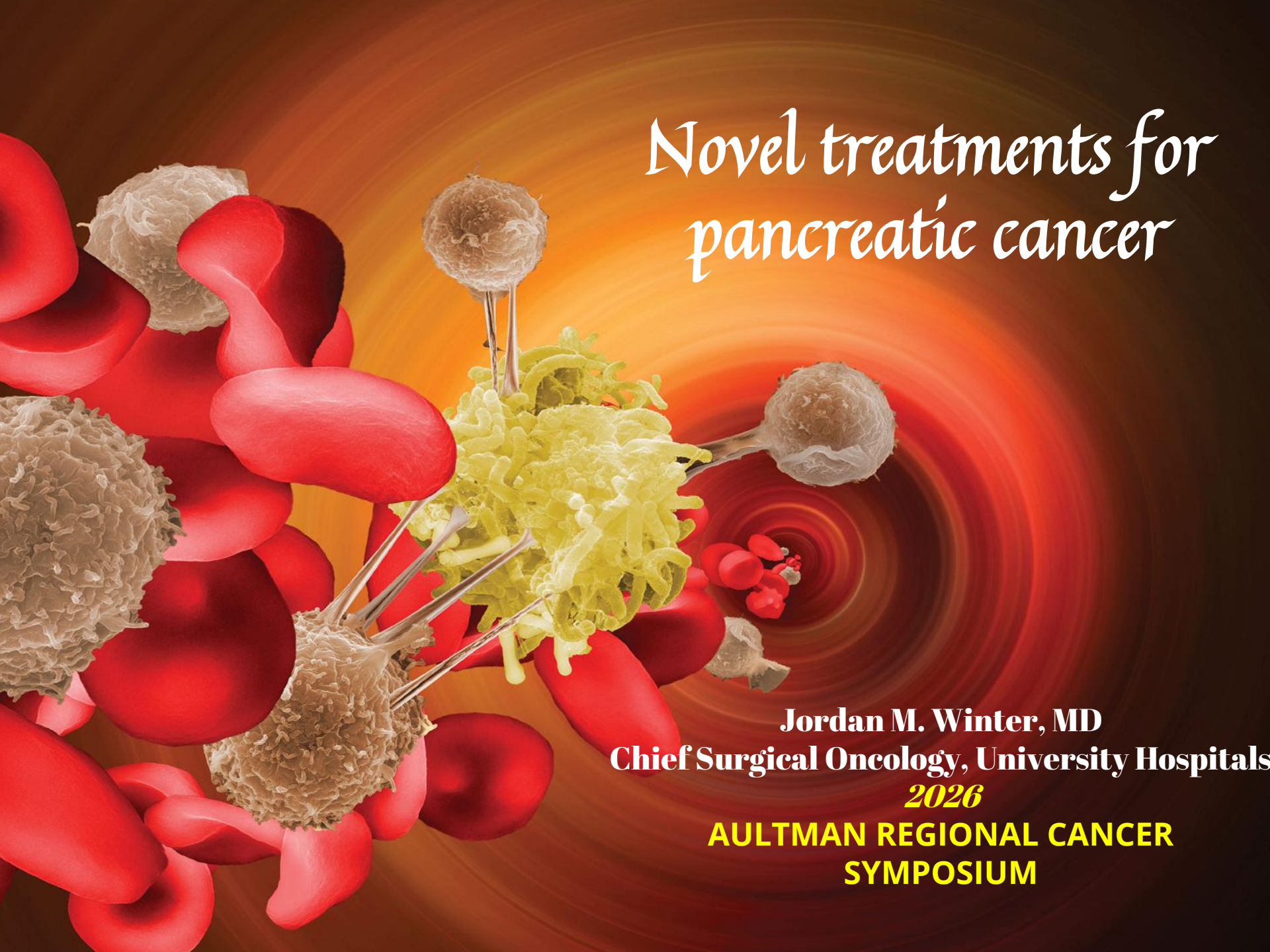




Novel treatments for pancreatic cancer

Jordan M. Winter, MD
Chief Surgical Oncology, University Hospitals
2026

**AULTMAN REGIONAL CANCER
SYMPOSIUM**

Deaths

#	Cancer	Deaths/Yr
1	Lung	124,990
2	Colorectal	55,230
3	Pancreas	52,740
4	Breast	42,670
5	Prostate	36,320
6	Liver	30,980
