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INTRACYSTIC INJECTION OF SUBMICRON PARTICLE PACLITAXEL (SPP) FOR THE TREATMENT OF MUCINOUS PANCREATIC CYSTIC LESIONS RESULTED IN REDUCTION IN CYST VOLUME, AN INTERIM REPORT

Biliary Tract Diseases
Endoscopy: EUS New Technology
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BACKGROUND & AIMS: Mucinous pancreatic cystic lesions (PCLs), branched duct IPMNs or mucinous cystic neoplasms havethe potential for malignant transformation. A novel intracystic therapy with SPP may prevent progression to cancer without corresponding systemic toxicities. A prior study has confirmed SPP remains present at the delivery site for at least 100 days, providing a slow release depot.We aimed to determine safety and preliminary efficacy of SPP for treatment of mucinous-PCLs using endoscopic ultrasound Fine Needle Injection (EUS-FNI).
METHODS: Subjects with confirmed mucinous-PCLs (size > 1.5 cm) received intracystic SPP via EUS-FNI at volumes equal to the aspirated cyst fluid volume in sequential cohorts at 6, 10, and 15 mg/mL in a standard '3+3' dose-escalation protocol. The highest dose was determined to have a good safety and tolerability profile and was taken into the second phase of the study where 9 additional subjects receive two injections of SPP 12 weeks apart. At the 12-week visit, cyst fluid was evaluated during EUS, prior to the second injection. Subjects were followed 6 months for clinical endpoints including: safety and tolerability, pharmacokinetic analysis of systemic paclitaxel drug levels, and cyst volume response (reported by imaging at 3, and 6 months). Significant reduction in cyst volume defined as 50% reduction of cyst volume in 6 months.
RESULTS:Seventeen patients have been enrolled in the study so far. Nine subjects have completed the dose escalation phase of the study. Another 8 (of 9 planned) have been enrolled to the two-injection phase with ongoing evaluations. No dose limiting toxicities, serious adverse events related to treatment, or clinically significant laboratory values have been reported. Mild adverse events potentially related to SPP include mild, transient abdominal pain/discomfort and nausea following the procedure which resolved on its own within 24 hours of th eprocedure. Systemic paclitaxel concentration did not exceed 3.5 ng/mL at any timepoint measured, and fell below 1ng/mL by week 2, supporting lack of systemic toxicity (Table 1). Cyst volumes in 8/9 completed subjects (dose escalation phase) reduced by month 6 (Table 2); significant reduction was seen in 6/9 patients
CONCLUSION:Single intracystic injection of SPP for the treatment of mucinous PCL at 6, 10, and 15 mg/mL in a volume equal to that of aspirated cyst fluid resulted in reduction of cyst volume, produced minimal systemic drug exposure, and no patients developed pancreatitis. Subject enrollment to the second phase (2 injections 12 weeks apart, at 15mg/mL) to maximize the reduction in cyst volume is ongoing.

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Table 1 Dose escalation Subjects; All branch duct IPMN cysts; CEA and PK (ng/mL) results

Subject	Pre-study cyst fluid CEA level (ng/mL)	SPP injected (mg)	PK 2 hours post-injection (ng/mL)	PK at 1 week	PK at 2 weeks	PK at 12 weeks	PK at 24 weeks
4001	not done (thick mucin)	21	0.463	BLQ	BLQ	BLQ	BLQ
4002	732	15	0.383	0.046	BLQ	BLQ	BLQ
4003	317	24	BLQ	BLQ	BLQ	BLQ	BLQ
4004	595	50	0.053	0.056	BLQ	BLQ	BLQ
4005	766	30	0.269	BLQ	BLQ	BLQ	BLQ
4006	2870	50	0.434	0.038	0.027	BLQ	pending
4007	380	105	BLQ	BLQ	BLQ	BLQ	pending
4008	591	112.5	0.663	0.07	0.0304	BLQ	pending
4009	43343	75	not done (hard stick)	2.83	0.843	pending	pending

*PK – lower level of quantitation 0.025ng/mL ; BLQ – below level of quantitation

Table 1 Dose escalation Subjects; All branch duct IPMN cysts; CEA and PK (ng/mL) results

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Table 2. Subject Cyst Volumes as Determined by CT Scan.

	Subject	Total SPP injected	Cyst Volume (mL)			% Change in Volume
		(mg)	Day 1	Week 12	Week 24	
Cohort 1 6mg/mL	4001	21	9.2	10.1	8.5	-7.6
	4002	15	8.2	3.6	2.7	-67.1*
	4003	24	10.3	5.5	1.2	-88.8*
Cohort 2 10mg/mL	4004	50	14.1	6.0	4.1	-70.7*
	4005	30	3.1	2.0	5.0	62.3
	4006	50	38.8	7.5	4.0	-89.7*
Cohort 3 15mg/mL	4007	105	31.1	19.3	15.4	-50.4*
	4008	112.5	10.0	8.8	9.0	-9.5
	4009	75	4.2	0.8	1.1	-73.7*

*Significant reduction (more than 50%)

Table 2. Subject Cyst Volumes as Determined by CT Scan

Disclosure: M. O. Othman: Abbvie: Consulting, Grant/Research Support; Boston Scientific: Consulting; ConMed: Consulting; Lumendi: Consulting; Nanology: Grant/Research Support; Olympus: Consulting; K. Patel: Abbvie: Speaking and Teaching; Conmed: Speaking and Teaching; S. G. Krishna: No Conflicts; A. H. Mendoza Ladd: No Conflicts; S. Verco: US Biotest Inc: Employment; J. Verco: US Biotest: Employment; A. wendt: No Answer; G. diZerega: NanOlogy: Stock Shareholder;
