IX SIMPOSIO · SYMPOSIUM | 2024
BIOPSIA LÍQUIDA · LIQUID BIOPSY
EL CAMINO A LA ONCOLOGÍA DE PRECISIÓN · THE WAY TO PRECISION MEDICINE

25, 26 Y 27 DE ENERO · JANUARY 25th, 26th and 27th

Pancreatic ductal adenocarcinoma: Advances in the liquid biopsy and opportunities for targeted and immunotherapy.

Julie Earl, Ramón y Cajal Health Research Institute (IRYCIS), Carretera Colmenar Km 9,100. 28034. Madrid, Spain

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PANCREATIC DUCTAL ADENOCARCINOMA: A CLINICAL CHALLENGE

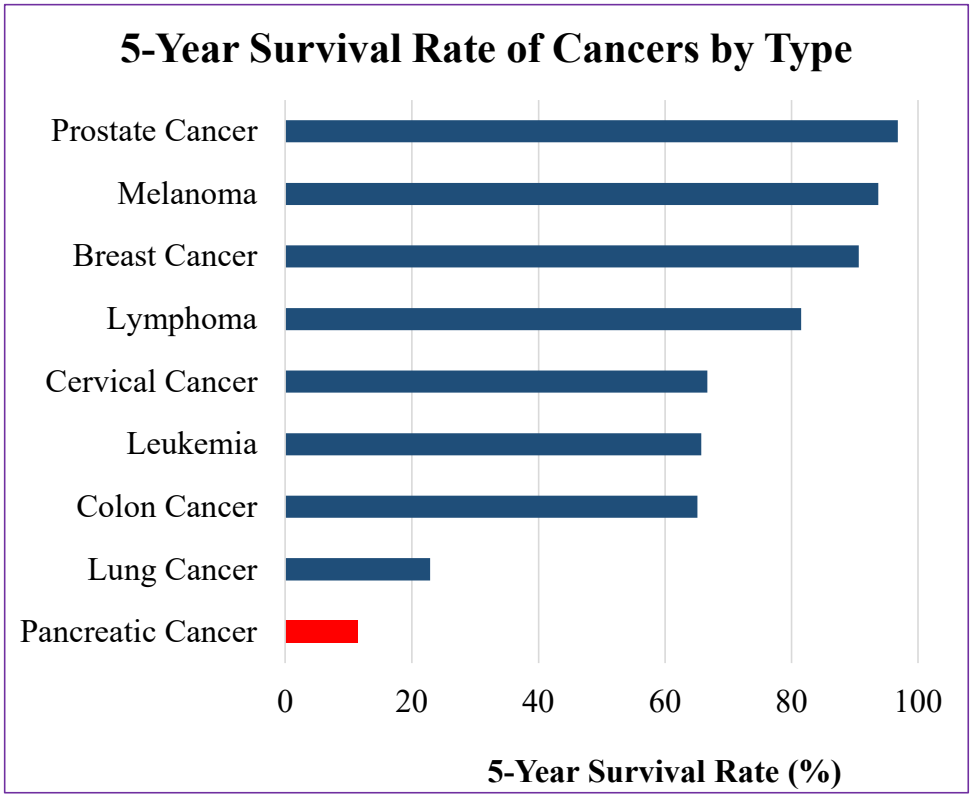
1 in 64 people will die from this disease

Almost everyone who gets pancreatic cancer **dies** from it

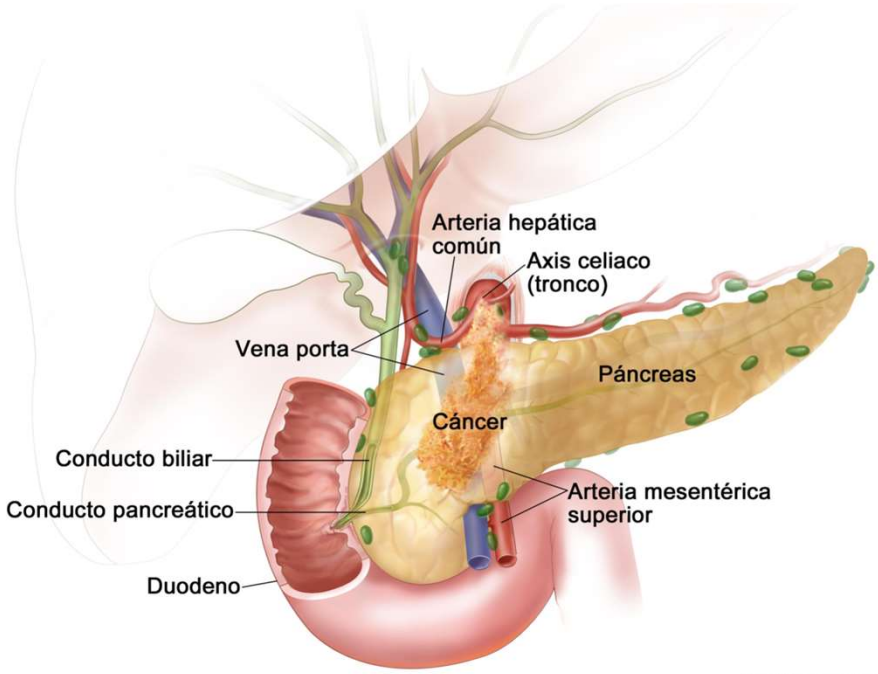
It is the **3rd** leading cause of cancer death and will become the **2nd** leading cause this decade- unless we change our strategy to tackle it