7	Leukemia	23,910
8	NHL	19,970
9	Brain	18,350
10	Bladder	17,870
11	Esophagus	16,290
12	Kidney	15,160

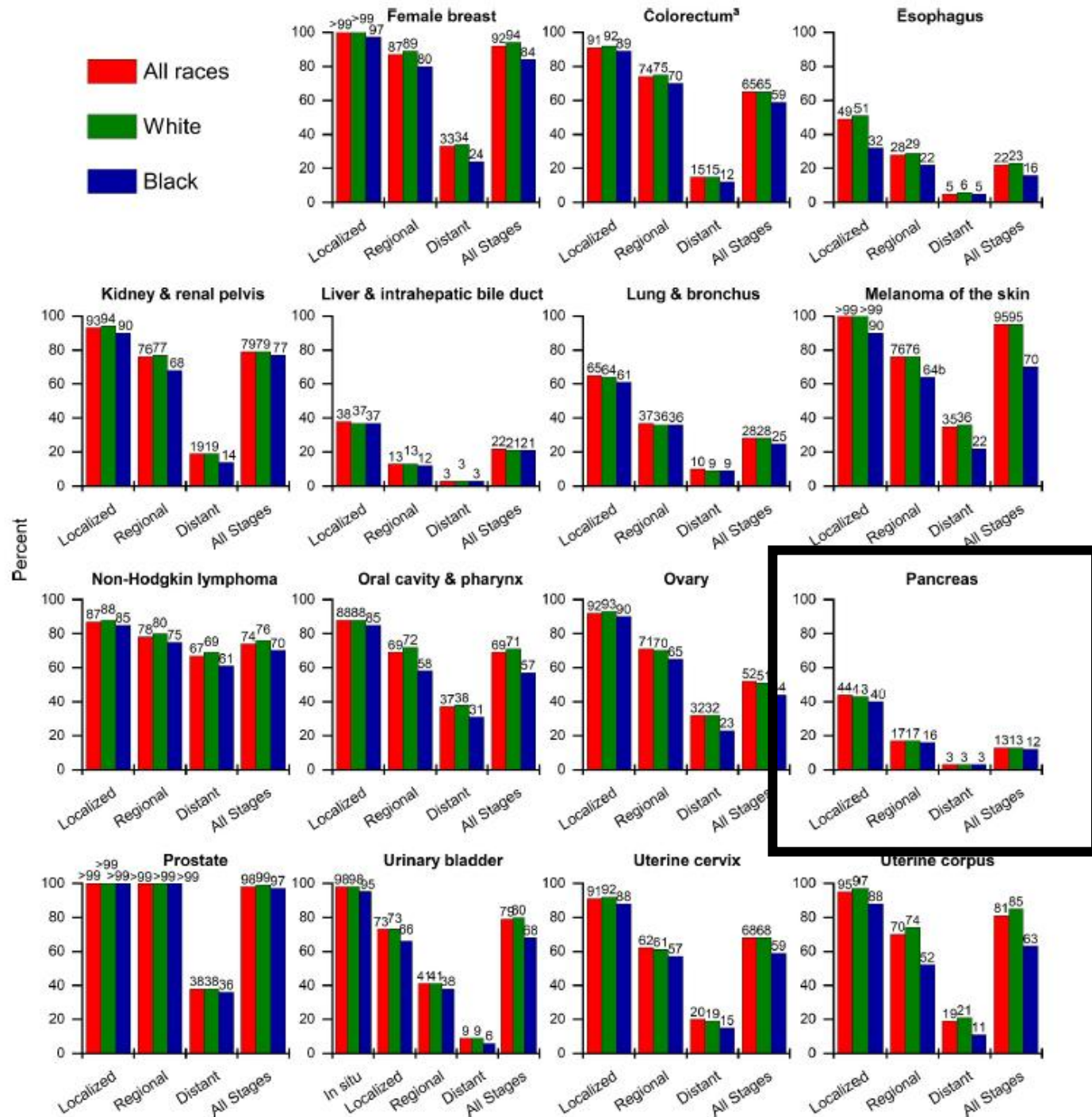
#	Cancer	Deaths/Yr
13	Uterine	14,450
14	Oral	13,150
15	Ovary	12,450
16	Myeloma	10,850
17	Stomach	10,740
18	Melanoma	8,510
19	Soft tissue	5,400
20	Bile duct	4,590
21	Cervix	4,200
22	Thyroid	3,960

