THE EFFICACY OF INTRACYSTIC INJECTION OF LARGE SURFACE AREA MICROPARTICLE PACLITAXEL (NANOPAC®) IN THE MANAGEMENT OF INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS: RESULTS FROM AN EXPANDED ACCESS PROTOCOL

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Background and Aims

- Branch duct (BD)-IPMNs with increased risk for malignant transformation are typically treated with surgical resection. Alternate therapies are needed for patients with prohibitive risks for perioperative complications.
- Injection of cysts with paclitaxel may prevent or reverse transformation, but current formulations are not retained in cysts to provide durable benefit.
- EUS-guided intracystic fine needle injection (EUS-FNI) with a novel large surface area microparticle paclitaxel (LSAM-PTX, NanoPac®, NanOlogy, Ft Worth, TX) has been investigated in an early phase 2a for this patient population. The clinical trial (NCT03188991) demonstrated negligible systemic absorption, lack of serious adverse events, and evidence of cyst size decrease.
- A diagnosis of BD-IPMNs was confirmed by EUS-guided confocal laser endomicroscopy and cyst fluid next generation sequencing.
- Subjects (deemed nonsurgical) received up to two doses of LSAM-PTX (15mg/mL concentration; 12 weeks apart) by EUS-FNI at volumes equal to the aspirated cyst-fluid as part of a multicenter clinical trial; only one needle-pass was used.

Methods

- Subjects at this study site were subsequently enrolled into an *expanded access protocol* where additional doses of LSAM-PTX were administered with EUS-FNI at similar doses and schedules.
- The volume of LSAM-PTX was at least equal or more than the volume of cyst-fluid aspirated with no restriction on the number of needle-passes.
- Cyst-fluid was aspirated for NGS analysis before EUS-FNI.
- Changes in cyst size were measured.

Results

- A total of 6 BD-IPMNs (mean diameter ±SD = 3.18±0.76 cm) in 5 subjects (mean age 66 years) were treated by EUS-FNI with LSAM-PTX (Table 1). The mean duration of follow-up from the first EUS-FNI was 21±11 months. In all, 22 doses of LSAM-PTX were administered with a mean range of doses from 47.5 mg to 128.75 mg per cyst.
- Mean (±SD) decrease in size during follow-up:
  - EUS measurement: 9±7 mm (27%±0.2%) decrease
  - MRI measurement: 7±5 mm (23%±0.2%) decrease
- EUS revealed changes in cyst morphology, with increased intracystic lobularity and fibrosis, **Fig. 1**. Cross-sectional imaging studies also revealed changes as shown in **Fig. 2.**
- No dose-limiting toxicities, study-related serious adverse events, or clinically significant changes in blood work were observed in the clinical trial phase. In the expanded access phase, one subject developed post-EUS mild acute pancreatitis following injection of maximum (180mg) dose of LSAM-PTX at a volume 7x more than that of the withdrawn (2 ml) fluid in a near-complete fibrotic appearing BD-IPMN (**Fig 1, "Cyst 1"**).

Conclusion

- EUS-FNI with LSAM-PTX is reasonably tolerated and can potentially ablate pathogenic epithelium in BD-IPMNs.
- Continued studies to establish the number of injections, dose delivered, and longer-term follow-up are needed to understand the durability of the benefits observed.

