## Patient Population

- Must be ≥ 50 years and ≤ 75 years of age
- Must not have acute pancreatitis or a history of chronic pancreatitis
- Must have received a CT, MRI, or EUS within 6 months prior to randomization that revealed one or more ≥ 1 cm pancreatic cyst(s)
- Patients of childbearing potential must not be known to be pregnant
- Must not have a prior diagnosis of pancreatic malignancy of any type
- Must not have a history of pancreatic resection
- Patients with only pancreatic lesions without malignant risk (pancreatic pseudocyst or classic serous cystic lesion) are not eligible
- Must not have a family history of pancreatic adenocarcinoma in one or more first-degree relatives (biological parents, full siblings or children)
- Must not have pancreatic cyst morphology that would prompt immediate surgical consideration (enhancing mural nodule, solid component in cyst, pancreatic duct ≥ 10 mm, cyst causing obstructive jaundice)
- Must not have a comorbid illness that precludes EUS or pancreatic cyst resection
- Must not be currently participating in pancreatic cyst surveillance defined as organized, periodic up-to-date imaging directed towards the pancreatic cyst of interest

## Surveillance Plan

### Arm A– low intensity surveillance:
- Pre-enrollment imaging (MRI or CT or EUS) within 6 months prior to study randomization
- MRI/CT (preferably same imaging modality) in 1 year from pre-enrollment imaging
- If EUS is indicated by imaging features (at any point) and the subsequent EUS does not indicate surgery, repeat MRI/CT in 1 year. If EUS is not indicated on a follow-up MRI/CT study, repeat the MRI/CT in 2 years
  - See protocol for EUS indication parameters
- Diagnostic EUS expected within 2 months of surveillance CT/MRI

### Arm B– high intensity surveillance:
- Pre-enrollment imaging (MRI or CT or EUS) within 6 months prior to study randomization
- Schedule next imaging from time of pre-enrollment imaging by specific schedule per protocol
- Frequency of surveillance is determined based on largest/most suspicious cyst at each evaluation
  - Cyst ≥ 1 and < 2 cm: CT/MRI every 6 months for 1 year, then every 12 months for 2 years, then increase interval to 24 months
  - Cyst ≥ 2 and < 3 cm: EUS within 6 months of pre-enrollment CT/MRI/EUS. If EUS negative repeat in 1 year. If next EUS negative, alternate CT/MRI and EUS every 12 months
  - Cyst ≥ 3 cm: Alternate CT/MRI with EUS every 3-6 months
  - See protocol for EUS indication parameters; diagnostic EUS within 2 months of surveillance CT/MRI
- If size of the cyst has changed and EUS is not indicated, the timing of the next surveillance scan will be determined by the new size (if < 1 cm, CT/MRI in 6 months, then every 2 years if no change)

Note: Patients meeting the indications for surgery but refuse surgery or are deemed inappropriate surgical candidates will remain on the protocol surveillance assigned at randomization.
Comparing the Clinical Impact of Pancreatic Cyst Surveillance Programs

Schema

Randomization

Arm A
Low Intensity Surveillance
Long-term Follow-up

Arm B
High Intensity Surveillance
Long-term Follow-up

Asymptomatic patients aged 60-75 with ≥ 1 cm pancreatic cyst

Accrual: n = 4606

1. Low Intensity Surveillance:
   - Pre-enrollment imaging (MRI or CT or EUS) study within 6 months prior to study randomization
   - Repeat MR/CT imaging (preferably same imaging modality) in 1 year
   - If no abnormalities on year 1 study, repeat every 2 years
   - If EUS is indicated by imaging features (at any point) and the subsequent EUS does not indicate surgery, repeat MRI/CT in 1 year. If imaging does not indicate EUS, then extend the interval to two years.

2. High Intensity Surveillance
   - Pre-enrollment imaging (MRI or CT or EUS) study within 6 months prior to study randomization
   - Subsequent evaluation depends upon index cyst size
   - Cyst ≥1 and <3 cm: CT/MRI every 6 months for 1 year, then every 12 months for 2 years, then increase interval to 24 months
   - Cyst ≥2 and <3 cm: EUS within 6 months of pre-enrollment CT/MRI/EUS. If EUS negative repeat in 1 year. If next EUS negative, alternate CT/MRI and EUS every 12 months.
   - Cyst ≥3 cm: Alternate CT/MRI with EUS every 3-6 months