Death Rate = case/deaths

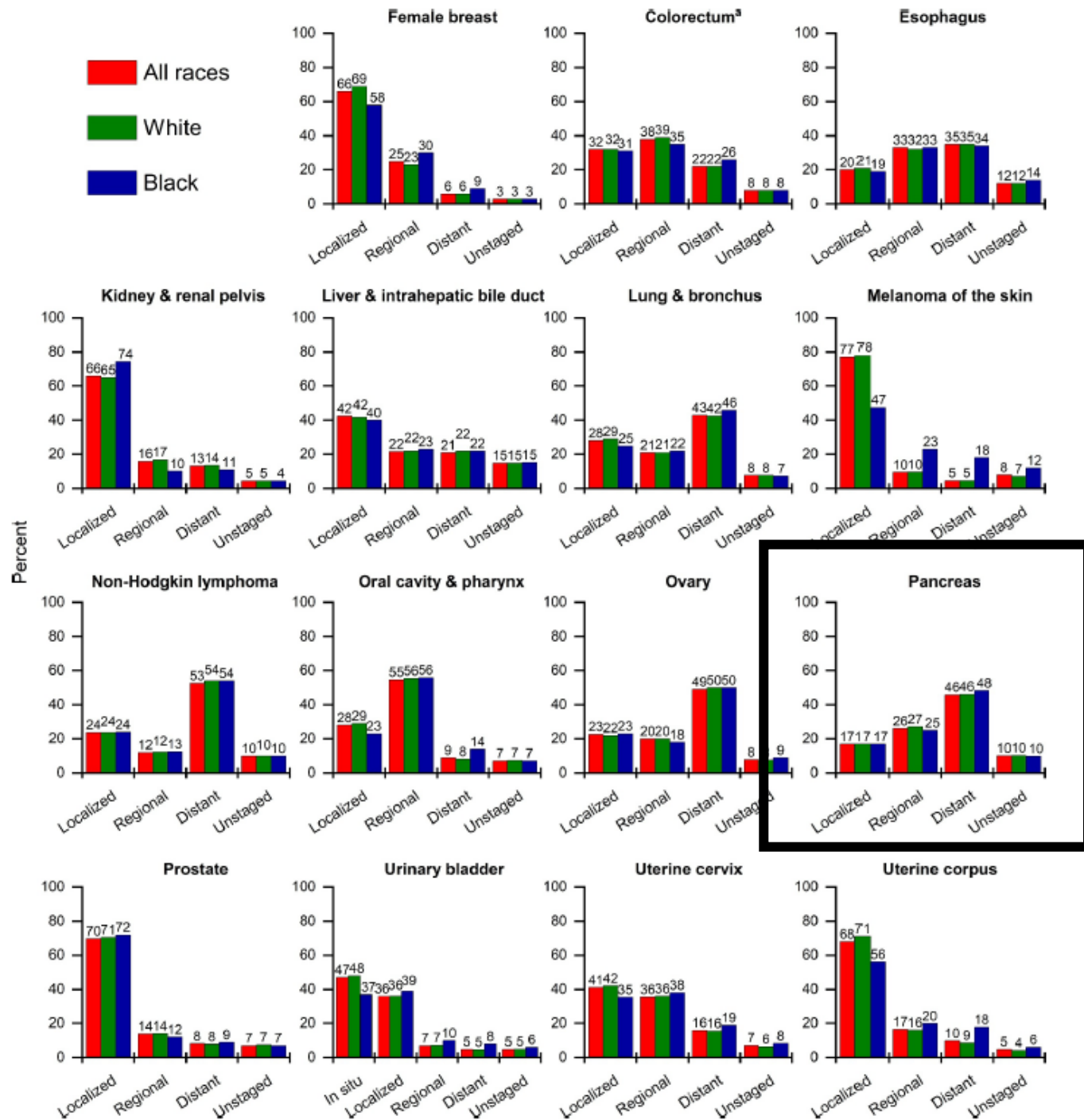
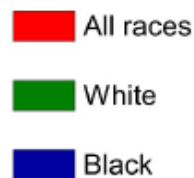
#	Cancer	Death rate
1	Pancreas	78.10%
2	Brain	74.17%
4	Liver	73.17%
3	Esophagus	72.30%
5	Ovary	59.26%
6	Lung	54.48%
7	Soft tissue	38.82%
8	Bile duct cancer	36.31%
9	Leukemia	35.27%
10	Colorectal	34.77%
11	Stomach	34.08%
12	Larynx	32.22%
13	Cervix	31.13%

