Phase 1 with Expansion Cohorts in a Study of NEO-201 in Adults with Chemo-Resistant Solid tumors

M. Pia Morelli[1], Nicole Houston[1], Stan Lipkowitz[1], Jung-min Lee[1], Alexandra Zimmer[1], Farah Zia[1], Kathrine Trewhitt[1], Erin Nichols[1], Mira Pavelova[1], Steven Hewitt[1], Massimo Fantini[2], Philip M. Arlen[2], Kwong Y. Tsang[2] and Christina M. Annunziata[1]

NATIONAL CANCER INSTITUTE Center for Cancer Research

[1]*Women's Malignancies Branch National Cancer Institute, National Institutes of Health, Bethesda, MD, USA.* [2]Precision Biologics, Inc., Rockville, MD, USA;

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Abstract #283199

Background: NEO-201 is a humanized IgG1 monoclonal antibody (mAb) generated against tumor-associated antigens (TAA) derived from tumor membrane fractions pooled from colorectal cancer surgical specimens. In preclinical data generated in our laboratory, we demonstrated that NEO-201 exerts anti-tumor activity by natural killer (NK)-mediated antibody-dependent cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC) against several tumor types. We identified NEO-201 antigen as a tumor-associated form of CEACAM-5 and -6, which is expressed by tumor tissue but is not present in the surrounding healthy tissue.

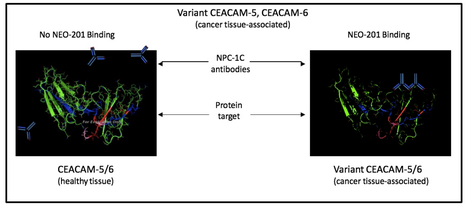
Methods: This is a first-in-human phase 1 study to determine the maximum tolerated dose (MTD) and recommended phase II dose (RP2D) of NEO-201 in adults with advanced solid tumors that have high likelihood of expression NEO201 antigen and have progressed to standard of treatments. This is a classic 3+3 dose escalation, with cohort expansion at the MTD. NEO-201 is administered intravenously every two weeks, and at four dose levels (DL1=1mg/kg, DL2=2mg/kg, DL3= 4mg/kg and DL4= 6mg/kg). Patients are evaluated for safety according to CTCAEv5.0., and for response according to RECISTv1.1. Biological samples are collected to understand NEO-201 pharmacokinetics, the effects on immune profile and the correlation with treatment toxicity and response.

Results: Here we report the safety data and pharmacokinetics from DL1 and 2. A total of 9 evaluable patients were enrolled. Prolonged neutropenia, defined as ≥ G2 neutropenia lasting for >7 days, was observed at DL2. The cohort was expanded to a total of 6 patients and no further DLTs were observed. Seven out of nine of the patients enrolled had colon cancer, two had pancreatic cancer and one had hormone positive breast cancer. The most frequent treatment-related AEs were infusion reaction which was observed in all patients, and moderate fatigue (33%). Best response was SD observed in two patients (one on each of DL1 and DL2). Dose escalation continues on DL3 and DL4. NEO201 antigen expression in patient tumor tissue, circulating CEACAM6/CEACAM5 (CEA), and MICA will be evaluated to correlate with response and toxicity.

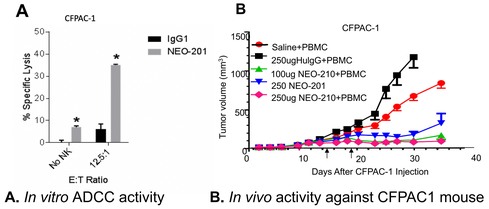
Conclusion: NEO201 has shown some promising activity. PK and PD studies are ongoing to better understand dosing schedule, toxicity profile and to identify biomarkers for patient selection. Clinical trial NCT number: NCT03476681

