Keck School of Medicine of USC

A Phase 1 Trial of FID-007, a Novel Nanoparticle Paclitaxel Formulation, in Patients with Solid Tumors

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Introduction

- FID-007 consists of paclitaxel encapsulated in a polyethyloxazoline (PEOX) polymer excipient designed to enhance PK, biodistribution, and tolerability
- In addition to allowing the drug to remain in solution until it can enter a cancer cell, the PEOX nanoparticle preferentially delivers paclitaxel to the tumor through the leaky hyperpermeable vasculature.
- In xenograft studies, FID-007 reduced or limited tumor growth in multiple tumor types including lung, gastric, breast, pancreatic, and ovarian cancer.
- FID-007 was more effective at lower or comparable taxane doses with fewer side effects. We present the first-in-human trial of FID-007.

Study Design

Objectives

1. To determine the MTD and RP2D of FID-007
2. To determine PK of total paclitaxel, free paclitaxel, and paclitaxel metabolites in patients treated with FID-007
3. To characterize safety and tolerability of FID-007
4. To obtain a preliminary assessment of anti-tumor activity of FID-007 using RECIST 1.1

Eligibility Criteria

- Histopathologically / cytologically confirmed advanced solid tumor
- ECOG performance status 0-2
- ANC ≥ 1500/mm^3, Platelet count 100,000/mm^3, Hemoglobin ≥ 8 g/dL, Serum Cr ≤ 1.5XULN, T. Bili ≤ 1.5XULN, AST/ALT ≤ 3XULN
- No more than 3 lines of prior cytotoxic chemotherapy for advanced disease
- Prior treatment with paclitaxel or nab-paclitaxel allowed if treating physician believes retreatment with taxane is clinically reasonable, but patients with taxane as most recent line of therapy were excluded

Treatment Plan

- FID-007 was given IV once a week for 3 weeks of a 28-day cycle.
- Infusion given over 60 minutes. 500cc of D5W with 1mEq/mL sodium bicarbonate administered before and after FID-007.
- Dose escalation in standard 3+3 design
- Doses ranged between 15 mg/m^2 to 125mg/m^2

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Results

Table 1: Patient Baseline Characteristics

Characteristic	Overall, N = 26
Years of Age, Median (Range)	61 (43, 75)
Gender	
Female	17 (65%)
Male	9 (35%)
Race/Ethnicity	
White or Caucasian	6 (23%)
Hispanic	11 (42%)
Black or African American	1 (3.8%)
Asian (including Indian)	8 (31%)
ECOG PS	
0	8 (31%)
1	17 (65%)
2	1 (3.8%)
Number of Prior Regimens, Median (Range)	3 (1, 7)
Tumor Type	
Pancreatobiliary	11 (42%)
Non-small cell lung	4 (15%)
Head and neck SCC	3 (12%)
Other	8 (31%)

Figure 1: FID-007 has Linear PK Between Doses 15 – 125mg/m2

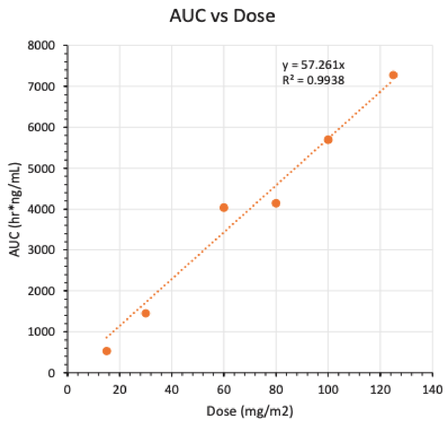
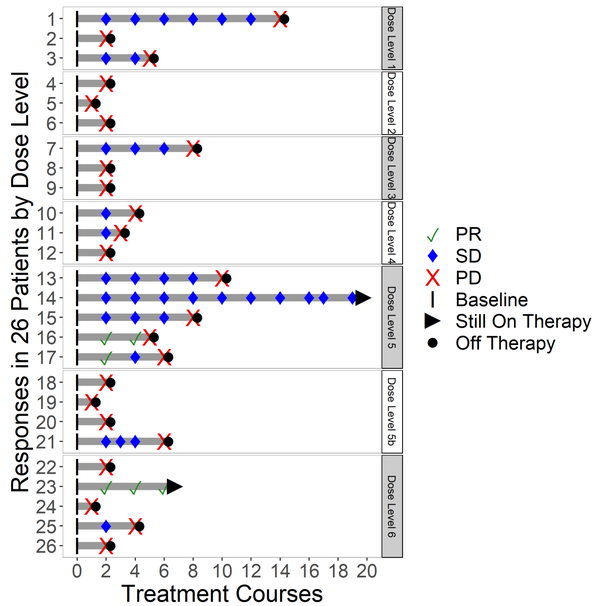