#	Cancer	Death rate
14	Myeloma	30.14%
15	NHL	25.18%
16	Oral	21.74%
17	Uterine	21.17%
18	Bladder	21.14%
19	Kidney	18.84%
20	Breast	13.15%
21	Prostate	10.88%
22	Melanoma	7.60%
23	Thyroid	5.13%

5 year survival



Stage distribution

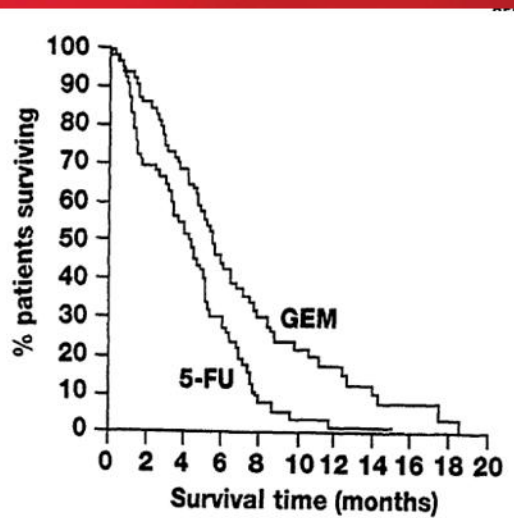


5 year survival for localized and metastatic cancer

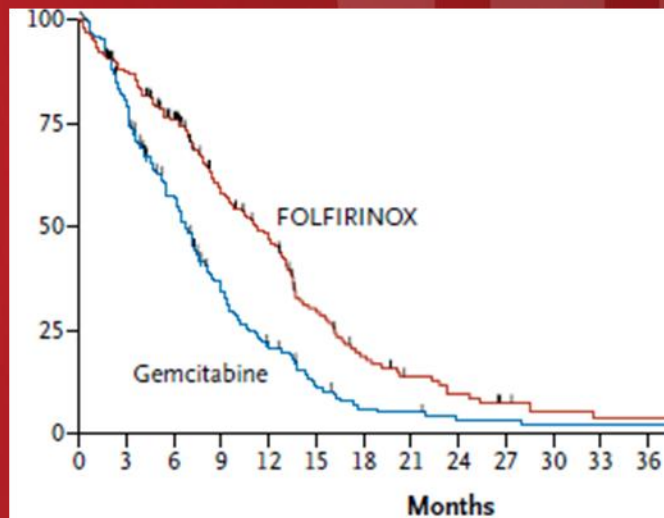
Cancer	Localized	Metastatic
Breast	>99%	33%
Prostate	>99%	38%
Lung	65%	10%
Colorectal	91%	15%
Melanoma	>99%	35%
Bladder	98%	9%
Kidney	93%	19%
NHL	87%	67%
Uterine	95%	19%
Pancreas	44%	3%

