Abstract 3094:

A Phase 1 Open-label Multicenter Single Dose Escalation and Multi-dose Study of a mAb Targeting CEACAM1 in Subjects with Selected Advanced or Recurrent Malignancies

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Background:

- The carcinomembryonic antigen cell adhesion molecule 1 (CEACAM1, CD66a) is a member of the CEA gene family.
- CEACAM1 has been associated with a number of different mechanisms of action, including adhesion (interacts homophillically and heterophilically with CEACAM5), angiogenesis/oncogenesis, and as an immune checkpoint as a ligand to TIM3, thus activating immune fatigue.
- CEACAM1 has been found to be relevant as a marker of tumor activity in a number of tumor types, and expression has been found to portend to a poorer prognosis.
- CEACAM1 is expressed on a variety of epithelial and hematological cells, including multiple types of cancer and activated lymphocytes.
- CM-24, a novel humanized anti-CEACAM1-specific antibody with nanomolar affinity to the N terminal domain of CEACAM1, blocks intercellular CEACAM1 interactions.
- In pre-clinical studies, CM-24 has demonstrated activity as a single agent and a synergistic anti-cancer effect in combination with αPDL-1.

Methods:

- Primary objective was to test the safety and tolerability of CM-24 in adult patients with advanced or recurrent cancer.
- Secondary objectives included assessment of CM24 PK/PD profiles, anti-tumor response and the recommended Phase 2 dose.
- 27 patients received IV infusion of CM-24 at 7 doses:

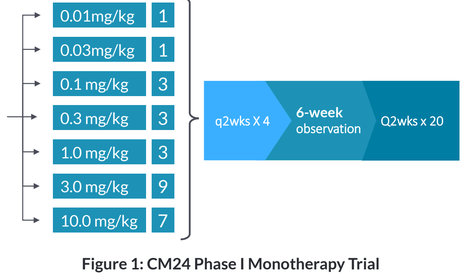
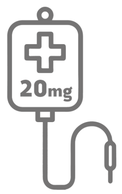


Figure 1: CM24 Phase I Monotherapy Trial

Summary of Demographic Characteristics	n (%)
Total	
	27 (100.0)
Gender	
Male	13 (48.1)
Female	14 (51.9)
Race	
Asian	2 (7.4)
African American	1 (3.7)
Caucasian	24 (88.9)
Age	
Age < 65 (Mean, SD)	20 (55.9, 7.6)
Age ≥ 65 (Mean, SD)	7 (69.6, 5.4)
Diagnosis	
Colorectal adenocarcinoma	11 (40.7)
Gastric carcinoma	3 (11.1)
Ovarian carcinoma	4 (14.8)
Melanoma	7 (25.9)
Non-Small Cell Lung Adenocarcinoma	2 (7.4)
Stage at Original Diagnosis	
Stage 1	1 (3.7)
Stage 2	3 (11.1)
Stage 3	9 (33.3)
Stage 4	13 (48.1)
Unknown	1 (3.7)
Number of Prior Lines of Therapy	
2	4 (14.8)
3	9 (33.3)
4	8 (29.6)
5	3 (11.1)
6	1 (3.7)
8	2 (7.4)

Table 1. Summary of Demographic Characteristics (Safety Population)

This Phase 1 monotherapy trial shows CM-24 (anti-CEACAM1) is safe and well-tolerated at doses up to 10mg/kg.



PK analysis reveals a two- week administration at 20mg/kg is the recommended dose and schedule for further clinical evaluation.

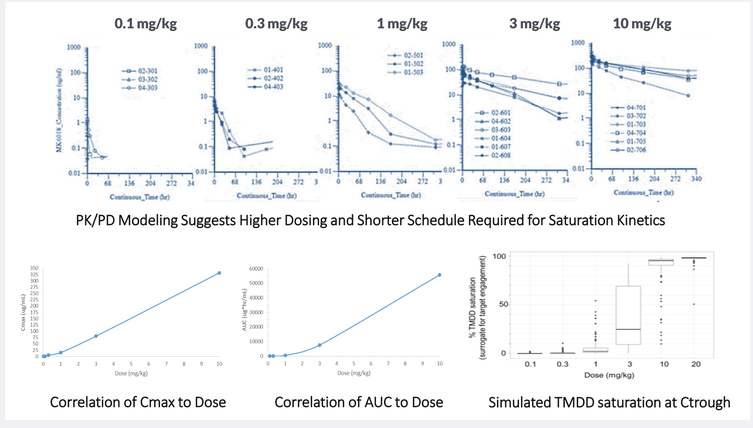
Results:

Treatment with CM-24 was overall well-tolerated without DLTs.

