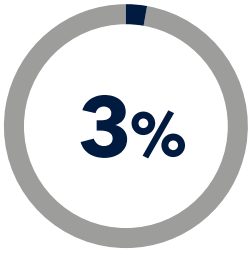
Avantect

Avantect Pancreatic Cancer Test

The only test that can detect Pancreatic Cancer at very early stages.

From stage IA and over

Early detection may make all the difference



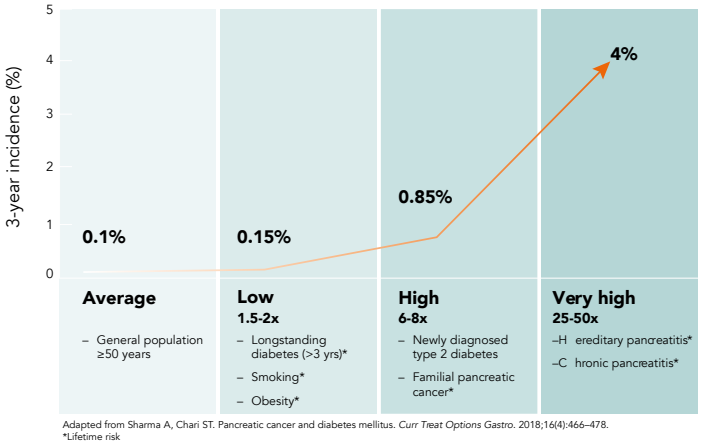
5-year relative survival for distant pancreatic cancer

vs

5-year survival at stage IA[2]

Pancreatic Cancer Risk Factors and relative risk

Risk increases with family history of pancreatic and other cancers, linked to gene mutations.



Adapted from Sharma A, Chari ST. Pancreatic cancer and diabetes mellitus. *Curr Treat Options Gastro.* 2018;16(4):466–478.
*Lifetime risk

Pancreatic cancer risk and 3-year case incidence.

Group or Affected Gene(s)	Risk of PaC
General Population	1
BRCA1	RR 2.26 (95% CI: 1.26-4.06)
BRCA2, PALB2	RR 3.5 to 6.2 (95% CI: 1.87-6.58)
Lynch Syndrome (*MLH1, MSH2, MSH6*)	RR 8.6 to 11
FAMM (*CKDN2A*)	RR 13 to 39
ATM	RR 3.92 (95% CI: 0.44-14.2)
Hereditary Pancreatitis (*PRSS1, SPINK1*)	SIR 53 (95% CI: 23-105)
Peutz-Jeghers Syndrome (*STK11*)	RR 132 (95% CI: 44-261)

Pancreatic cancer (PaC) predisposition syndromes and relative risk of the disease. RR, relative risk; SIR, standardized incidence ratio

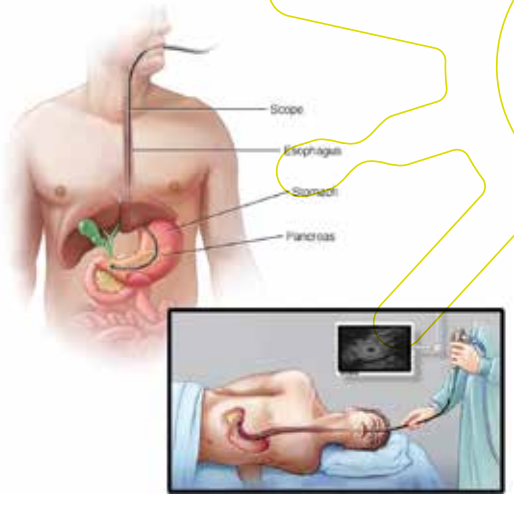
Recommended Avantect surveillance for individuals with hereditary and familial risk

The best surveillance method for high-risk individuals would be, alternately, an MRI/EUS exam and after 6 months to a year, an Avantect test, after exceeding the international guidelines' suggested age for screening initiation.

The advantages of the recommended surveillance model suggested:

1 Less invasive than endoscopic ultrasound (EUS has the highest sensitivity and specificity from other screening methods, but it is highly invasive and impractical for routine surveillance and demand high expertise from the physician who will use it).

