ExoLuminate: Observational Registry Study for Detection of Pancreatic Adenocarcinoma (PDAC) in High-Risk or Clinically Suspicious Patients

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Background

- Pancreatic Ductal Adenocarcinoma (PDAC) is the most common form of pancreatic cancer and one of the deadliest cancers in the U.S. The low 5-year survival rate (~11%) is mainly because PDAC is often diagnosed too late (at the regional or distant state) when the window for curative resection has narrowed.
- The lack of high accuracy biomarkers poses a challenge for early diagnosis.
- We developed **a liquid biopsy test, the ExoVita™ Pancreas**, that has high sensitivity and specificity for the detection of PDAC at stages I and II.[1,2]
- ExoVita™ Pancreas measures protein biomarkers on extracellular vesicles (EV) isolated using an alternating current electrokinetics (ACE) technology.
- Data acquisition and data analysis workflows are in Figures 1 and 2.
- Performance characteristics of the ExoVita™ Pancreas in early stages PDAC are in Table 1.

Purpose of the Study

- Here we describe the ExoLuminate study, an ongoing registry study that aims to generate real-word evidence for **early detection of PDAC in high-risk and clinically suspicious patients.** The study will also expand the validation of the **ExoVita™ Pancreas test**.
- The study includes patients that are 1). at high-risk of developing PDAC (due to family history, germline mutations, precursor lesions, hereditary pancreatitis, new onset diabetes) and 2). Biopsy-proven PDAC or clinically- suspicious.

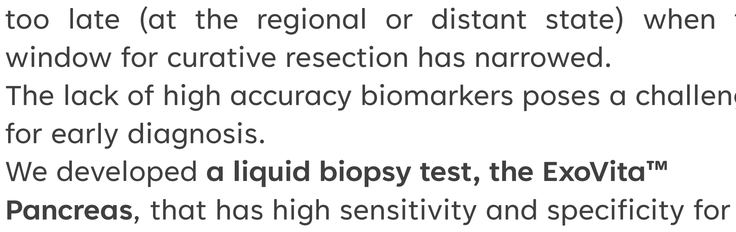

Figure 1. Data Acquisition Workflow. Samples are collected in K_2EDTA plasma and the EVs are isolated on the Verita™ Platform (Biological Dynamics). Protein concentration on isolated EVs are evaluated with a commercial multiplex immunoassay.

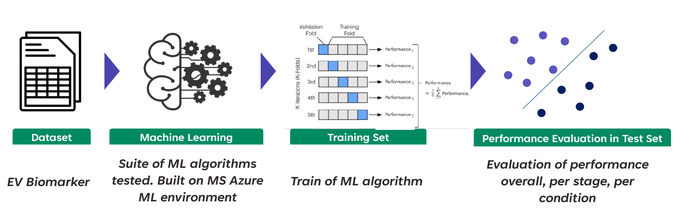

Figure 2. Data Analysis Workflow. The dataset containing EV biomarker information and subject information is input into a machine learning (ML) pipeline that evaluates a suite of ML algorithms to find the optimal one to differentiate cases (PDAC stages I and II) vs. controls.

Table 1. Performance Summary in Training and Test Sets for Baseline Model

Cohort	Training Set (95% CI)			Test Set (95% CI)		
	N	Sensitivity, %	Specificity, %	N	Sensitivity, %	Specificity, %
PDAC Cases	105	**93.3** (86.9 – 96.7)		20	**95.0** (76.4 – 99.1)	
Stage I	39	94.9 (83.1 – 98.6)		10	100.0 (72.2 – 100)	
Stage II	66	92.4 (83.5 – 96.7)		10	90 (59.6 – 98.2)	
Controls	545		**91.0** (88.3 – 93.1)	31		**96.8** (83.8 – 99.4)

Study Overview

Study Overview

- Prospective, multi-center, observational, registry study.
- Target enrollment n > 5000 subjects with >20 sites nationwide.
- Duration: 3 years (2-year accrual, 1 year follow-up).
- Q-6months timepoints per patient (baseline, 6mo, 1 year) (Figure 3).

