668P: First-in-Human Phase I Dose Escalation Study of ALG.APV-527, a 5T4 Tumor Antigen-Conditional 4-1BB Bispecific Antibody, in Patients with Advanced Solid Tumors, Demonstrates Positive Safety, Signals of Biological Activity and Patients with Lasting Stable Disease

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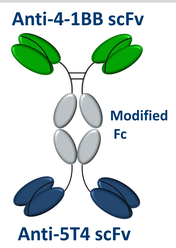
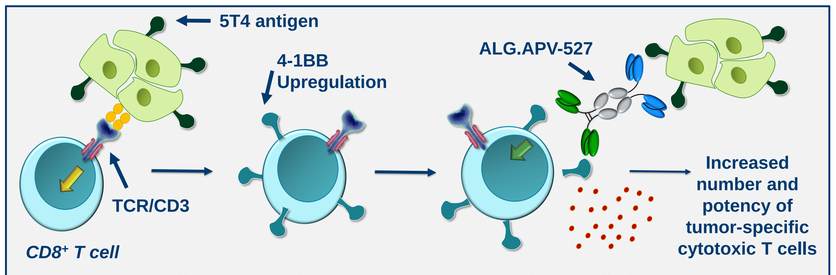
About ALG.APV-527

- ALG.APV-527 is a bispecific therapeutic containing binding domains targeting the co-stimulatory receptor 4-1BB and the oncofetal antigen 5T4, expressed on multiple solid tumor types. These 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 (Alligator Bioscience) and optimized for use in the bispecific ADAPTIR™ format (Aptevo Therapeutics)
- ALG.APV-527 features targeted T cell stimulation, optimized stability, good manufacturing properties with potential for better risk-benefit in humans than monospecific 4-1BB antibodies



ALG.APV-527 Mode of Action



ALG.APV-527 directs the stimulation of CD8⁺ T and NK cells by 5T4⁺ tumors and is designed to minimize the toxicity observed with other 4-1BB therapeutics

Study Design

The Phase I study is a first-in-human, open-label, multicenter trial consisting of up to six cohorts (0.1-15 mg/kg) with a 3+3 dose escalation of ALG.APV-527 monotherapy, administered IV Q2W, in adult patients with advanced solid tumors. Eligibility is limited to patients with tumor types identified as likely to express 5T4 antigen.

Clinical Trials Number: NCT05934539

Key Objectives

- Characterize **safety & tolerability profile** of **ALG.APV-527**
- Identify **MTD** and/or **RP2D**
- Characterize **PK profile** after single and repeated IV administration
- Assess potential **immunogenicity and PD** effects
- Obtain a preliminary assessment of **anti-tumor activity**

Baseline Characteristics

Dose mg/kg Total n=18	Median age (range)	Gender (%) F	Gender (%) M	ECOG PS (%) 0	ECOG PS (%) 1	Tumor Types
Cohort 1 0.1 (n=4)	75.5 (71-82)	2 (50)	2 (50)	0	4 (100)	Breast, Colorectal (2) Esophagus
Cohort 2 0.5 (n=3)	58.0 (56-74)	1 (33)	2 (67)	0	3 (100)	Breast, Pancreatic (2)
Cohort 3 2.0 (n=6)	56.5 (39-72)	5 (83)	1 (17)	2 (33)	4 (67)	H&N SCC, Pancreatic Colorectal (4)
Cohort 4 6.0 (n=3)	47.0 (44-60)	2 (67)	1 (33)	1 (33)	2 (67)	NSCLC, Colorectal (2)
Cohort 5 12.0 (n=2)	56.0 (51-61)	2 (100)	0	0	2 (100)	Renal CC, NSCLC

Prior Anti-Cancer Therapy	n (%); median (range)
Surgery	8 (44); 1 (1-3)
Radiotherapy	12 (67); 1 (1-3)
Systemic Therapy	18 (100); 6 (2-8)

Prior Systemic Therapy	n (%)
Chemotherapy & other antineoplastic therapies	18 (100)
Immune and antibody therapies*	13 (72)

n= number of patients; *bevacizumab (8), pembrolizumab (3), nivolumab (2), ipilimumab, IL-2, cetuximab, panitumumab, durvalumab, cemiplimab

