CT136

Interim Safety and Efficacy Results from a Phase 1b Study of CM24 in Combination with Nivolumab in Adults with Advanced Solid Tumors

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BACKGROUND

- The carcinoembryonic antigen cell adhesion molecule 1 (CEACAM1) has a number of important roles in the cancer phenotype, including angiogenesis, mediation of neutrophil extracellular trap activity, regulation of NK and CD8+ T-cells, the immune exclusion phenotype of therapy resistance, as well as regulation of TIM3.
- The monoclonal antibody CM24 has been found to block CEACAM1 interactions.

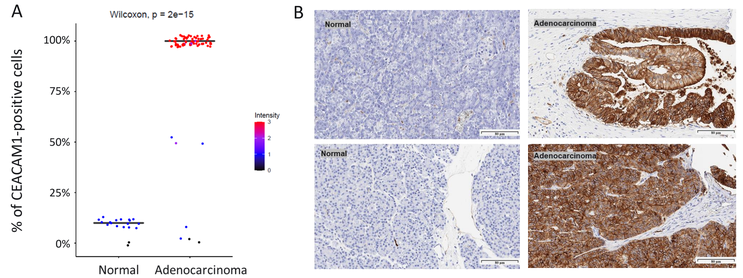

Figure 1: Upregulation of CEACAM1 in Pancreatic Cancer
CEACAM1 immunostaining in pancreatic cancer and normal tissues. (A) Comparison between CEACAM1 staining extent and intensity in pancreatic adenocarcinoma samples (40 cases/80 cores) and normal pancreatic tissues (10 cases/20 cores). (B) Representative examples of CEACAM1 immunohistochemical images of pancreatic adenocarcinoma and normal tissues.

METHODS

- A Phase 1/2 study (NCT 04731467) to assess the safety, tolerability, pharmacokinetics, pharmacodynamics and efficacy of CM24 in combination with nivolumab in adults with advanced solid tumors has been initiated. In the Phase 1 part, patients with indicated refractory cancers were administered CM24 at 10, 15, and 20mg/kg q2w and nivolumab 480mg q4w. The primary objective of this part of the study is to evaluate safety, tolerability, pharmacokinetics and determine the recommended Phase 2 dose (RP2D). Safety was assessed according to CTCAE v5 and preliminary anti-tumor activity was assessed by the investigators according to RECISTv1.1 using CT/MRI. CM24 and CEACAM1 measurements in serum, biopsy specimens, and TILs, as well as tumor and TILs PD-L1 levels are being determined.
- In the Phase 2 part of this study, patients with NSCLC relapsed from or refractory to first-line immune checkpoint inhibitors will be treated with CM24 and nivolumab, and patients with advanced/metastatic pancreatic adenocarcinoma relapsed from or refractory to first-line therapy will be treated with CM24, nivolumab, and chemotherapy. The objectives of these parts of the study will be to evaluate safety and preliminary efficacy of the combination treatments.

Dose Escalation

CM24 Doses: 10, 15, 20mg/kg q2w + nivolumab (480mg q4w)
3+3 design
$9 \leq n \leq 15$

Indications: NSCLC, Pancreatic, Ovarian, CRC, Melanoma, Papillary Thyroid Carcinoma

Expansion cohorts

I/O refractory NSCLC; 2nd line
CM24 (@RP2 dose) q2w + nivolumab (480mg) q4w
n=13+14 (Simon 2 Stage Design)

Locally advanced/ metastatic pancreatic cancer; 2nd line
Arm#1: CM24 (@RP2 dose) q2w + nivolumab (480mg) q4w + nab-paclitaxel
Arm #2: CM24 (@RP2 dose) q2w + nivolumab (240mg) q2w + 5FU/Nal-IRI
Each arm: n=9+8 (Simon 2 Stage Design)

Figure 2: CM24 in Combination with Nivolumab or with Nivolumab and chemotherapy

RESULTS

Patients: As of March 8th, 2022, a total of 13 patients were enrolled in the dose escalation phase, and 11 patients were evaluable for dose limiting toxicity (DLT) determination, including 8 with pancreatic cancer (PDAC), two with colorectal cancer (CRC) and one with papillary thyroid cancer (PTC). Nine patients had received 2 prior regimens for metastatic disease and two patients had one previous line for metastatic disease .

Demographics of patients treated with CM24 (10, 15, 20mg/kg) in combination with nivolumab (480mg)			
Median age, years (range)	65 (49-76)	Prior Lines of Therapy, n (%)	
Sex, n (%)		1	2 (18%)
Male	5 (45%)	2	9 (82%)
Female	6 (55%)	Diagnosis , n (%)	
Ethnicity, n (%)		Pancreatic cancer	8 (73%)
Not Hispanic or Latino	10 (91%)	Papillary Thyroid cancer	1 (9%)
Hispanic or Latino	1 (9%)	Colorectal cancer	2 (18%)
Race, n (%)		Median Time from Initial Diagnosis months (range)	23 (11-73)
White	10 (91%)	ECOG, n (%)	
Black or African American	1 (9%)	0	7 (64%)
		1	4 (36%)

Table 1: Demographics of patients

Safety: Six Grade 3 adverse events (AEs) (unrelated to CM24 or nivolumab), were observed, each in a single patient, including diarrhea, hypokalemia, abdominal pain, small bowel obstruction, atrial flutter, and GI bleed. No Grade 4 AEs or deaths were reported.

