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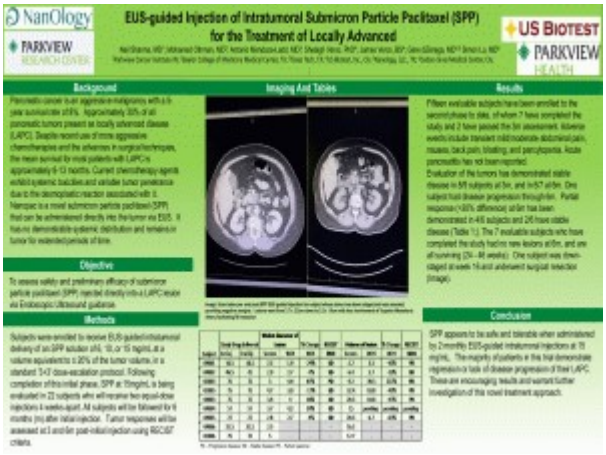
EUS-GUIDED INJECTION OF INTRATUMORAL SUBMICRON PARTICLE PACLITAXEL (SPP) FOR THE TREATMENT OF LOCALLY ADVANCED PANCREATIC ADENOCARCINOMA (LAPC):PHASE 2 STUDY



Technologies and Procedural Innovation
Endoscopy: New Therapeutic Technology
Presented on Saturday, May 2, 2020 12:30 PM

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Pancreatic cancer is an aggressive malignancy with a 5-year survival rate of 8%. Approximately 30% of all pancreatic tumors present as locally advanced disease (LAPC). Despite recent use of more aggressive chemotherapies and the advances in surgical techniques, the mean survival for most patients with LAPC is approximately 8-13 months. Current chemotherapy agents exhibit systemic toxicities and variable tumor penetrance due to the desmoplastic reaction associated with it. Nanopac is a novel submicron particle paclitaxel (SPP) that can be administered directly into the tumor via EUS. It has no demonstrable systemic distribution and remains in tumor for extended periods of time.

AIMS: To assess safety and preliminary efficacy of submicron particle paclitaxel (SPP) injected directly into a LAPC lesion via Endoscopic Ultrasound guidance.

METHODS:

Subjects were enrolled to receive EUS-guided intratumoral delivery of an SPP solution of 6, 10, or 15 mg/mL at a volume equivalent to ≤ 20% of the tumor volume, in a standard '3+3' dose-escalation protocol. Following completion of this initial phase, SPP at 15mg/mL is being evaluated in 22 subjects who will receive two equal-dose injections 4 weeks apart. All subjects will be followed for 6 months (m) after initial injection. Tumor responses will be assessed at 3 and 6m post-initial injection using RECIST criteria.

RESULTS:

Fifteen evaluable subjects have been enrolled to the second phase to date, of whom 7 have completed the study and 2 have passed the 3m assessment. Adverse events include transient mild/moderate abdominal pain, nausea, back pain, bloating, and pancytopenia. Acute pancreatitis has not been reported.

Evaluation of the tumors has demonstrated stable disease in 8/9 subjects at 3m, and in 6/7 at 6m. One subject had disease progression through 6m. Partial response (>30% difference) at 6m has been demonstrated in 4/6 subjects and 2/6 have stable disease (Table 1;). The 7 evaluable subjects who have completed the study had no new lesions at 6m, and are all surviving (24 - 46 weeks). One subject was down-staged at week 16 and underwent surgical resection (Image).

CONCLUSION:

SPP appears to be safe and tolerable when administered by 2 monthly EUS-guided intratumoral injections at 15 mg/mL. The majority of patients in this trial demonstrate regression or lack of disease progression of their LAPC. These are encouraging results and warrant further investigation of this novel treatment approach.

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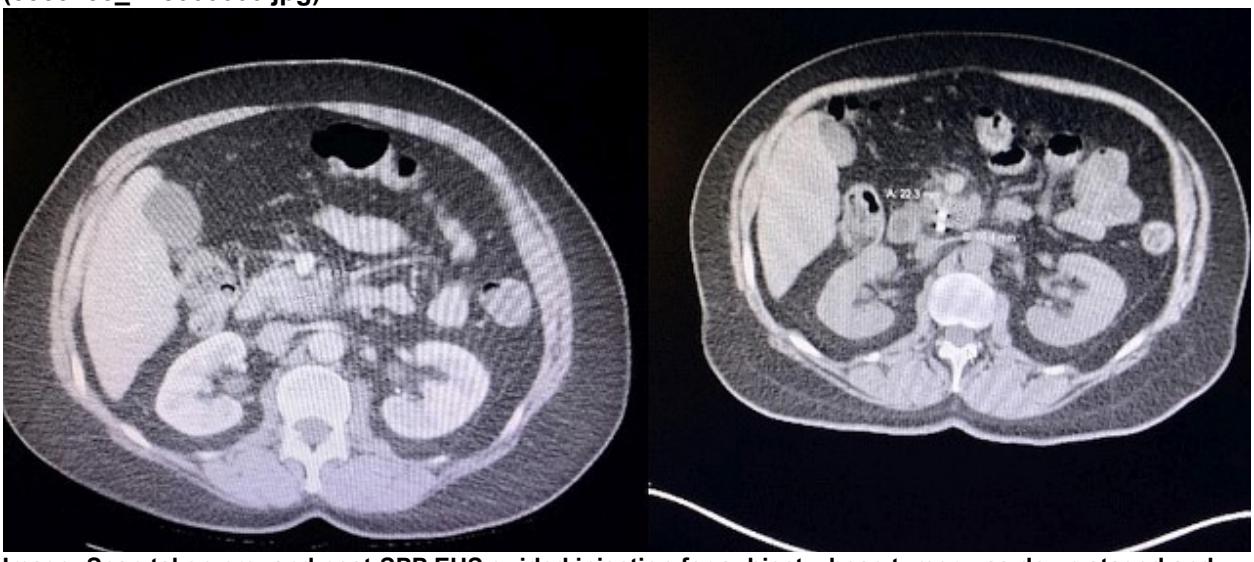

Image: Scan taken pre- and post-SPP EUS guided injection for subject whose tumor was down staged and was resected, providing negative margins. Lesions went from 2.7 x 2.2cm down to 2.2 x 1.6cm with less involvement of Superior Mesenteric Artery facilitating R0 resection.

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	Study Drug delivered		Widest diameter of Lesion		% Change	RECIST	Volume of lesion		% Change	RECIST
Subject	1st inj	2nd inj	Screen	W24	W24	W24	Screen	W24	W24	W24
04001	16.5	16.5	2.5	1.9	-24%	SD	5.7	3.3	-42%	PR
04002	46.5	42	2.9	2.7	-7%	SD	6.4	5.7	-11%	SD
05003	75	75	3	4.4	47%	PD	9.2	39.3	327%	PD
02005	75	75	4.7	3.9	-17%	SD	32.4	18.8	-42%	PR
04003	75	75	3.4	4	18%	SD	20.5	10.8	-47%	PR
04004	57	57	3.7	4.2	14%	SD	15	*pending*	*pending*	*pending*
04005	27	27	2.8	2.7	-4%	SD	20.3	6.7	-67%	PR
04006	31.5	31.5	2.3	-	-	-	16.3	-	-	-
02006	75	75	5	-	-	-	12.7	-	-	-

PD – Progressive disease; SD – Stable disease; PR – Partial response

Table 1: RECIST evaluation – Tumor Diameter (largest) and Tumor Volume - in subjects receiving two SPP injections, one month apart.

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