Abstract # 3026: A Phase 1 Trial of FID-007, a Novel Nanoparticle Paclitaxel Formulation, in Patients with Solid Tumors

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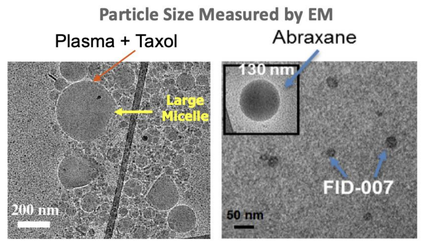
Background/Methods

- 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.



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, over 30-60 minutes, once a week for 3 weeks of a 28-day cycle.
- Sodium bicarbonate infusion (pre- and post-treatment dose) was used to prevent potential kidney toxicity in patients receiving dose levels 1-6. Sodium bicarbonate infusion was omitted at dose level 6b as no evidence of kidney toxicity observed at any dose level.
- Dose escalation in standard 3+3 design with doses ranged between 15 mg/m^2 to 160mg/m^2.
- Dexamethasone pre-medication added for dose level 6b, given only in cycle 1

Results

Table 1: Patient Baseline Characteristics

Characteristic	Overall, N = 40
Years of Age, Median (Range)	61 (32 - 75)
Gender	
Female	23 (58%)
Male	17 (43%)
Race/Ethnicity	
White or Caucasian	11 (28%)
Hispanic	19 (48%)
Black or African American	1 (3%)
Asian (including Indian)	9 (23%)
ECOG PS	
0	11 (28%)
1	28 (70%)
2	1 (3%)
Number of Prior Regimens, Median (Range)	2 (1 - 5)
Tumor Type	
Pancreatobiliary	11 (28%)
Non-small cell lung	4 (10%)
Head and neck SCC	11 (28%)
Other	14 (35%)

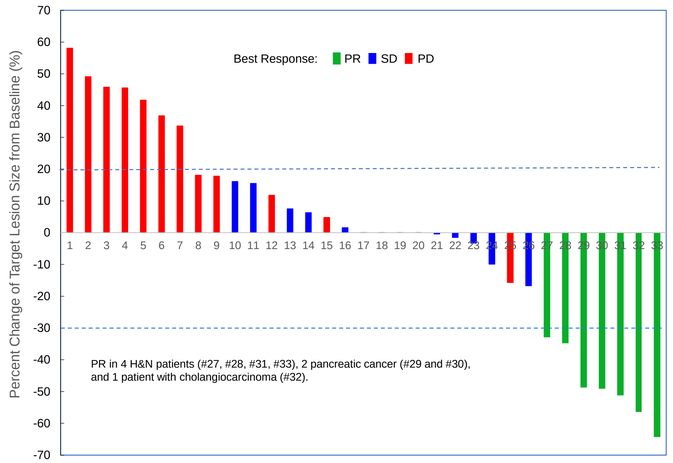
Table 2: Dose Levels Evaluated

Dose Level	FID-007 (mg/m^2)	No. of Patients	No. of Evaluable Patients	DLTs Observed	DLT Type
1	15	3	3	0	
2	30	3	3	0	
3	60	3	3	0	
4	80	3	3	0	
5	100	5	5	2[a]	Rash
5b	100	4	3	0	
6	125	9	6	1	Gr4 neutropenia
7	160	3	3	1	Gr3 febrile neutropenia
6b[b]	125	7	6	1	Gr4 neutropenia

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 and above to allow for grade 3 rash that resolves within 7 days. No further patients had DLT for rash in the subsequent dose levels.

b. Cohort 6b used modified pre-medication by removing sodium bicarbonate infusion and addition of corticosteroid pre-medication for C1 only. One patient had to be replaced.

Figure 1: Waterfall Plot for Best Response



FID-007 has a manageable safety profile with preliminary evidence of antitumor activity, including in patients treated with prior taxanes.

