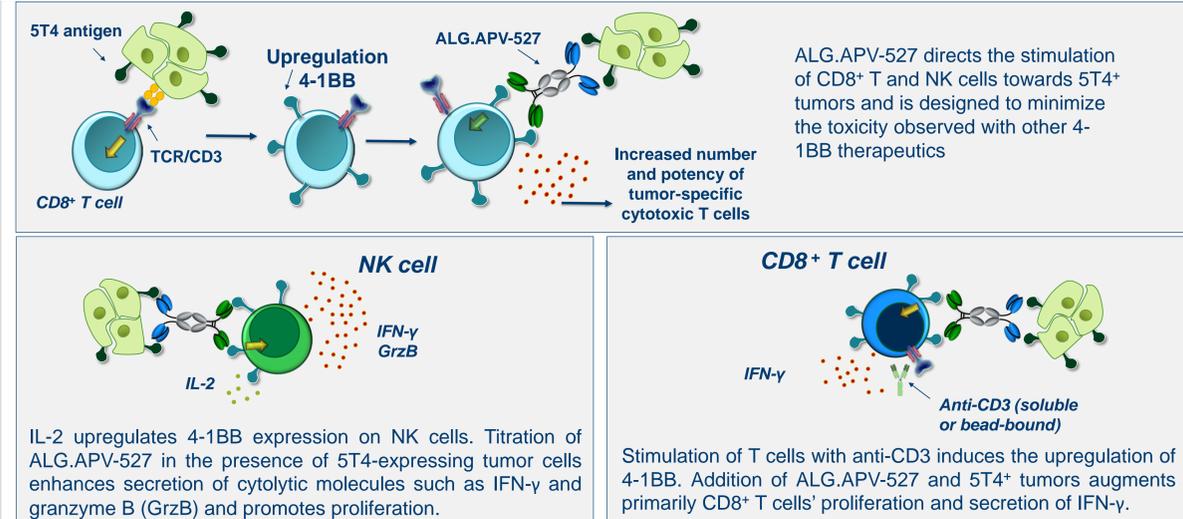
- Primary Conclusions:**
- 5T4 was found to be co-expressed with CD8 expression (infiltration) across a range of solid tumor indications.
 - Co-expression of 5T4 and 4-1BB was highest in lung tumors, head and neck tumors (oral cavity and pharyngeal tumors), sarcomas, mesotheliomas, and in some breast tumors.
 - 5T4 expression was detected in neoplasms of the oral cavity and pharynx, respiratory system neoplasms, sarcomas and mesotheliomas and finally in breast and cervical cancer. Lowest expression was detected in neoplasms of the lower digestive tract, melanomas and brain tumors.
 - Together, these observations suggest a broad range of solid tumors to be optimal for treatment by ALG.APV-527 as they present potential microenvironment rich in CD8 infiltration, active 4-1BB stimulation and abundance of the 5T4 target.

Co-expression of 5T4, 4-1BB & CD8 in solid tumors and in the tumor microenvironment. Expression analyses of the three genes were performed by Nebion using curated and QC compendia of tumor mRNA-seq data and GENEVESTIGATOR tools. Bulk tumor samples and single-cell tumor-derived cells were evaluated. (A) Expression of 5T4 in mRNASeq data from Breast or Head and Neck Cancer patients. (B) Expression of 5T4, 4-1BB and CD8 in mRNASeq data from Lung Cancer patients.

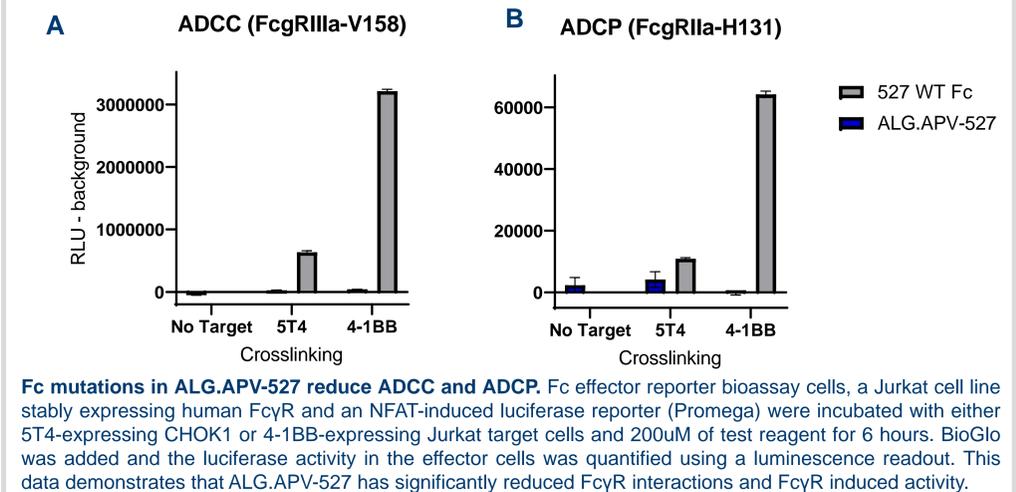
ALG.APV-527 enhances tumor cell killing



ALG.APV-527 Mode of Action



Fc mutations in ALG.APV-527 reduce Fc γ R interactions and functional activity



Summary and Conclusions

- 5T4 and 4-1BB targets are co-expressed in a variety of solid tumor indications
- ALG.APV-527 augments CD3-activated CD8⁺ T cell killing of tumors cells in a 5T4-dependent manner
- ALG.APV-527 is designed with Fc mutations that reduce ADCC and ADCP activity thereby reducing the risk of T cell depletion

>The anti-4-1BB x anti-5T4 targeting ADAPTIR molecule, ALG.APV-527, has the potential to be a unique anti-cancer therapeutic agent with an improved safety profile for the treatment of numerous 5T4-expressing solid tumors