Abstract # 6042: Efficacy from the phase 1 study of FID-007, a novel nanoparticle paclitaxel formulation, in patients with head and neck squamous cell carcinoma

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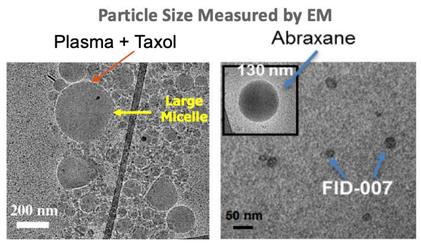
Background/Methods

- 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 (HNSCC only)

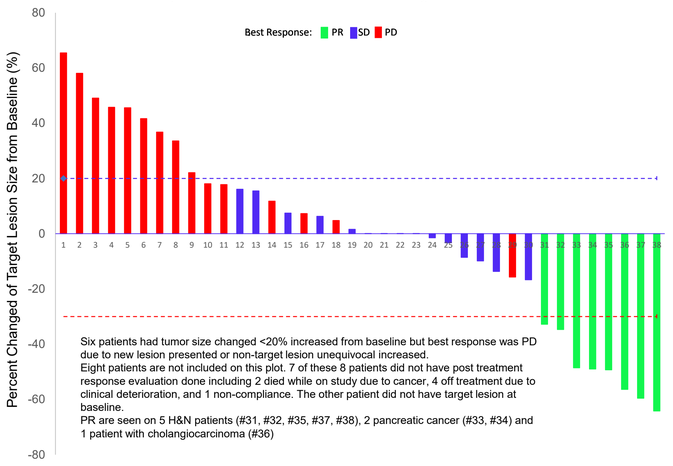
Characteristic	Overall, N = 11
Years of Age, Median (Range)	61 (53 - 75)
Gender	
Female	4 (36%)
Male	7 (64%)
Race/Ethnicity	
White or Caucasian	2 (18%)
Hispanic	6 (55%)
Black or African American	1 (9%)
Asian (including Indian)	2 (18%)
Number of Prior Regimens, Median (Range)	3 (1 - 5)
Tumor Type	
Nasopharynx	2 (18%)
Sinonasal	2 (18%)
Oropharynx	5 (45%)
Oral Cavity	1 (9%)
Occult Primary	1 (9%)

ECOG performance status was 1 in all HNSCC pts.

All HSNCC pts had received prior immune checkpoint inhibitor.

Seven patients (64%) had received prior taxane chemotherapy.

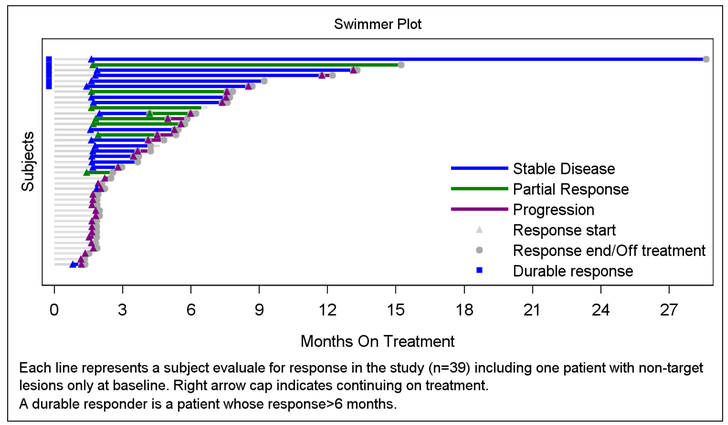
Figure 1: Waterfall Plot for Best Response



Six patients had tumor size changed <20% increased from baseline but best response was PD due to new lesion presented or non-target lesion unequivocal increased.
Eight patients are not included on this plot. 7 of these 8 patients did not have post treatment response evaluation done including 2 died while on study due to cancer, 4 off treatment due to clinical deterioration, and 1 non-compliance. The other patient did not have target lesion at baseline.
PR are seen on 5 H&N patients (#31, #32, #35, #37, #38), 2 pancreatic cancer (#33, #34) and 1 patient with cholangiocarcinoma (#36)

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



Each line represents a subject evaluale for response in the study (n=39) including one patient with non-target lesions only at baseline. Right arrow cap indicates continuing on treatment.
A durable responder is a patient whose response>6 months.

Table 2: Treatment-related select AE categories (>= 10%) (All patients)

Toxicity	Number Of Patients With Maximum Grade Toxicity Experienced (N=46)		
	Grade 1 or 2	Grade 3	Grade 4
Alopecia	24 (52%)	0	0
Pruritus	20 (43%)	0	0
Rash maculo-papular	17 (37%)	16 (35%)	0
Fatigue	17 (37%)	0	0
Nausea	13 (28%)	0	0
White blood cell decreased	12 (26%)	6 (13%)	3 (7%)
Anorexia	12 (26%)	1 (2%)	0
Neutrophil count decreased	10 (22%)	3 (7%)	6 (13%)
Dry skin	10 (22%)	1 (2%)	0
Dysgeusia	10 (22%)	0	0
Anemia	9 (20%)	8 (17%)	0
Peripheral sensory neuropathy	9 (20%)	0	0
Palmar-plantar erythrodysesthesia syndrome	9 (20%)	0	0
Constipation	6 (13%)	0	0
Vomiting	6 (13%)	0	0
Diarrhea	6 (13%)	0	0

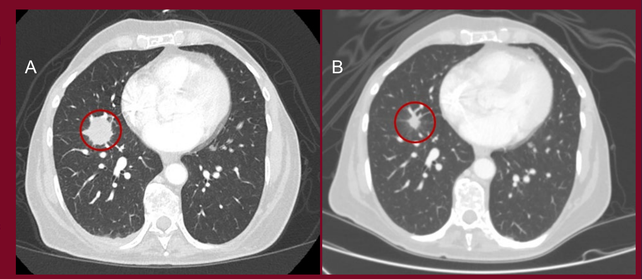
Table 3: Tumor Responses and Outcomes

Characteristic	Overall, N = 46	HNSCC, N = 11
Total Courses Completed, Median (Range)	2 (1 - 30)	5 (2-16)
Best Response*		
PR	8 (17%)	5 (45%)
SD	16 (35%)	3 (27%)
PD	21 (46%)[a]	3 (27%)
Inevaluable	1 (2%)	0 (0%)
Duration of Follow-up (Months), Median (Range)	12.1 (1.1, 45.9)	4.0 (1.0-15.0)

a. PD includes 4 patients who had clinical deteriorations prior to RECIST evaluation.
* One patient with inevaluable response; off-treatment due to non-compliance. No response evaluation was performed.

Figure 3: 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

- FID demonstrates preliminary evidence of anti-tumor activity in heavily pre-treated HNSCC pts across different primary tumor sites, with an ORR 45%.
- 3 out of the 5 patients who achieved a PR had received prior taxane.
- There has been no grade 3 or higher peripheral neuropathy.
- Phase 2 study of FID combination with cetuximab in pts with HNSCC has begun enrollment.