Study Objectives

- ExoVita™ Pancreas is non-inferior to standard-of-care surveillance (SOC) for early detection of PDAC in high-risk patients or patients with clinical suspicion of PDAC.
- Optimize sensitivity for early detection of cancer in high-risk populations.

Study Endpoints

- Performance of ExoVita™, stage shift, time to diagnostic resolution, comparison to SOC surveillance (e.g. imaging, CA19-9).

Conclusions

- A new novel liquid biopsy using EV protein signatures has high sensitivity and specificity in PDAC at early stages.
- This study, which aims to demonstrate our test in *high-risk* patients (family history of PDAC, known germline mutations, precursor lesions, hereditary pancreatitis, new onset diabetes) will provide real-world evidence on the performance of the ExoVita test, as well as generate the data involved in clinically stage-shifting patients with hopes to improve patient outcomes in pancreatic cancer.

ExoLuminate Study (NCT# 05625529)

NOW ENROLLING

The ExoLuminate Study

A clinical study for those at risk for developing pancreatic cancer

Subject Cohorts and Timing

Cohort 1 | High Risk Population

- Germline mutations known to be associated with cancer (see Table 2).
  - STK11 (**Peutz-Jeghers syndrome**), any age.
  - CDKN2A, p16 (**Familial atypical multiple mole and melanoma; FAMMM**), any age.
  - BRCA1, BRCA2, ATM, PALB2, age ≥45 or 10 years younger than youngest afflicted relative.
  - MLH1, MSH2, MSH6, PMS2, EPCAM, TP53 (**HNPCC or Lynch Syndrome**), age ≥50 or 10 years younger than youngest afflicted relative.
  - **Hereditary Pancreatitis** with confirmed PRSS1 mutation, age ≥40.
- Family member(s) who have at least one first-degree relative (FDR) affected by pancreatic cancer, age ≥50 or 10 years younger than youngest afflicted relative.
- Intraductal papillary mucinous neoplasms (IPMNs), any age.
- Personal history of pancreatitis, any age.
  - Acute pancreatitis.
  - Chronic Pancreatitis.
- New-onset Diabetics (NOD), age ≥50.

Cohort 2 | Clinically-Suspicious or Pathologically-Confirmed

- Clinical findings suspicious for early stage PDAC.
- Biopsy-proven, PDAC stages I-IV.

Table 2: Genetic mutations associated with pancreatic cancer

BRCA1	BRCA2	PALB2
CDKN2A	ATM	TP53
STK11	MLH1	MSH2
MSH6	PMS2	PRSS1
EPCAM		

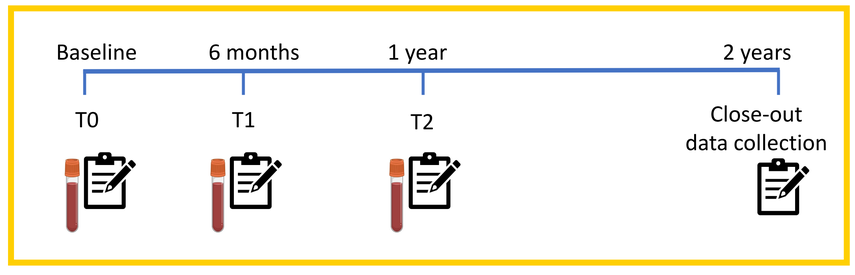

Figure 3. Study visits occur every 6 months with additional data collection 2 years after baseline.

Disclosures & References

Disclosures

This study is sponsored by Biological Dynamics, Inc.

References

1. Hinestrosa et al. *Front. Bioeng. Biotech.* **2020**, *8*, 581157
2. Hinestrosa et al. *Commun. Med.* **2022**, *2*, 29

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