						Largest diameter (cm)			Cyst fluid mutations		Changes in EUS cyst morphology	
Cyst ID	**Age**	**Sex**	**Total EUS-FNI**	**F/u months**	**Mean dose (mg)**	**1st EUS-FNI (cm)**	**Final EUS-FNI**	**Difference (%)**	**Mutations (diagnostic)**	**Mutations at final EUS-FNI**	**Increase septations / lobularity**	**Fibrosis**
1	60	M	6	31	128.75	4	3.5	12.50%	KRAS, GNAS	None	Yes	Yes
2	66	F	4	27	48.75	2.4	2.4	0%	KRAS, GNAS	KRAS, GNAS	Yes	Yes
3	68[1]	F	2	3	47.5	3.1	2.4	33%	GNAS, BRAF	None	Yes	No
4	70	F	4	28	78.5	3.2	1.7	47%	KRAS, GNAS	KRAS, GNAS	Yes	Yes
5	66[2]	M	4	26	80.63	4.1	2	52%	KRAS, GNAS	None	Yes	Yes
6	66[2]	M	2	9	52.5	2.3	1.9	17%	KRAS, GNAS	None	No	Yes
Mean ± SD				21±11	73±31	3.2±0.8	2.3±0.6	↓27±0.2%				

[1] Patient course complicated by pneumonia (unrelated to intracystic injection of LSAM-PTX) and and unable to receive additional EUS-FNI of LSAM-PTX. [2] Cysts 5 and 6 are in the same subject.
EUS-FNI: EUS-guided intracystic fine needle injection

Table 1. Demographic and cyst characteristics in study subjects receiving Large Surface Area Microparticle Paclitaxel (LSAM-PTX) for Branch Duct Intraductal Papillary Mucinous Neoplasms (BD-IPMN).

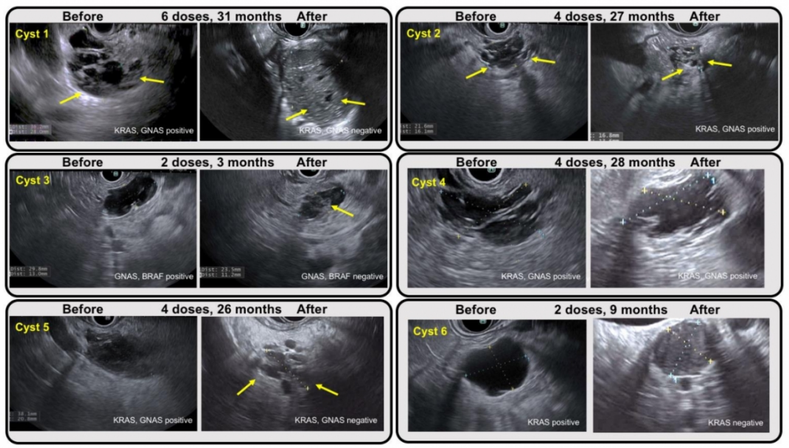

Figure 1. Pre-and-post EUS imaging of BD-IPMN following intracystic injection of Large Surface Area Microparticle Paclitaxel (LSAM-PTX)

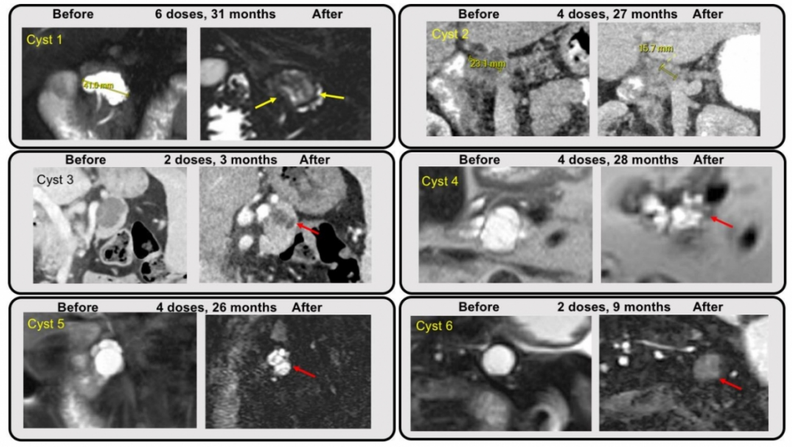

Figure 2. Pre-and-post cross-sectional imaging of BD-IPMN following intracystic injection of Large Surface Area Microparticle Paclitaxel (LSAM-PTX)