Early detection of pancreatic cancer is the key

POOR OVERALL SURVIVAL OF PDAC



Only 15-20% of patients are eligible for a surgical resection



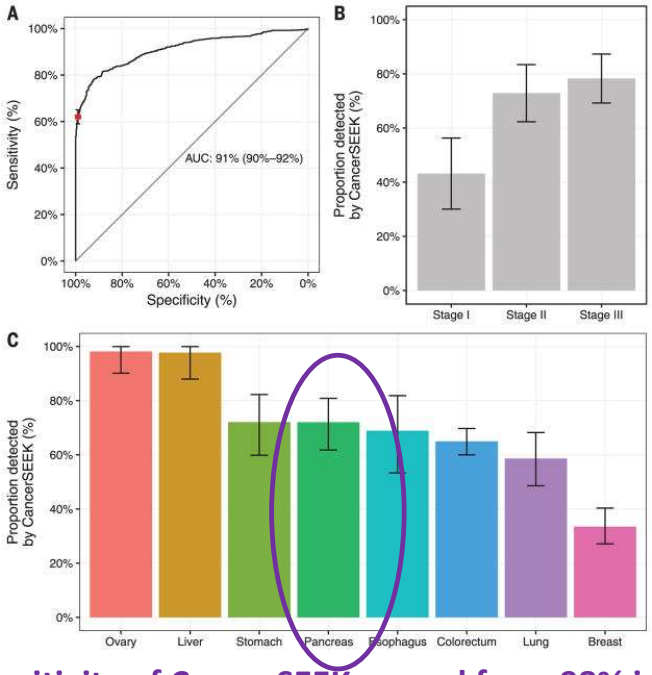
MULTI-CANCER TESTING VS PDAC SPECIFIC TESTING

Science. 2018 Feb 23;359(6378):926-930. doi: 10.1126/science.aar3247. Epub 2018 Jan 18.

Detection and localization of surgically resectable cancers with a multi-analyte blood test

Joshua D Cohen [1 2 3 4 5], Lu Li [6], Yuxuan Wang [1 2 3 4], Christopher Thoburn [3], Bahman Afsari [7], Ludmila Danilova [7], Christopher Douville [1 2 3 4], Ammar A Javed [8], Fay Wong [1 3 4], Austin Mattox [1 2 3 4], Ralph H Hruban [3 4 9], Christopher L Wolfgang [8], Michael G Goggins [3 4 9 10 11], Marco Dal Molin [4], Tian-Li Wang [3 9], Richard Roden [3 9], Alison P Klein [3 4 12], Janine Ptak [1 2 3 4], Lisa Dobbyn [1 3 4], Joy Schaefer [1 3 4], Natalie Silliman [1 2 3 4], Maria Popoli [1 3 4], Joshua T Vogelstein [13], James D Browne [14], Robert E Schoen [15 16], Randall E Brand [15], Jeanne Tie [17 18 19 20], Peter Gibbs [17 18 19 20], Hui-Li Wong [17], Aaron S Mansfield [21], Jin Jen [22], Samir M Hanash [23], Massimo Falconi [24], Peter J Allen [25], Lhibin Zhou [1 3 4], Chetan Bettegowda [1 3 4], Luis A Diaz Jr [1 3 4], Cristian Tomasetti [26 4 7], Kenneth W Kinzler [27 3 4], Bert Vogelstein [27 2 3 4], Anne Marie Lennon [26 4 8 10 11], Nickolas Papadopoulos [27 3 4]