AE Term	Total	Grade 1	Grade 2	Grade 3	Grade 4/5
Diarrhea	5	4		1	
Abdominal pain	4	1	3		
Fever	4	2	2		
Headache	4	3	1		
Fatigue	4	4			
Nausea	3	1	2		
Creatinine increased	3	2	1		
Hypokalemia	2			2	
Dyspnea	2	1		1	

AE Term	Total	Grade 1	Grade 2	Grade 3	Grade 4/5
Constipation	2	2			
Cough	2	2			
Abdominal pain aggravated	1			1	
Alkaline phosphatase increase	1			1	
Atrial flutter	1			1	
C-Diff Colitis	1			1	
GI bleed	1			1	
Leukocytosis	1			1	
Small bowel obstruction	1			1	

Table 2: Most frequent and severe adverse events (AEs)

Efficacy: For the 11 evaluable patients, best overall response included one confirmed PR (PDAC patient) three SD (two PDAC and one PTC patient) for a disease control rate of 36%. As of March 8th, 2022, 9/11 of the evaluable patients are in follow-up.

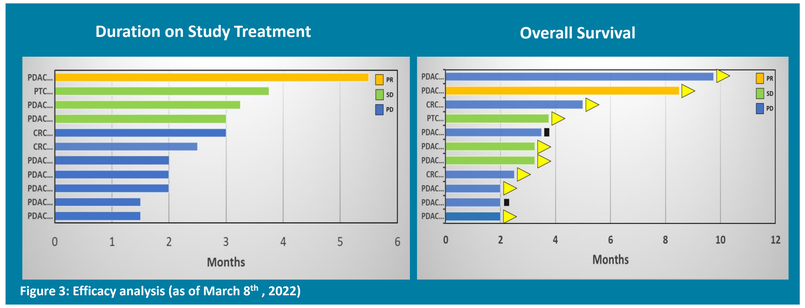

Figure 3: Efficacy analysis (as of March 8th , 2022)

Partial Response patient: PDAC patient, previously treated with FOLFIRINOX and gemcitabine/nab-paclitaxel, had a germline NF1 VUS, with MSS and PDL-1 IHC 2+ and 5% staining.

- After initial treatment, the patient had a Partial Response of 40%, with a definite reduction of the para-tracheal adenopathy and liver lesions and 58% reduction in CA19-9 levels.

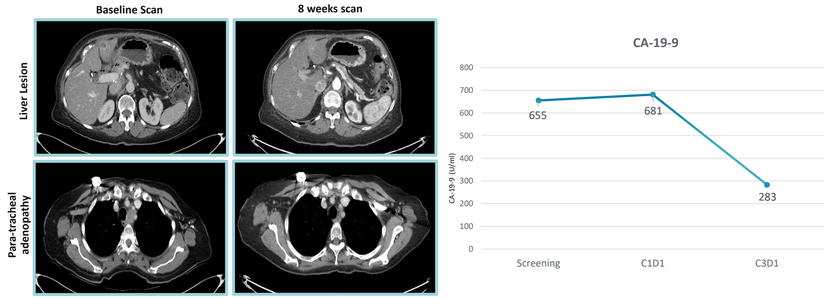

Figure 4: CT scans and CA-19-9 levels during treatment

Pharmacokinetics: Pharmacokinetic analysis of CM24 shows exposure is dose-proportional.

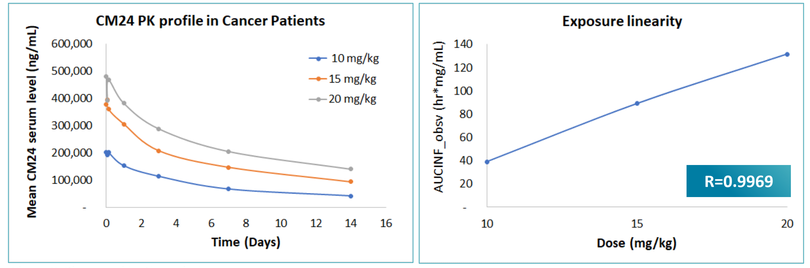

Figure 5: Pharmacokinetic analysis

CEACAM1 Receptor occupancy by CM24: Complete receptor occupancy of peripheral CEACAM1 receptors on T cells and neutrophils was demonstrated at CM24 doses of 15 and 20mg/kg.

CONCLUSIONS

- No DLTs were observed across all dose levels; no Grade 4 AEs or treatment related deaths have been reported.
- The most frequent AEs were diarrhea, abdominal pain, fever, headache and fatigue; Severe AEs were noted in 6/13 patients (46%).
- Best overall response in previously treated patients was 1 PR and 3 SDs for a disease control rate of 36%
- Pharmacokinetic analysis of CM24 shows exposure is dose-proportional across the 3 doses in this study; Complete receptor occupancy of peripheral CEACAM1 receptors on T cells and neutrophils was demonstrated at CM24 doses of 15 and 20mg/kg.
- The Phase 2 portions of the study will be initiated at the conclusion of this dose-escalation part.
- The Investigators wish to thank the patients and their families for their participation in the study.

The study is sponsored by Purple Biotech Ltd as part of a clinical collaboration with Bristol Myers Squibb; no conflicts of interest to declare