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Interim results of the Randomized Phase 2 Cohort of Study FW-2020-01 Assessing the Efficacy, Safety and Pharmacodynamics of CM24 in Combination with Nivolumab and Chemotherapy in Advanced/Metastatic Pancreatic Cancer

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BACKGROUND

The novel monoclonal antibody CM24 blocks the activity of Carcinoembryonic Antigen Cell Adhesion Molecule 1 (CEACAM1), known to have key roles in cancer progression, immune evasion, and metastasis. We present the interim efficacy and safety data from the global multi-center, open label, randomized Phase 2 study (NCT 04731467) in patients with advanced/metastatic pancreatic ductal adenocarcinoma (PDAC) who progressed after 1st line therapy, treated with CM24, nivolumab and chemotherapy vs. chemotherapy.

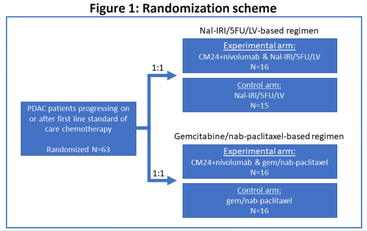
Here we report interim results for the patients who were randomized to receive CM24 and nivolumab with liposomal irinotecan (Nal-IRI), 5 fluorouracil (5FU) and leucovorin (LV; Nal-IRI/5FU/LV) or only Nal-IRI/5FU/LV. Data from the gemcitabine/nab-paclitaxel arm is not yet mature for analysis.

METHODS

Patients with advanced/metastatic PDAC progressing after 1 prior line of systemic therapy including fluoropyrimidine/irinotecan or gemcitabine/nab-paclitaxel, having ≥1 measurable lesion, ≥18-year-old, ECOG ≤1 and adequate organ function were allocated to the treatment groups based on prior chemotherapy regimen received. Randomization to the experimental and control arms was at a ratio of 1:1 with experimental arms administered with CM24 (20mg/kg, q2wk), nivolumab (240mg/kg, q2wk) and one of the following chemotherapy regimens, NI-IRI (70mg/m^2), 5FU (2400mg/m^2) and LV (200mg/m^2) administered q2wk, or gemcitabine (1000mg/m^2) and nab-paclitaxel (125mg/m^2), administered q1wkx3, or to the control arms with one of the chemotherapy regimens alone.

This was a Bayesian design trial with a total planned sample size of approximately 60 patients with Overall Survival (OS) as the primary endpoint. Secondary endpoints include progression free survival (PFS), objective response rate (ORR), disease control rate (DCR) and clinical and exploratory biomarkers.

Figure 1: Randomization scheme



RESULTS

Patients: As of May 8, 2024, a total of 31 PDAC patients were randomized to the Nal-IRI/5FU/LV-based study regimen with a median follow up of 8.3 months.

Table 1: Patient characteristics

Characteristic		Experimental (n=16)	Control (n=15)
Age (median)		66	68
Age **≥65** (n, %)		8 (50.0)	4 (26.7)
Male (n, %)		10 (62.5)	8 (53.3)
Female (n, %)		6 (37.5)	7 (46.7)
Race/ white (n, %)		15 (93.8)	14 (93.3)
BMI		23.4	23.1
ECOG (n, %)	0	5 (31.3)	3 (20.0)
	1	11 (68.8)	12 (80.0)
Time from initial diagnosis (median, mo)		18	18
Time from most recent disease progression (median, mo)		0.94	0.89
CR/PR/SD to prior line (%)		43.8	60.0

Safety: Treatment-emergent adverse events (TEAEs) were manageable.

Table 2: Grade ≥3 Treatment Emergent Adverse Events reported in ≥2 patients/arm

Grade ≥3 TEAE, n (%)	CM24/nivolumab+ Nal-IRI/5FU/LV (n=16)	Nal-IRI/5FU/LV (n=15)
Any Grade ≥3 TEAE	15 (94)	10 (67)
Diarrhea	3 (19)	1 (7)
Fatigue	3 (19)	1 (7)
Hypokalemia	1 (6)	2 (13)
Asthenia	2 (13)	- (0)

Efficacy: Median OS for the experimental arm was 7.72m (95% CI: 4.00-8.11) vs. 5.62m (95% 3.22 -7.89) for the control arm (HR: 0.74; 95% CI: 0.31-1.77).

Median PFS for the experimental group was 3.8m (95% 1.8-5.0) vs. 1.9m (95% 0.9, 3.6) for the control arm (HR 0.72; 95% CI: 0.33-1.60). ORR and DCR for the experimental arm were 25% and 62.5%, and for the control arm 6.7% and 40%, respectively.