Metastatic pancreatic cancer

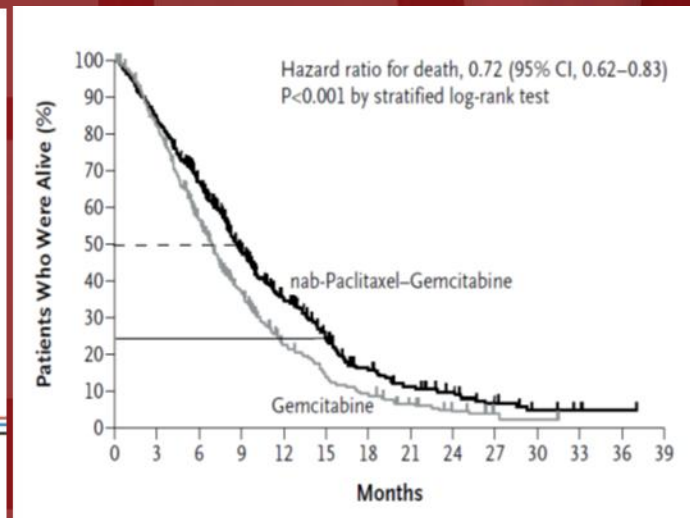
Gem v 5Fu, 1996



Gem v FOLFIRINOX, 2011



Gem v Gem/Abraxane, 2013



	GEM	5FU
Survival	5.6	4.4
Response	5%	0%
SD	39%	19%
PFS	2.3	1

	GEM	FOLFIRINOX
Survival	6.8	11.1
Response	9%	32%
SD	42%	39%
PFS	3.3	6.4

	GEM	GEM/ABRAX
Survival	6.7	8.5
Response	7%	23%
SD	26%	25%
PFS	3.7	5.5

STATE OF PANCREATIC CANCER RESEARCH



KRAS inhibitors and pancreatic cancer vaccines

SCIENCE

F.D.A. Approves Drug Poised to Transform Care for Pancreatic Cancer

In a key clinical trial, patients who got the pill, daraxonrasib, lived twice as long as those who got chemotherapy.

By Gina Kolata, Rebecca Robbins and Carolyn Y. Johnson

AUG. 26

PRINT EDITION F.D.A. Nod for Promising Pancreatic Cancer Pill | August 27, 2026, Page A1



SCIENCE

The Race to Develop More Medicines Like the New Pancreatic Cancer Drug

Companies are testing dozens of similar drugs in cancers of the pancreas, lung, colon and more.