CancerSEEK



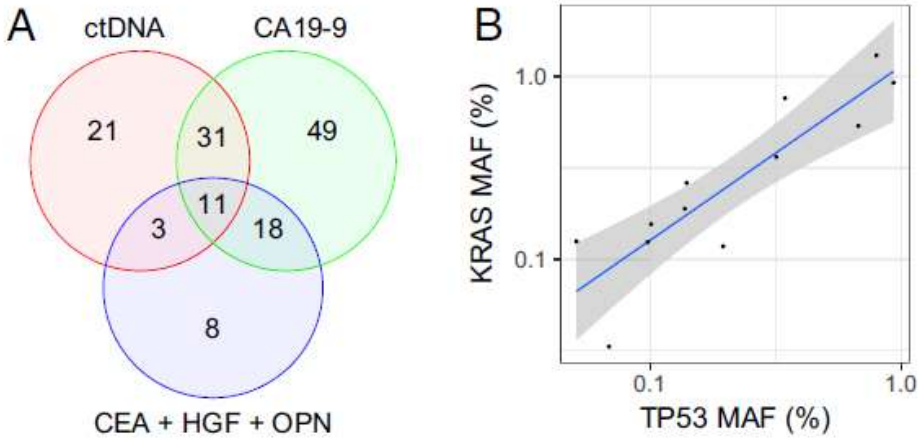
The median sensitivity of CancerSEEK ranged from 98% in ovarian cancers to 33% in breast cancers, with a specificity of >99%.

The median sensitivity of CancerSEEK was 43% for stage I, 73% for stage II and 78% for stage III cancers.

PNAS

Combined circulating tumor DNA and protein biomarker-based liquid biopsy for the earlier detection of pancreatic cancers

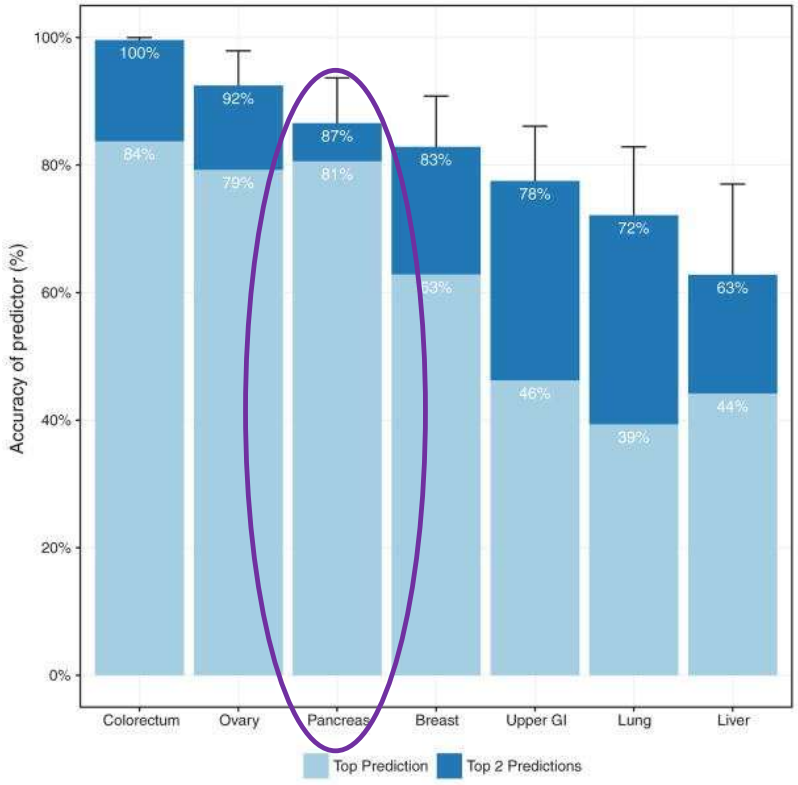
Joshua D. Cohen[a,b,c,d,e], Ammar A. Javed[f], Christopher Thoburn[c], Fay Wong[a,b,c,d], Jeanne Tie[g,h,i], Peter Gibbs[g,h,i], C. Max Schmidt[j,k], Michele T. Yip-Schneider[l], Peter J. Allen[f], Mark Schattner[m], Randall E. Brand[n], Aatur D. Singhi[o], Gloria M. Petersen[p], Seung-Mo Hong[q], Song Cheol Kim[r], Massimo Falconi[s], Claudio Doglioni[t], Matthew J. Weiss[f], Nita Ahuja[f], Jin He[f], Martin A. Makary[f], Anirban Maitra[u], Samir M. Hanash[v], Marco Dal Molin[d], Yuxuan Wang[a,b,c,d], Lu Li[c], Janine Ptak[a,b,c,d], Lisa Dobbyn[a,b,c,d], Joy Schaefer[a,b,c,d], Natalie Silliman[a,b,c,d], Maria Popoli[a,b,c,d], Michael G. Goggins[c,d,w,x], Ralph H. Hruban[c,d,x], Christopher L. Wolfgang[f], Alison P. Klein[c,d,y], Cristian Tomasetti[c,y,z], Nickolas Papadopoulos[a,c,d], Kenneth W. Kinzler[a,c,d], Bert Vogelstein[a,b,c,d,1], and Anne Marie Lennon[d,w,1]