Figure 2: Efficacy analysis, Overall Survival

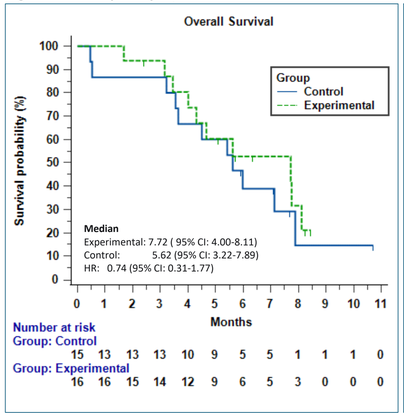


Figure 3: Efficacy analysis, progression Free Survival

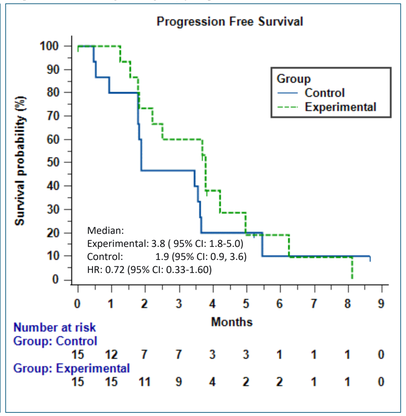
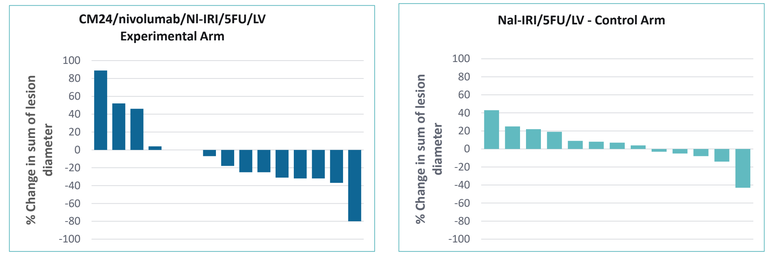


Table 3: efficacy summary

Parameter	Experimental (n=16)	Control (n=15)
OS (mo, median; 95% CI)	7.72 (4.00-8.11)	5.62 (3.22 -7.89)
OS HR (95% CI)	0.74 (0.31-1.77)	
6 mo OS (%)	52.7	38.9
PFS (mo, median; 95% CI)	3.8 (1.8-5.0)	1.9 (0.9-3.6)
PFS HR (95% CI)	0.72 (0.33-1.60)	
3 mo PFS (%)	60.0	46.7
6 mo PFS (%)	19.0	10.0
ORR (%)	25.0	6.7
DCR (%)	62.5	40.0

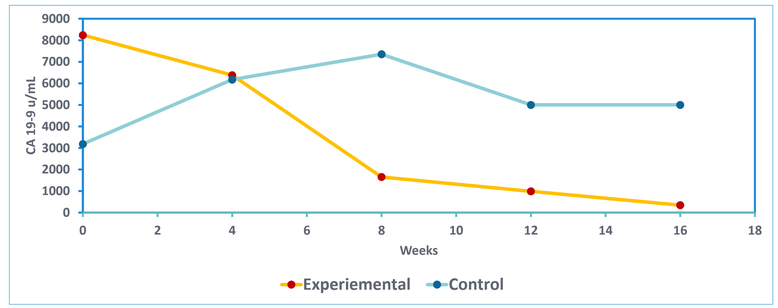
ORR: Responses in the study included PR in 4/16 patients of the experimental arm and 1/15 patients of the control arm.

Figure4: Percent change in tumor size



Median CA 19-9 levels: CA 19-9 decrease in the experimental group

Figure 5: Median CA 19-9 levels



CONCLUSIONS

- The interim analysis demonstrates clinically meaningful benefit and risk reduction on OS and PFS:
  - ✓ A 26% reduction in the risk of death combined with median OS prolongation of 2.1 months
  - ✓ A 28% reduction in the risk of progression or death with median PFS prolongation of 1.9 months
  - ✓ Over 3x increase in ORR
  - ✓ CA 19-9 consistent decrease in the experimental arm vs. control arm
  - ✓ CM24 plus nivolumab and Nal-IRI/5FU/LV were well tolerated
- Biomarker analysis is ongoing (serum CEACAM1, CEACAM1+ lymphocytes, NET marker-MPO)
- Results support further clinical evaluation of CM24/nivolumab with Nal-IRI/5FU/LV in patients with PDAC in the second line

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