By Rebecca Robbins and Carolyn Y. Johnson

AUG. 27



BUSINESS

A \$480,000-a-Year Pill Reflects a New Normal for Cancer Drugs

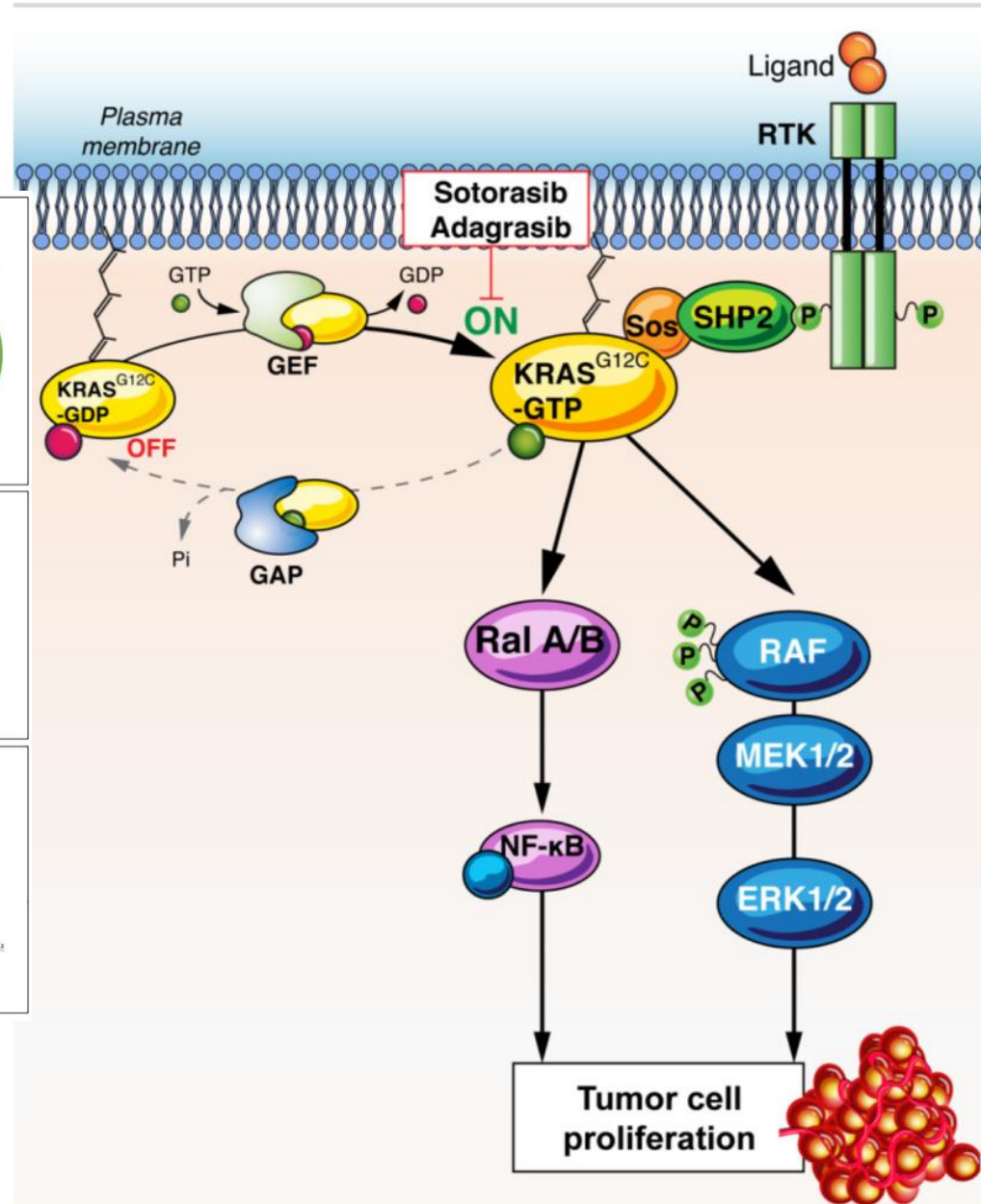
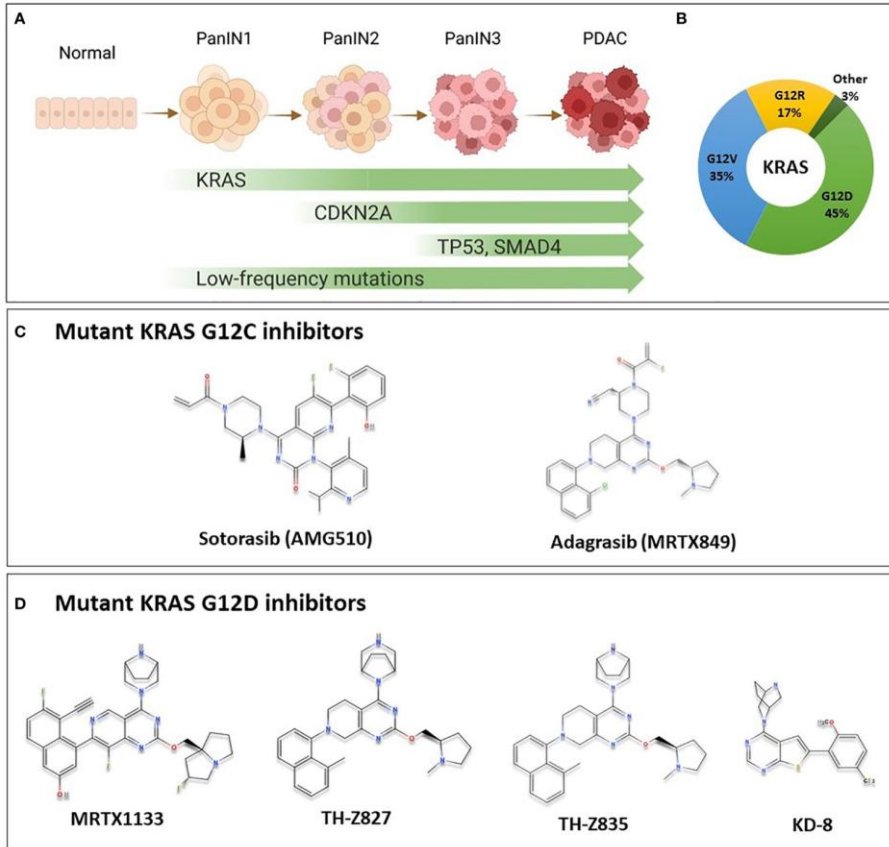
Rasonque, the new pancreatic cancer treatment from Revolution Medicines, illustrates the huge inflation in cancer drug prices over the past two decades.

