Intracystic Injection of Large Surface Area Microparticle Paclitaxel for Chemoablation of Intraductal Papillary Mucinous Neoplasms: Insights from an Expanded Access Protocol

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BACKGROUND and AIMS

Branch duct (BD) – Intraductal Papillary Mucinous Neoplasms (IPMNs) represent 80% of incidentally identified pancreatic cystic lesions (PCLs). Guideline-directed risk assessment is suboptimal and about 60% patients undergo unnecessary surgical resection. Thus, minimally invasive treatments are increasingly being utilized.

A phase 1 clinical trial evaluated the safety, tolerability, and preliminary efficacy of EUS-guided fine needle injection (EUS-FNI) with novel particle-engineered form of paclitaxel with large surface area microparticles (LSAM-PTX, NanoPac®, CritiTech, Lawrence, KS) in mucinous PCLs.

We prospectively evaluated the safety and response of EUS-FNI of LSAM-PTX to chemoablate BD-IPMNs in an expanded access protocol (EAP).

METHODS

Subjects diagnosed with BD-IPMNs and deemed non-surgical received up to two doses of LSAM-PTX (15mg/mL; 12 weeks apart) by EUS-FNI as part of a multicenter clinical trial (NCT03188991). Subjects at our center were subsequently enrolled into an EAP where additional doses of LSAM-PTX were administered by EUS-FNI on similar schedules (Figure 1).

RESULTS

Six BD-IPMNs measuring (mean ± standard deviation (SD)) 3.18 ± 0.76 cm in diameter among 5 subjects (mean age: 66 years) were treated by EUS-FNI of LSAM-PTX. Two to six doses of LSAM-PTX (mean dose/cyst: 73 ± 31 mg)) were administered, and subjects were followed for up to 32 months.

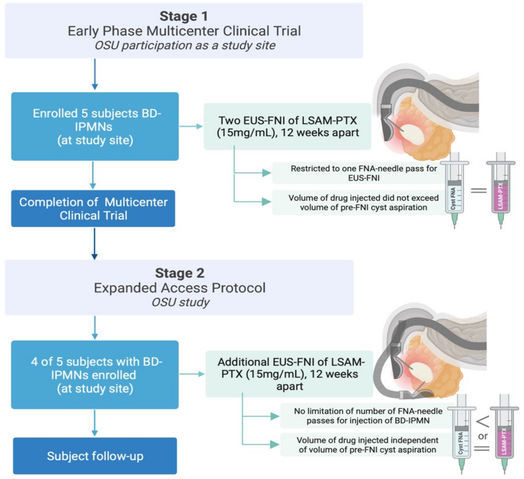

Figure 1. Study flow chart

The mean volume reduction of the treated cysts was 42-89% (absolute volume change from 9.58 ± 5.1ml to 2.2 ± 1.1ml (p=0.016)), Figure 2. The mean surface area was reduced from 31-83% (absolute reduction from 21.9 ± 8.7cm2 to 5.7 ± 2.5cm2 (p=0.009)), Figure 2.

Higher dosing-frequency of EUS-FNI of LSAM-PTX significantly correlated with a reduction in cyst volume (R2=0.87, p=0.03) and surface area (R2=0.83, p=0.04), Figure 3.

Comparing pre-and-post ablation, molecular analysis of the cyst fluid demonstrated loss of the cyst-associated mutations in 5 (83.3%) with reemergence in 1 and persistence in 1, and intracystic changes of fibrosis or calcification were observed in 83.3% (n=5) BD-IPMNs (Figure 4).

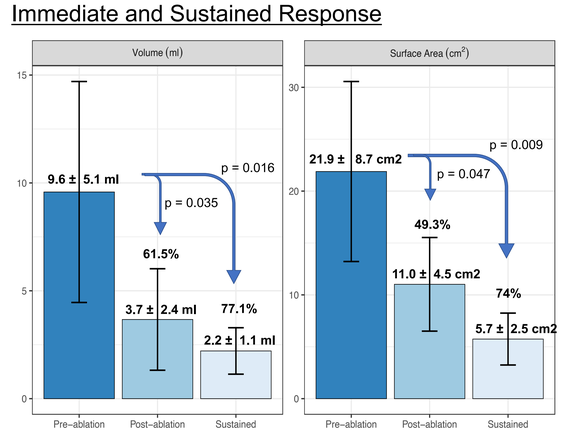

Figure 2. Changes in BD-IPMN volume and surface comparing pre-ablation, immediate and sustained response; box-plot with 95% CI.

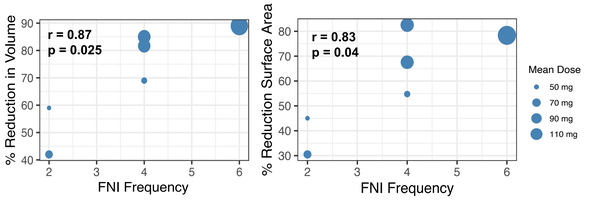

Figure 3. Reduction in BD-IPMN volume and surface and correlation with frequency and dosing of LSAM-PTX

ADVERSE EVENTS

One subject developed mild acute pancreatitis following EUS-FNI (5th dose) of LSAM-PTX in a fibrotic BD-IPMN.

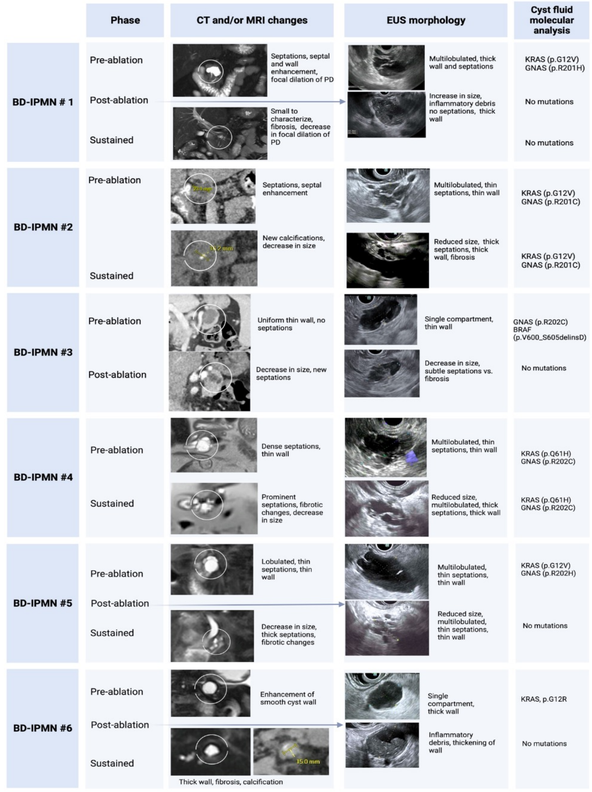

Figure 4. Morphological changes observed in cross-sectional imaging and EUS after EUS-guided chemoablation with LSAM-PTX

CONCLUSION

In this extended access protocol, EUS-FNI of LSAM-PTX into BD-IPMNs was safe and resulted in volume and surface area reduction, morphological changes, and loss of pathogenic mutations.