Figure 2: Swimmer Plot for Responses over Time

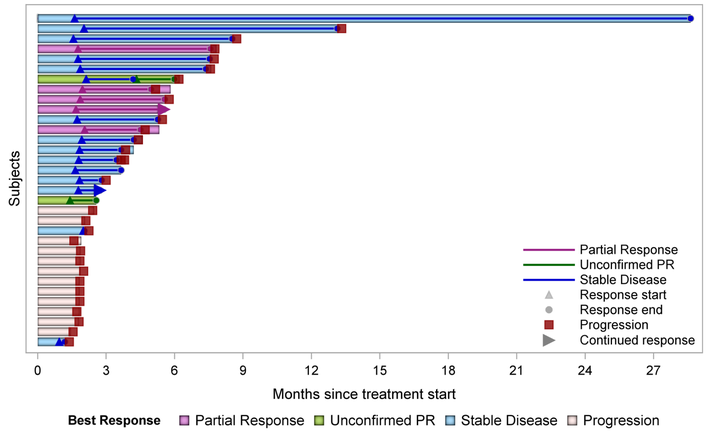


Table 3: Treatment-related select AE categories (>= 10%)

Toxicity	Number Of Patients With Maximum Grade Toxicity Experienced		
	Grade 1 or 2	Grade 3	Grade 4
Alopecia	21 (53%)	0	0
Rash maculo-papular	16 (40%)	11 (28%)	0
Pruritus	16 (40%)	0	0
Fatigue	15 (38%)	0	0
Anorexia	12 (30%)	1 (3%)	0
Nausea	12 (30%)	0	0
White blood cell decreased	11 (28%)	5 (13%)	3 (8%)
Anemia	10 (25%)	6 (15%)	0
Dysgeusia	10 (25%)	0	0
Neutrophil count decreased	9 (23%)	3 (8%)	5 (13%)
Peripheral sensory neuropathy	9 (23%)	0	0
Dry skin	8 (20%)	0	0
Palmar-plantar erythrodysesthesia syndrome	7 (18%)	0	0
Constipation	6 (15%)	0	0
Vomiting	6 (15%)	0	0
Diarrhea	5 (13%)	0	0
Arthralgia	4 (10%)	0	0
AST	4 (10%)	0	0

Table 4: Tumor Responses and Outcomes

Characteristic	Overall, N = 40
Total Courses Completed, Median (Range)	2 (1 - 30)
Best Response*	
PR	7 (18%)
SD	14 (35%)
PD[a]	18 (45%)
Duration of Follow-up (Months), Median (Range)	12.0 (0.4, 38.9)

a. PD includes 4 patients who had clinical deteriorations prior to RECIST evaluation.

* One patient response is pending

Figure 3: FID-007 PK

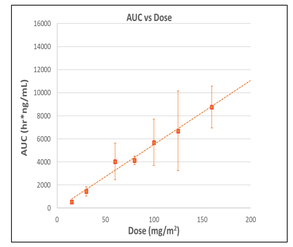
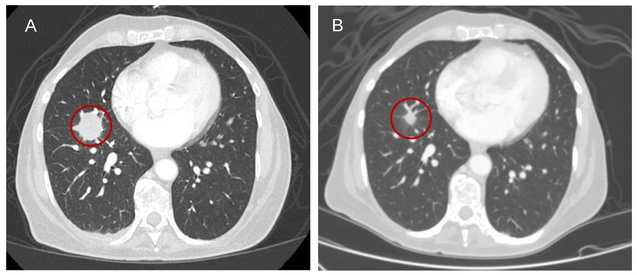


Figure 4: Partial Response in Patient with Head and Neck SCC

- Panel A at baseline, panel B after 2 cycles of FID-007
- Prior therapies (best response):
  - Pembrolizumab + 5-FU + carboplatin (SD)
  - Cetuximab (SD)
  - Docetaxel (PR 9 months)
  - NK cell + EGFR bi-specific Ab (PD)
- Response ongoing > 6 months



Conclusions

- Enrollment in a 10-patient expansion cohort at RP2D continues
- Based on overall tolerability, pharmacokinetics, and efficacy, the dose of 125mg/m2 has been chosen as the RP2D.
- There has been no grade 3 or higher peripheral neuropathy
- Combination studies are planned, including a phase 2 study in head and neck SCC