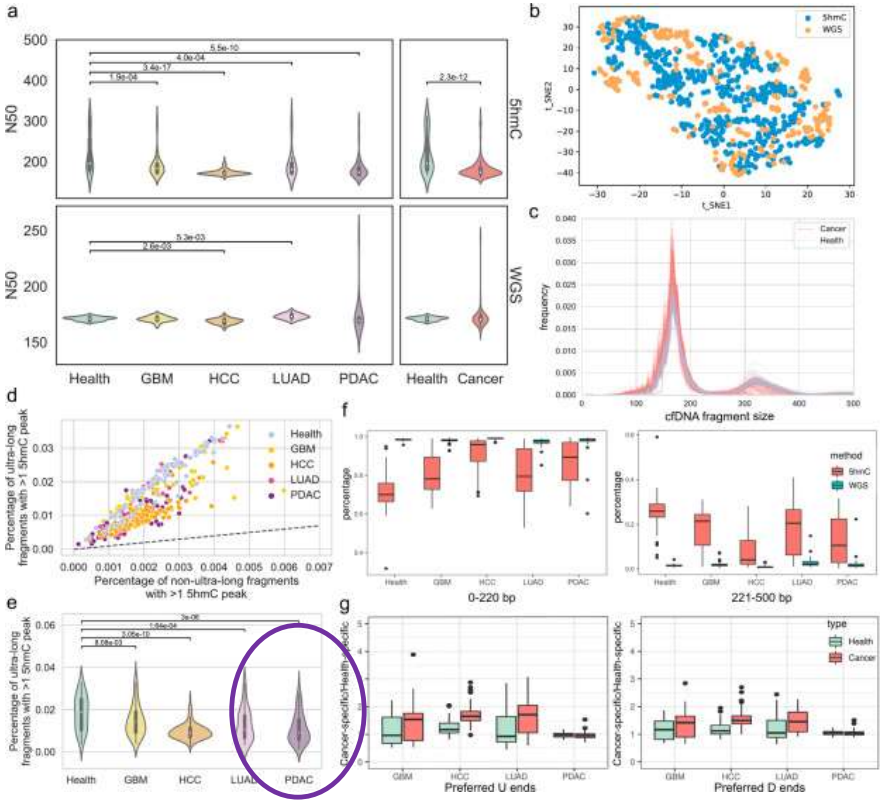
KRAS in conjunction with four thresholded protein biomarkers (CA19-9, CEA, hepatocyte growth Factor (HGF) and osteopontin (OPN)) had a sensitivity of 64% and 99.5% specificity.

TUMOR OF ORIGIN TESTING

Cancer SEEK



Epigenetic markers (5-Hydroxymethylcytosine) and fragmentomics of cell-free DNA



Driver gene mutations are usually not tissue-specific, the vast majority of the localization information was derived from protein markers.


Translational Oncology

Original Research

Integrated fragmentomic profile and 5-Hydroxymethylcytosine of capture-based low-pass sequencing data enables pan-cancer detection via cfDNA

Zhidong Zhang [1,*], Xuenan Pi [1,*], Chang Gao [1], Jun Zhang [1], Lin Xia [1], Xiaoqin Yan [1], Xinlei Hu [1], Ziyue Yan [1], Shuxin Zhang [1], Ailin Wei [1], Yuer Guo [1], Jingfeng Liu [1], Ang Li [1], Xiaolong Liu [1], Wei Zhang [1], Yanhui Liu [1], Dan Xie [1,*]