	Severity					
Adverse Event Common Diagnosis	Mild	Moderate	Severe	Life-Threatening	Death	Total
Alanine Aminotransferase Increased	14 (6, 22.2)	1 (1, 3.7)	1 (1, 3.7)			16 (7, 25.9)
Vomiting	14 (8, 29.6)	1 (1, 3.7)				15 (8, 29.6)
Fatigue	10 (8, 29.6)	3 (3, 11.1)				13 (11, 40.7)
Nausea	13 (8, 29.6)					13 (8, 29.6)
Headache	10 (8, 29.6)	2 (2, 7.4)				12 (9, 33.3)
Abdominal Pain	8 (8, 29.6)	2 (2, 7.4)	1 (1, 3.7)			11 (9, 33.3)
Anorexia	9 (7, 25.9)	2 (2, 7.4)				11 (7, 25.9)
Aspartate Aminotransferase Increased	7 (4, 14.8)	2 (2, 7.4)	1 (1, 3.7)			10 (6, 22.2)
Anemia	2 (2, 7.4)	3 (2, 7.4)	4 (2, 7.4)			9 (4, 14.8)
Alkaline Phospatase Increased	1 (1, 3.7)	5 (4, 14.8)	2 (1, 3.7)			8 (5, 18.5)
Fever	6 (6, 22.2)	1 (1, 3.7)				7 (7, 25.9)
Constipation	4 (4, 14.8)	2 (2, 7.4)				6 (5, 18.5)
Creatine Kinase Increased	4 (3, 11.1)	1 (1, 3.7)	1 (1, 3.7)			6 (3, 11.1)
Gamma glutamyl transferase Increased			3 (3, 11.1)	3 (3, 11.1)		6 (4, 14.8)
Weakness	3 (3, 11.1)	2 (2, 7.4)	1 (1, 3.7)			6 (5, 18.5)
Weight Loss	3 (3, 11.1)	2 (2, 7.4)	1 (1, 3.7)			6 (4, 14.8)
Dizziness	4 (2, 7.4)	1 (1, 3.7)				5 (3, 11.1)
Dyspnea	4 (4, 14.8)		1 (1, 3.7)			5 (5, 18.5)
Rash	4 (3, 11.1)	1 (1, 3.7)				5 (4, 14.8)
Abdominal Pain Worsening		4 (4, 14.8)				4 (4, 14.8)
Bilirubin Inceased	2 (2, 7.4)	1 (1, 3.7)				3 (3, 11.1)
Constipation Worsening		3 (1, 3.7)				3 (1, 3.7)
Cough Worsening		3 (3, 11.1)				3 (3, 11.1)
Edema in extremities	1 (1, 3.7)	2 (2, 7.4)				3 (2, 7.4)
Gastroenteritis	2 (2, 7.4)	1 (1, 3.7)				3 (3, 11.1)
Hematuria		2 (1, 3.7)	1 (1, 3.7)			3 (1, 3.7)
Pain in extremity	1 (1, 3.7)		2 (1, 3.7)			3 (2, 7.4)
Paroxysmal Headache Worsening	2 (1, 3.7)	1 (1, 3.7)				3 (1, 3.7)
Bowel Obstruction		1 (1, 3.7)				2 (2, 7.4)
Chest pain	1 (1, 3.7)	1 (1, 3.7)				2 (2, 7.4)
Fatigue Worsening	1 (1, 3.7)	1 (1, 3.7)				2 (1, 3.7)
Hypertension	1 (1, 3.7)		1 (1, 3.7)			2 (2, 7.4)
Pneumonia	1 (1, 3.7)	1 (1, 3.7)				2 (2, 7.4)
Pruritus	1 (1, 3.7)	1 (1, 3.7)				2 (2, 7.4)
Shoulder pain worsening		2 (2, 7.4)				2 (2, 7.4)

Table 2. Most Frequent Incidence of Adverse Events by Adverse Event Diagnosis and Severity for Frequent Events (Safety Population)

- Eight subjects (33%) achieved SD by RECIST criteria as BOR.
- Most responding patients were at the two highest dose levels (3&10mg/kg).
- Drug elimination results suggested non-linear pharmacokinetics, and moreover, target mediated drug disposition modelling suggested dose and schedule of CM-24 should be 20mg/kg administered every 2 weeks.



Correlation of Cmax to Dose | Correlation of AUC to Dose | Simulated TMDD saturation at Ctrough

Conclusion:

This Phase 1 monotherapy trial shows CM-24 is safe and well-tolerated at doses up to 10mg/kg. PK analysis reveals a two-week administration at 20mg/kg is the recommended dose and schedule for this mAb. A phase 1b/2a clinical trial evaluating CM-24 in combination with nivolumab in patients with NSCLC and pancreatic cancer, including assessment of CEACAM1 expression, is being planned.

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