Treatment-Related AEs

>1 Patient; 18 total patients	n (%) E
Any TRAE	16 (89) 87
Fatigue	4 (22) 6
Diarrhea	3 (17) 4
Infusion-related reaction	3 (17) 6
Nausea	2 (11) 2
ALT increase	2 (11) 2
Anemia	2 (11) 4
Neutrophil count decrease	2 (11) 2
WBC count decrease	2 (11) 3
Myalgia	2 (11) 2
Pruritus	2 (11) 3

Serious Treatment-Related AEs	n (%) E
Any Serious TRAE	4 (22) 5
Febrile neutropenia*	1 (6) 1
Ulcerative colitis	1 (6) 1
Hemorrhagic diarrhea	1 (6) 1
GI hemorrhage	1 (6) 1
Nausea	1 (6) 1

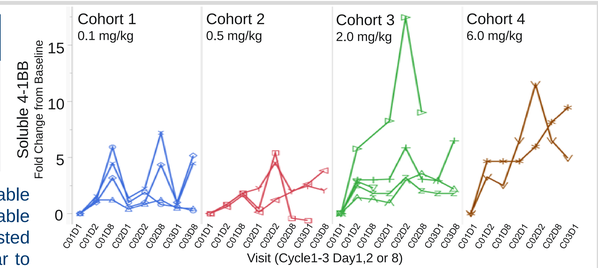
Overall, ALG.APV-527 was safe and well tolerated.

*Case of Gr4 febrile neutropenia, classified as a DLT, and resolved following Filgrastim treatment.
n= number of patients, E= number of events

Favorable PK profile and increase in soluble 4-1BB in blood following treatment

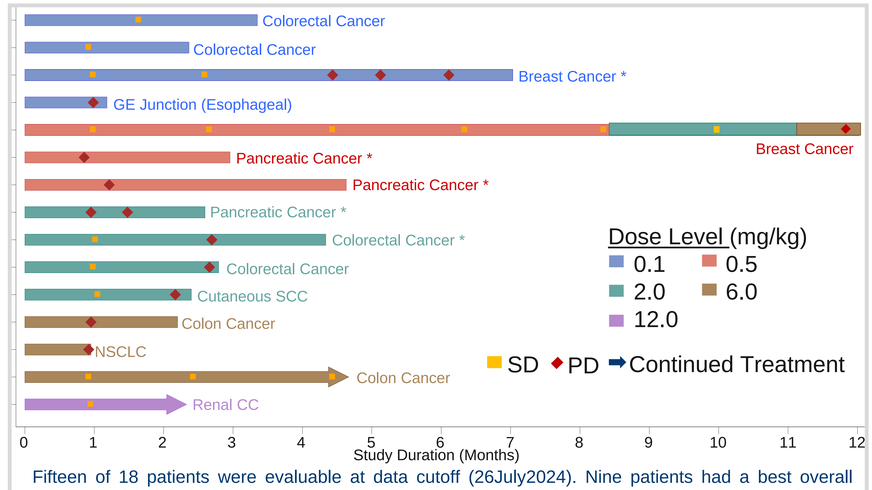
Cmax	mcg/mL
Cohort 1	2.26-4.04
Cohort 2	10.5-22.7
Cohort 3	45.1-105.0
Cohort 4	282.0-362.0

ALG.APV-527 displays a favorable PK profile; the drug is detectable in the serum of all patients tested thus far and exposure is similar to the human PK prediction from NHP studies.



Serum soluble 4-1BB increases with dosing of ALG.APV-527, generally peaking at days 2-8. Data cutoff 26 July 2024.

Duration on Study



Fifteen of 18 patients were evaluable at data cutoff (26July2024). Nine patients had a best overall response of SD. Cohort 2 breast cancer patient increased dosing from 0.5 to 2.0, then to 6.0 mg/kg.

SD= stable disease, PD= progressive disease *Patients were allowed to stay on study with PD events if agreed upon with the treating physician

Summary and Conclusions

ALG.APV-527 demonstrates good tolerability, safety, and biological activity. Serum concentration of ALG.APV-527 was consistent with the administered dose. Based on RECIST 1.1 and iRECIST, nine of 15 evaluable patients (60%) had a best overall response of SD, with the longest SD duration in a breast cancer patient >11 months. One colon cancer patient with sustained SD is still on study. Dose escalation is ongoing. An MTD has yet to be determined.