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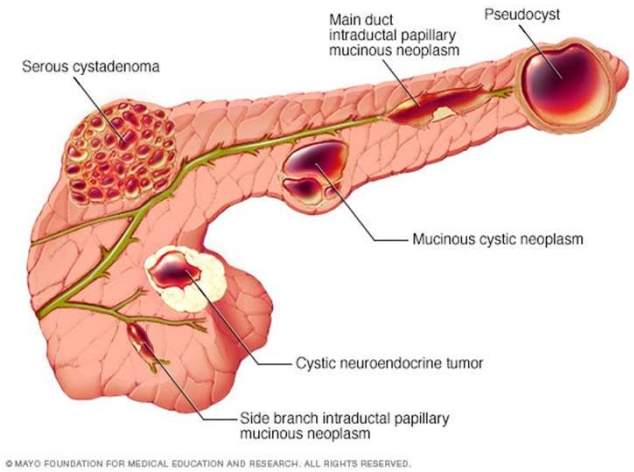
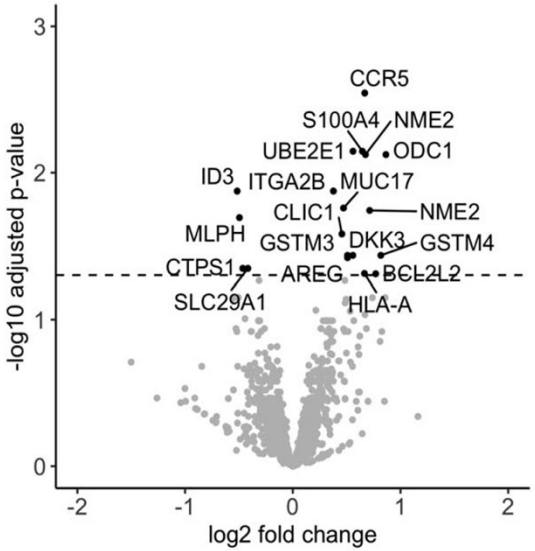
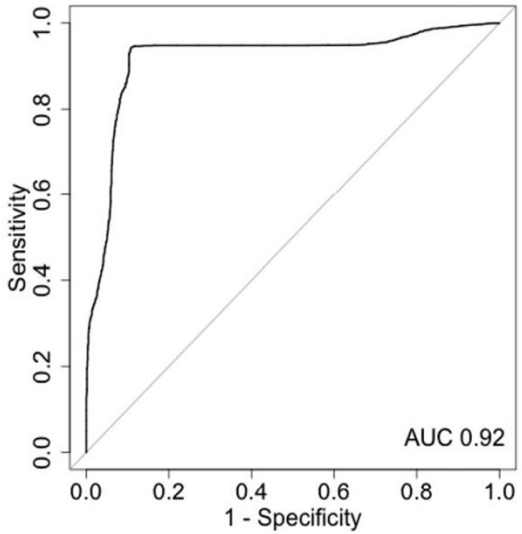
INTRAPAPILLARY MUCINOUS NEOPLASMS: IPMN







Susanne Roth et al. Noninvasive Discrimination of Low and High-risk Pancreatic Intraductal Papillary Mucinous Neoplasms. Annals of Surgery Volume 273, Number 6, June 2021

MUC17, ID3, AREG, ITGA2B, CSF2RA and CCR5 distinguish between low and high grade IPMN

NEW EARLY DETECTION BIOMARKERS ON THE HORIZON

PANCAID

PANcreatic CAncer Initial Detection via liquid biopsy

Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or European Health and Digital Executive Agency (HADEA). Neither the European Union nor the granting authority can be held responsible for them.

Funded by the European Union

The main objective of PANCAID is to provide a minimally invasive blood test using a comprehensive panel of liquid biopsy diagnostics (LBx) for early detection of pancreatic cancer and the malignant conversion of premalignant to invasive lesions.

PI Coordinator: Klaus Pantel and Matthias Lohr.

PLATAFORMA ISCIII BIOBANCOS Y BIOMODELOS

Primary Tumor Tissue: Fresh, FFPE

Liquid samples: Serum, Plasma, Saliva, Urine, Stool

Clinical Data: High Quality

Biomodels: 2D & 3D invitro, in vivo

PDAC EARLY DETECTION IN HIGH RISK GROUPS

More than 50 international registries of pancreatic cancer that offer high-risk screening

PRECEDE
The Pancreatic Cancer Early Detection Consortium

Highest Risk for individuals without history of PDAC meeting any of the following criteria:

1. 2+ relatives with PDAC on same side of family where 2 affected are first degree related to each other and at least 1 affected is first degree related to subject; **age 50+** or ≤10 years younger than earliest PDAC in family at time of diagnosis.
2. 2 affected first degree relatives with PDAC; **age 50+ or 10 years younger** than earliest PDAC in family
3. *BRCA1*, *BRCA2*, *PALB2*, *ATM*, *MLH1*, *MSH2*, *MSH6*, *PMS2*, *EPCAM* pathogenic or likely pathogenic variant AND 1 first or second degree relative with PDAC; **age 50+ or 10 years younger** than earliest PDAC in family
4. Familial Atypical Moles and Malignant Melanoma (FAMMM) with pathogenic or likely pathogenic *CDKN2A* variant; **age 40+**
5. Peutz-Jegher syndrome with *STK11* pathogenic or likely pathogenic variant; **age 35+**
6. Hereditary pancreatitis with *PRSS1* pathogenic or likely pathogenic variant and history of pancreatitis; **age 40+**

ExoVita™ Pancreas Assay: exosomes

ClearNote™ : epigenetics of cell free DNA

Biological Dynamics

ClearNote™ HEALTH

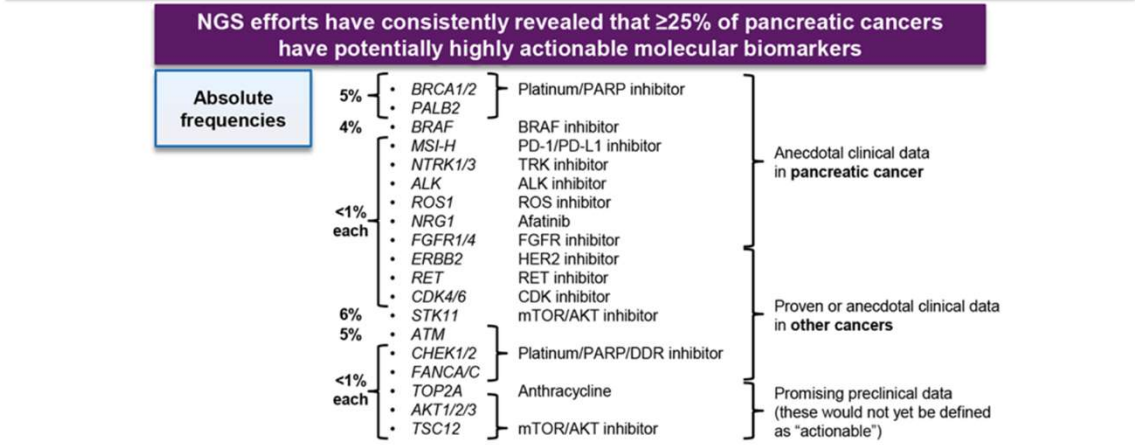
Avantect
EARLY CANCER DETECTION

PDAC ONCOLOGICAL TREATMENT

Adjuvant therapy after surgery
- Gemcitabine +/- Capecitabine
- FOLFIRINOX

Disseminated disease
- Gemcitabine
- Gemcitabine - Nab-Paclitaxel
- FOLFIRINOX
- 5FU-NalIRI

Actionable Findings in Pancreatic Cancer[1-11]



1. Singhi AD et al. *Gastroenterology*. 2019;156:2242-2253.e4. 2. Pishvaian MJ et al. *Clin Cancer Res*. 2018;24:5018-5027. 3. Heeke AL et al. *JCO Precis Oncol*. 2018;2018. 4. Aguirre AJ et al. *Cancer Discov*. 2018;8:1096-1111. 5. Witkiewicz AK et al. *Nat Commun*. 2015;6:6744. 6. Lowery MA et al. *Clin Cancer Res*. 2017;23:6094-6100. 7. Waddell N et al. *Nature*. 2015;518:495-501. 8. Bailey P et al. *Nature*. 2016;531:47-52. 9. Biankin AV et al. *Nature*. 2012;491:399-405. 10. Collisson EA et al. *Nat Med*. 2011;17:500-503. 11. Pishvaian MJ, Brody JR. *Oncology (Williston Park)*. 2017;31:159-166.

WHERE CAN BE APPLY TARGETED THERAPY IN PDAC?