2 Higher sensitivity and specificity than any other screening methods in very early pancreatic cancer stages IA-II



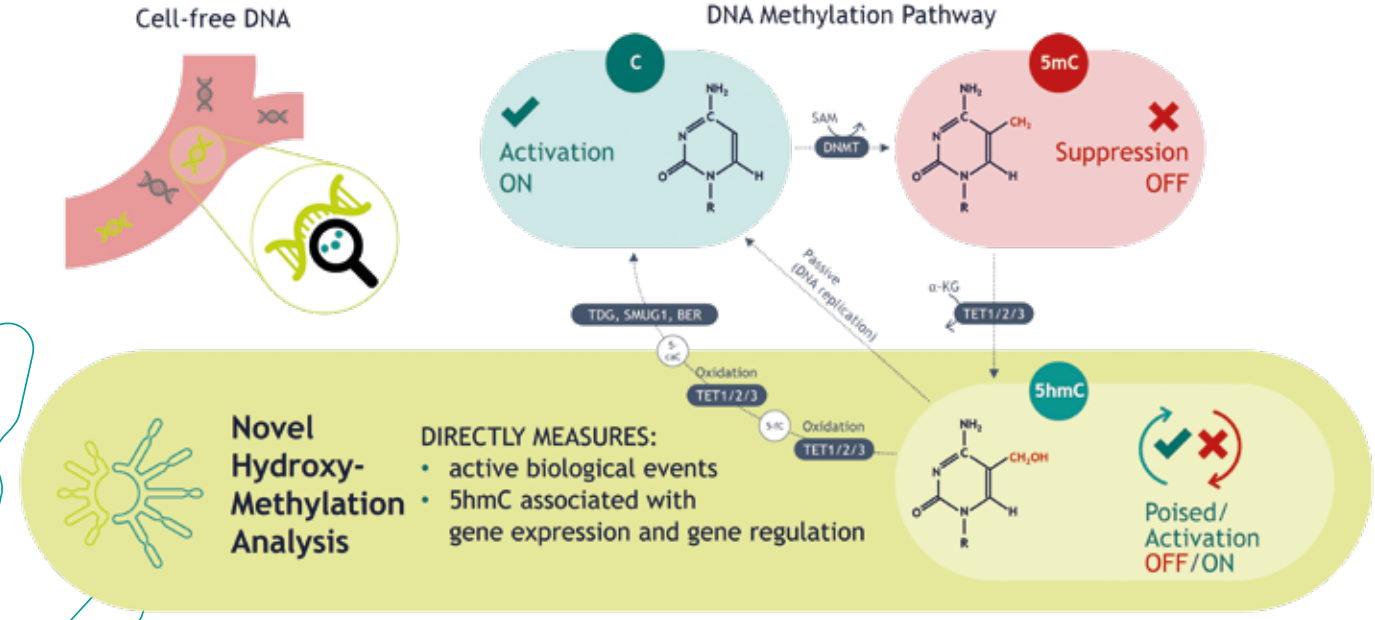
Technical Details

The science that sees beyond the code

Epigenetic changes are present in the earlier stages of pancreatic cancer. [4]Chemical modifications of DNA such as 5-hydroxymethylcytosine (5hmC) have now been identified as powerful biomarkers for pancreatic cancer. The Avantect test uses a combination of 5hmC profiling and whole-genome sequencing in a single, DNA-based blood test to identify pancreatic cancer at very early stages of disease where interventions have been shown to improve survival.