Figure 2: Swimmer Plot for Responses over Time



SD > 6 months in cutaneous SCC (ID#1), ampullary cancer (ID#7), head and neck SCC (ID#13), adenoid cystic carcinoma (ID#14), Gallbladder (ID#15)

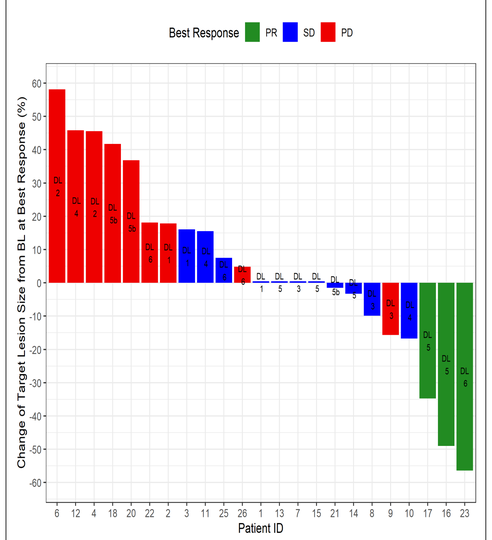
Table 2: Dose Levels Evaluated

Dose Level	FID-007 (mg/m^2)	No. of Patients	DLTs Observed
1	15	3	0
2	30	3	0
3	60	3	0
4	80	3	0
5	100	5	2[a]
5b	100	4	0
6	125	5	1[b]

a. Two patients in dose level 5 had DLT of grade 3 maculopapular rash. Rash resolved with supportive care and/or dose delays in both patients and treatment was successfully continued safely without recurrence of grade 3 rash. DLT definition was modified for dose levels 5b/6 to allow for grade 3 rash that resolves within 7 days. No further patients had DLT for rash in dose levels 5b and 6

b. One DLT was observed for grade 4 neutropenia in dose level 6. A sixth patient is still in cycle 1.

Figure 3: Waterfall Plot for Best Response



PR in Head and neck SCC (ID#17), pancreatic Adenocarcinoma (ID#16), and cholangiocarcinoma (ID#23)

Table 3: Tumor Responses and Outcomes

Characteristic	Overall, N = 26
Total Courses Completed, Median (Range)	2 (1, 19)
Best Response	
PR	3 (12%)
SD[a]	11 (42%)
PD[b]	12 (46%)
Duration of Follow-up (Months), Median (Range)	6 (1, 18)

a. 5 patients had SD for 6 months or longer.

b. PD includes 3 patients who were not RECIST evaluable yet had clinical deteriorations before end of cycle 1.

Table 4: Treatment-related select AE categories (>= 10%)

Toxicity	Number Of Patients With Maximum Grade Toxicity Experienced		
	Grade 1-2	Grade 3	Grade 4
Rash maculo-papular[a]	12 (46%)	5 (19%)	0
Alopecia	15 (58%)	0	0
Pruritus	12 (46%)	0	0
Anemia	6 (23%)	5 (19%)	0
White blood cell decreased	7 (27%)	3 (12%)	1 (4%)
Fatigue	10 (38%)	0	0
Anorexia	8 (31%)	1 (4%)	0
Dysgeusia	9 (35%)	0	0
Nausea	8 (31%)	0	0
Neutrophil count decreased	4 (15%)	1 (4%)	3 (12%)
Peripheral sensory neuropathy	7 (27%)	0	0
Constipation	5 (19%)	0	0
Arthralgia	4 (15%)	0	0
Diarrhea	4 (15%)	0	0
Palmar-plantar erythrodysesthesia syndrome	4 (15%)	0	0
Dry skin	3 (12%)	0	0
Fever	3 (12%)	0	0
Vomiting	3 (12%)	0	0

a. Maculopapular rash seen in 17/26 (65%) of patients resolved prior to cycle 2 in majority of patients

Conclusions

- FID-007 has a manageable safety profile with MTD not reached. Accrual is continuing at 125 mg/m2. (NCT03537690)
- PK is linear, dose proportional and comparable to that of nab-paclitaxel.
- There is preliminary evidence of anti-tumor activity in heavily pre-treated pts across different tumor types.
- Combination studies with immunotherapeutic agents are planned.