Background

TAA derived mAb NEO-201 selectively binds tumor tissue



NEO-201 activity in pre-clinical models



A. *In vitro* ADCC activity

B. *In vivo* activity against CFPAC1 mouse model

NEO201 First in Human Phase I Trial

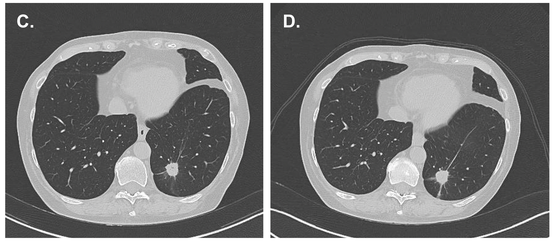
Dose Escalation Schedule		
Cohorts	Dose (mg/kg)	Number of Patient
DL 1	1	3-6
Level 1.5**	1.5	3-6
DL 2	2	3-6
Level 2.5**	3	3-6
DL 3	4	3-6
Level 3.5**	5	3-6
DL 4*	6	3-6
* Additional doses may be investigated if no DLTs or clinical activity is observed		
** Dose de-escalation cohorts		

Results

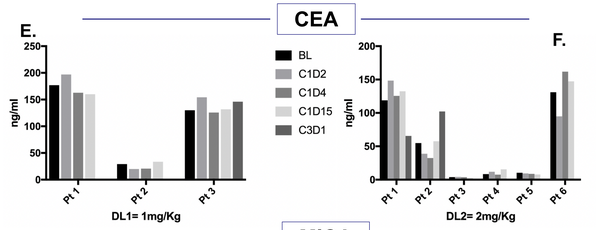
Patients Characteristics	DL 1 (1 mg/Kg)	DL 2 (2 mg/Kg)
Age, years		
• Range	48-70	43-73
Sex		
• Female	2	3
• Male	1	3
Primary histology		
• Colon	2	1
• Rectum/Sigma	1	4
• Pancreas		1
ECOG		
• 0	1	3
• 1	2	3
Prior Therapy		
• Chemotherapy	3	6
• Radiotherapy	0	3
• Anti-EGFR	2	3
• Anti- VEGF	3	4
• Immunotherapy	2	1
• Surgery	2	5
Biological Characteristics		
• KRAS wt	2	4
• KRAS mut	0	2
• BRAF wt	2	4
• BRAF mut	1	0
• MSS	3	6

Adverse Events	DL 1 (1 mg/Kg)						DL 2 (2 mg/Kg)					
	Grade 1/2		Grade 3		Grade 4		Grade 1/2		Grade 3		Grade 4	
	No	%	N	%	N	%	No	%	N	%	N	%
Fatigue	3/3	100					4/6	66				
Neutropenia					3	100					6	100
Infusion Reaction	3/3	100					3/6					
DVT/PE							1/6	16				

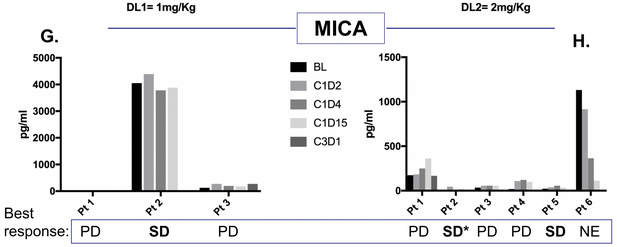
Baseline **C5 D1 (4 months)**



C,D, 1/6 patients in DL2 showed SD after 4 months of treatment.



E, F, Depict CEA level fluctuation at different time point from treatment



G, H, Depict MICA level at different time point from treatment

Best response: PD **SD** PD PD **SD*** PD PD **SD** NE

*Off study for drug unrelated complication

Conclusion

- This is a first in human clinical trial of the monoclonal Ab against a TAA form of CEACAM5/6
- NEO201 most common AE were infusion reaction, fatigue, and neutropenia.
- G4 prolonged neutropenia was the DLT, and was observed in DL2
- Promising activity data were observed at DL2
- Activity may correlate with baseline CEA and/or MICA level