Avantect's cutting-edge epigenomics

Directly measures active biology as cells become cancerous



Purpose-built

Specifically designed for early detection of pancreatic cancer

Easy-to-use

A routine blood draw makes it easy to incorporate into clinical management protocols

Actionable report

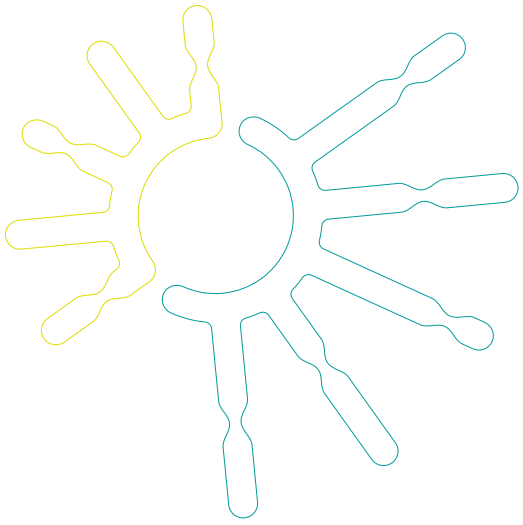
Clear results with recommendations for next steps

Who and when should be tested according to NCCN Guidelines

Gene	Absolute Risk	Management	Age for Surveillance**
ATM	~5%–10%	Screen P/LP* variant carriers with a family history of pancreatic cancer	50-55 years old
BRCA1	≤5%	Screen P/LP variant carriers with a family history of pancreatic cancer	50-55 years old
BRCA2	5%–10%	Screen P/LP variant carriers with a family history of pancreatic cancer	50-55 years old
CDKN2A	>15%	Screen P/LP variant carriers	40 years old
MSH2, MLH1, MSH6, EPCAM	<5%–10%	Screen P/LP variant carriers with a family history of pancreatic cancer	50-55 years old
PALB2	2%–5%	Screen P/LP variant carriers with a family history of pancreatic cancer	50-55 years old
STK11	>15%	Screen P/LP variant carriers	30-35 years old
TP53	~5%	Screen P/LP variant carriers with a family history of pancreatic cancer	50-55 years old

* *Pathogenic (P)/Likely Pathogenic (LP)*

** *or 10 years younger than the earliest exocrine pancreatic cancer diagnosis in the family, whichever is earlier.*



NCCN GUIDELINES 2024

PANCREATIC CANCER SCREENING

Emerging data have examined the efficacy of pancreatic cancer screening in select individuals at increased risk for exocrine pancreatic cancer. To date, most such studies have restricted pancreatic cancer screening to individuals with:

1 A known P/LP germline variant in a pancreatic cancer susceptibility gene (*ATM, BRCA1, BRCA2, CDKN2A, MLH1, MSH2, MSH6, EPCAM, PALB2, STK11*, and *TP53*; see GENE-A and a family history of pancreatic cancer (first-degree or second-degree relative) from the same side of the family as the germline P/LP variant ; or

2 A family history of exocrine pancreatic cancer in ≥1 first-degree and ≥1 second-de-gree relatives from the same side of the family, even in the absence of a known P/LP germline variant (many centers would enroll individuals with one affected first-degree and one second-degree relative); or

3 Some groups have recommended pancreas surveillance for P/LP variant carriers in the absence of a family history.

- For individuals considering pancreatic cancer screening, the panel recommends that screening be performed in experienced high-volume centers. The panel recommends that such screening only take place after an in-depth discussion about the potential limitations to screening, including cost, the high incidence of benign or indeterminate pancreatic abnormalities, and uncertainties about the potential beneits of pancreatic cancer screening.

- Consider screening using annual contrast-enhanced MRI/magnetic resonance chol- angiopancreatography (MRCP) and/or endoscopic ultrasound (EUS), with con- sideration of shorter screening intervals, based on clinical judgment, for individ- uals found to have potentially concerning abnormalities on screening. Studies have typically started screening with contrast-enhanced MRCP and/or EUS in individuals at increased risk for pancreatic cancer. The panel emphasizes that most small cystic lesions found on screening will not warrant biopsy, surgical resection, or any other intervention.

Genekor's retrospective data of the positive samples to P/LP variants associated with pancreatic cancer.

From the 7.000 total Heredi-GENE-tested individuals, the following results came out:

857

examinees were positive in ***ATM, MLH1, MSH2, MSH6, TP53, PALB2, BRCA1 AND BRCA2*** gene mutations.

