2560: Dose Escalation of Davoceticept, a Conditional CD28 Costimulator and Dual Checkpoint Inhibitor, in Advanced Malignancies (NEON-1)

Diwakar Davar[1], Justin C Moser[2], Michael Millward[3], Mark Voskoboynik[4], Nehal J Lakhani[5], Rachel E Sanborn[6], Jaspreet Singh Grewal[7], Ajita Narayan[8], Mario Sznol[9], Allison G. Chunyk[10], Russell J. Sanderson[10], Tiffany C. Blair[10], J. Lori Blanchfield[10], Sherri Mudri[10], Heidi N. LeBlanc[10], Gary Means[10], Stacey R. Dillon[10], Keren Schieber[10], Hany Zayed[10], Christine Marie Dela Cruz[11], Graciela Noemi Perez[12], Stanford L Peng[10]

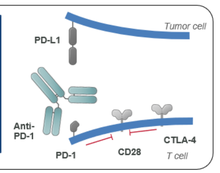
[1]University of Pittsburgh Hillman Cancer Center, Pittsburgh, PA; [2]HonorHealth Research and Innovation Institute, Scottsdale, AZ; [3]Linear Clinical Research & University of Western Australia, Perth, Australia; [4]The Alfred Hospital and Monash University, Melbourne, Australia; [5]START Midwest, Grand Rapids, MI; [6]Earle A Chiles Research Institute, Providence Cancer Institute, Portland, OR; [7]Norton Cancer Institute, Louisville, KY; [8]Horizon Oncology Research, Lafayette, IN; [9]Yale Cancer Center, New Haven, CT; [10]Alpine Immune Sciences, Seattle, WA; [11]PRA Health Sciences, Singapore; [12]PRA Health Sciences, San Diego, CA

Background:

- Inadequate CD28 activity may account for treatment resistance during checkpoint inhibition.
- Davoceticept is designed to localize CD28 costim to the TME, and inhibit PD-L1 and CTLA-4
- NEON-1 is a FIH study of davoceticept monotherapy in advanced malignancies. Dose escalation enrolled subjects at 0.001-10 mg/kg Q1W or Q3W.

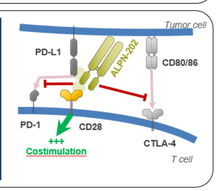
Checkpoint-Only Inhibition

- Inhibits PD-1/PD-L1
- Releases inhibition of, but does not activate, CD28



Davoceticept (ALPN-202)

- Inhibits PD-L1 and CTLA-4
- Mediates PD-L1-dependent CD28 costimulation



Davoceticept safely achieves CD28 costimulation along with dual checkpoint inhibition

- Antitumor activity observed despite a heavily-pretreated solid-tumor population
- Pharmacodynamic analyses (↑ICOS, ↑T_{CM}, ↓T_{reg}) and immune-related AE (irAE) incidence suggest optimal biologic doses of 1-3 mg/kg Q3W
- Expansions in melanoma, renal cell, and PD-L1+ tumors planned; supports study of multiple combinations

Correspondence: davard@upmc.edu; stanford.peng@alpineimmunesciences.com

Well-Tolerated; No G4-5 TR-AEs

Characteristic	Subjects (N = 58)
TR-AEs, G3+	**6 (10%)**
TR-SAEs / G3+	**3 (5%) / 3 (5%)**
AEIs	**25 (43%)**
irAEs / Gr 3+	19 (33%) / 3 (5%)
IRRs[3] / Gr 3+	9 (16%) / 0
Cytokine Release	0
DLT (Gastritis)	**1 (2%)**

[3] Infusion-related reaction

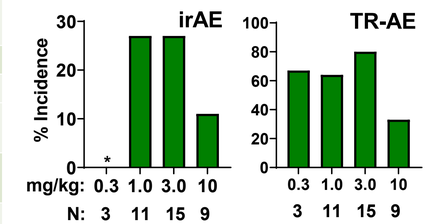
Participants with G3 TR-AEs

Dose	Adverse Event(s)	SAE	irAE	DLT
3Q3W	Gastritis	X	X	X
0.1Q1W	Acute Kidney Injury Testicular Pain	X	X	
3Q3W	Dehydration	X		
10Q3W	Urticaria		X	
3Q3W	Anemia Lipase Increased			
3Q3W	Diarrhea Edema Peripheral			
3Q3W	Hypokalemia			