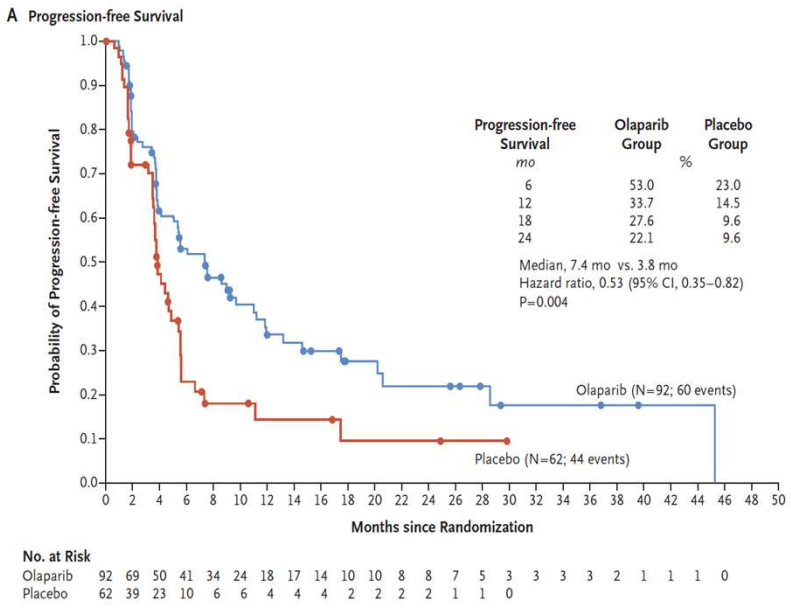
Germline BRCA mutations significantly increase risk of developing pancreatic cancer and can be found in up to 8% of patients with pancreatic cancer

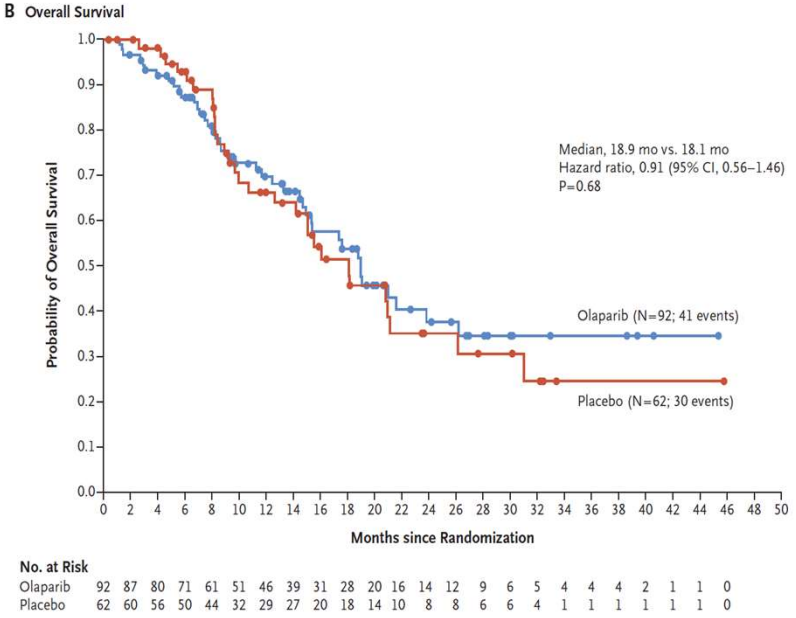
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Maintenance Olaparib for Germline *BRCA*-Mutated Metastatic Pancreatic Cancer

Talia Golan, M.D., Pascal Hammel, M.D., Ph.D., Michele Reni, M.D., Eric Van Cutsem, M.D., Ph.D., Teresa Macarulla, M.D., Ph.D., Michael J. Hall, M.D., Joon-Oh Park, M.D., Ph.D., Daniel Hochhauser, M.D., Ph.D., Dirk Arnold, M.D., Ph.D., Do-Youn Oh, M.D., Ph.D., Anke Reinacher-Schick, M.D., Ph.D., Giampaolo Tortora, M.D., Ph.D., Hana Algül, M.D., Ph.D., M.P.H., Eileen M. O'Reilly, M.D., David McGuinness, M.Sc., Karen Y. Cui, M.D., Ph.D., Katia Schlienger, M.D., Ph.D., Gershon Y. Locker, M.D., and Hedy L. Kindler, M.D.