8,8%

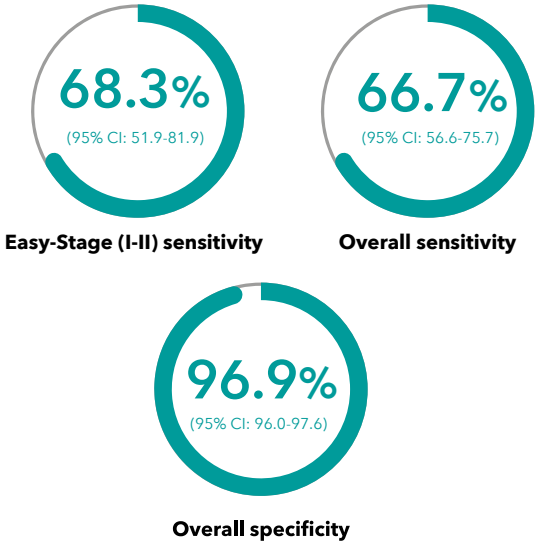
of them also had a family history of pancreatic cancer.

So, a total of

78

patients should undergo the Avantect test when at the right age to start the screening, according to NCCN guidelines.

Optimized performance in high-risk patients



The Avantect test has been validated in patients at high risk for pancreatic cancer.

Pancreatic cancer is an exceptionally lethal malignancy with increasing incidence. The key challenge in the treatment of pancreatic cancer is that the diagnosis is usually made at a late stage when potentially therapeutic surgical resection is no longer an option. Understanding and identifying patients with common risk factors for developing pancreatic cancer is crucial to enable timely deployment of potentially lifesaving, state-of-the-art early detection methods such as blood-based cfDNA testing.

ATM

85 patients

- 43 BrCa
- 3 Colon
- 6 Pancreatic
- 3 Ovarian
- 30 Other cancer type

12

with Family History of Pancreatic Cancer (14%)

MLH1

23 patients

- 2 BrCa
- 12 Colon
- 5 Ovarian
- 4 Other cancer type

0

with Family History of Pancreatic Cancer (0%)

MSH2

17 patients

- 8 Colon
- 2 Ovarian
- 7 Other cancer type

3

with Family History of Pancreatic Cancer (17.6%)

MSH6

16 patients

- 5 BrCa
- 3 Colon
- 8 Other cancer type

1

with Family History of Pancreatic Cancer (6.25%)

TP53

17 patients

- 9 BrCa
- 3 Ovarian
- 5 Other cancer type

1

with Family History of Pancreatic Cancer (5.88%)

PALB2

80 patients

- 50 BrCa
- 5 Ovarian
- 2 Pancreatic
- 23 Other cancer type

6

with Family History of Pancreatic Cancer (7.5%)

BRCA1

374 patients

- 212 BrCa
- 52 Ovarian
- 5 Pancreatic
- 105 Other cancer type

27

with Family History of Pancreatic Cancer (7.2%)

BRCA2

274 patients

- 131 BrCa
- 21 Ovarian
- 2 Pancreatic
- 88 Other cancer type

13

with Family History of Pancreatic Cancer (5.3%)

Note: Family history is dynamic and shifting information. In case an individual's first or second degree relative develops pancreatic cancer, then the individual should begin screening according to guidelines.

Avantect | PANCREATIC CANCER TEST

Important information

The **Avantect Pancreatic Cancer Test** is an early detection test. The test does not establish a diagnosis of pancreatic cancer, and results should be considered in the context of other clinical criteria. A definitive diagnosis of cancer is rendered by clinical providers through a combined use of diag-nostic testing, imaging, biopsy, and pathological findings. Not all pancreatic cancers will be detect-ed. Some patients with pancreatic cancer may have a "Signal not detected" result. Some patients without pancreatic cancer may have a "Signal detected" result. False-negative and false-positive results are possible. A "Signal not detected" result does not guarantee that no pancreatic cancer is present. In some cases, no result is obtained. While this is very uncommon, it may be caused by shipping delays or when there is not enough cell-free DNA for the test in the patient's blood. If this happens, additional blood samples may be required to produce a patient result.

The test was developed in the ClearNote Health CLIA-certified (CLIA# 05D2249973) and CAP-ac-cred-ited (CAP# 9219174) laboratory and has not been cleared or approved by the US Food and Drug Ad-ministration (FDA).

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