Immune-Related AEs (irAEs)

irAEs, All Cohorts	Subjects (N=58)
Skin/Subcutaneous Tissue • Rash Maculo-Papular • Rash Macular • Pruritus, Urticaria • Night Sweats, Rash Papular, Rosacea	**14 (24%)** • 7 (12%) • 5 (9%) • 2 (3%) each • 1 (2%) each
Endocrine • Hypothyroidism • Hyperthyroidism	**5 (9%)** • 5 (9%) • 2 (3%)
Gastrointestinal • Colitis, Gastritis, Terminal Ileitis	**3 (5%)** • 1 (2%) each
Musculoskeletal • Arthralgia, Arthritis, Myalgia	**2 (3%)** • 1 (2%) each
Other • Acute Kidney Injury, ALT Increased, Chills, Testicular Pain	• 1 (2%) each

irAE* Highest at 1-3 mg/kg



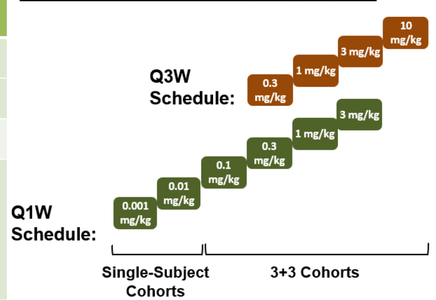
Subject Characteristics

Characteristic		Total (N = 58)
Prior Tx[1]		**4.0 (1-9)**
Prior PD-(L)1		**17 (29%)**
PD-L1[2] ≤ 10 / > 10		**67% / 33%**
Tumor	Colorectal	14 (24%)
	Pancreatic	11 (19%)
	Esophageal	5 (9%)
	Other	28 (48%)

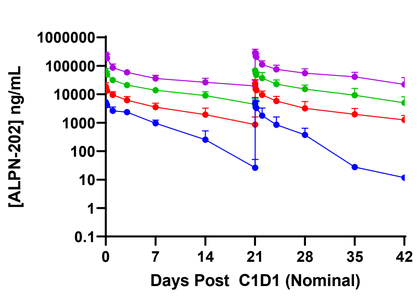
[1] median (range)
[2] CPS by 22C3

Data Extract: 13APR2022

Dose Escalation Included Two Schedules: Q1W, Q3W

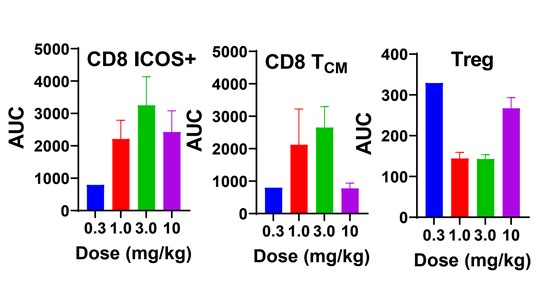


Dose-Dependent Pharmacokinetics*

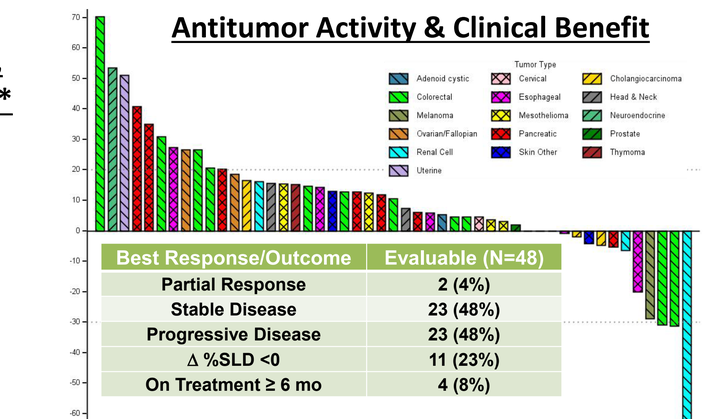


*Q3W schedule (Q1W not shown)

Most Favorable Changes Seen in T_{reg}, Activated and T_{CM} CD8+ at 1-3 mg/kg*



Antitumor Activity & Clinical Benefit



Best Response/Outcome	Evaluable (N=48)
Partial Response	2 (4%)
Stable Disease	23 (48%)
Progressive Disease	23 (48%)
Δ %SLD <0	11 (23%)
On Treatment ≥ 6 mo	4 (8%)