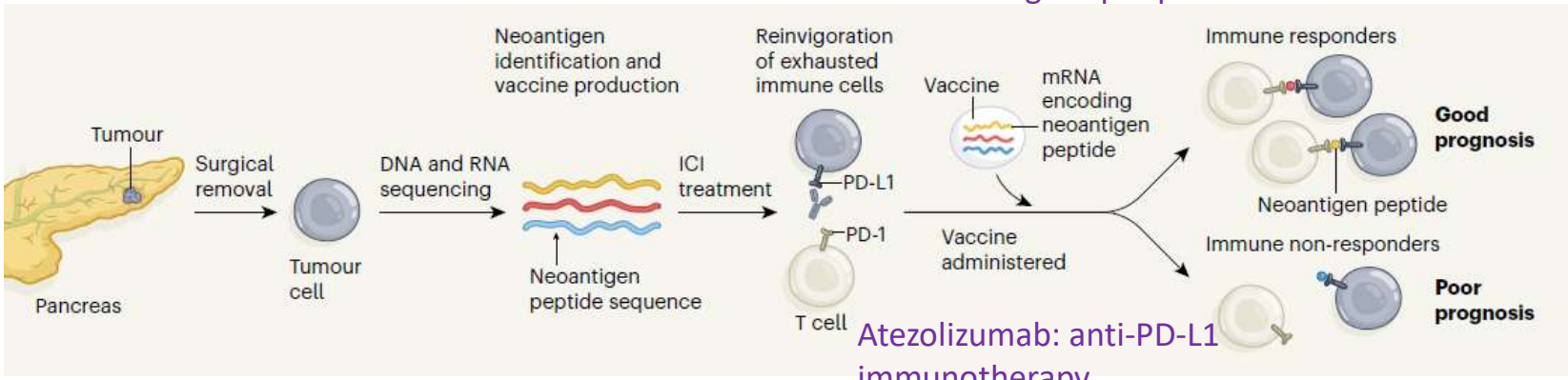


Platinum-based chemotherapies and poly (ADP-ribose) polymerase inhibitors are effective treatment options which may offer survival benefits in BRCA+ cases and HRD

WHERE CAN BE USE IMMUNOTHERAPY?

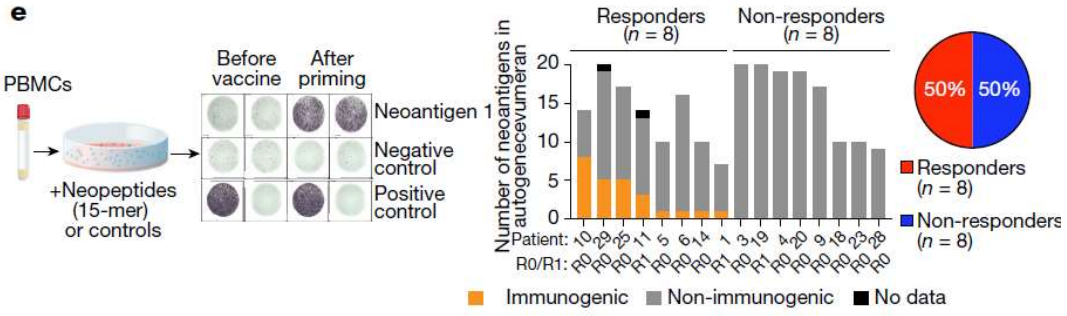
Vaccine boosts T cells that target pancreatic tumours

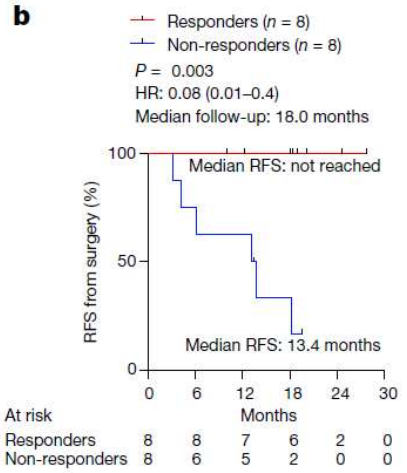
a maximum of 20
neoantigens per patient

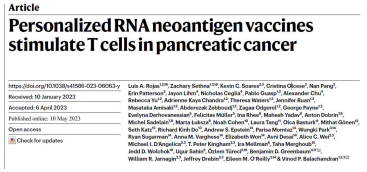


chemotherapy
mFOLFIRINOX

Atezolizumab: anti-PD-L1
immunotherapy






Article
Personalized RNA neoantigen vaccines stimulate T cells in pancreatic cancer

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CONSIDERATIONS FOR THE LIQUID BIOPSY IN PDAC

- The liquid biopsy is an important resource due to the limited availability of tumor tissue for molecular studies
- Effective multi modal biomarkers are needed for PDAC early detection
- Validation of biomarkers in multicenter International and European cohorts
- Targeted therapy and immunotherapy are possible treatment in selected patients, with a potential role of the liquid biopsy for patient management in the future?

INSTITUTO RAMÓN Y CAJAL DE INVESTIGACIÓN SANITARIA IRYCIS

PANGENFAM
SPANISH FAMILIAL PANCREATIC CANCER REGISTRY

THANK YOU

PLATAFORMA ISCIII
BIOBANCOS Y BIOMODELOS

PRECEDE
The Pancreatic Cancer Early Detection Consortium

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