By Rebecca Robbins

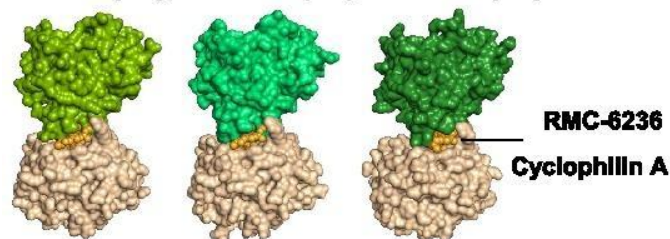
AUG. 31



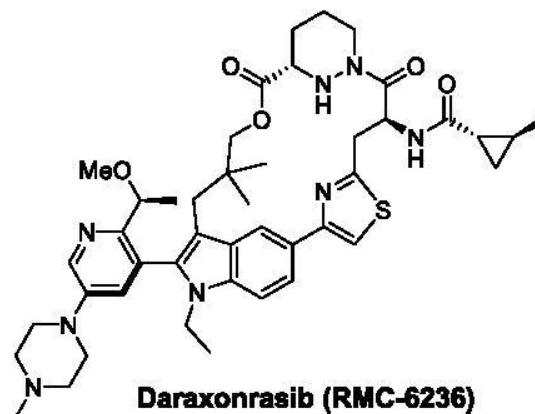
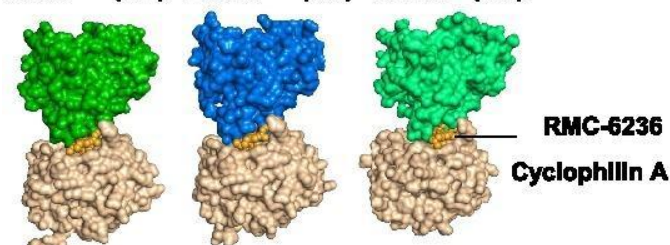
KRAS inhibition



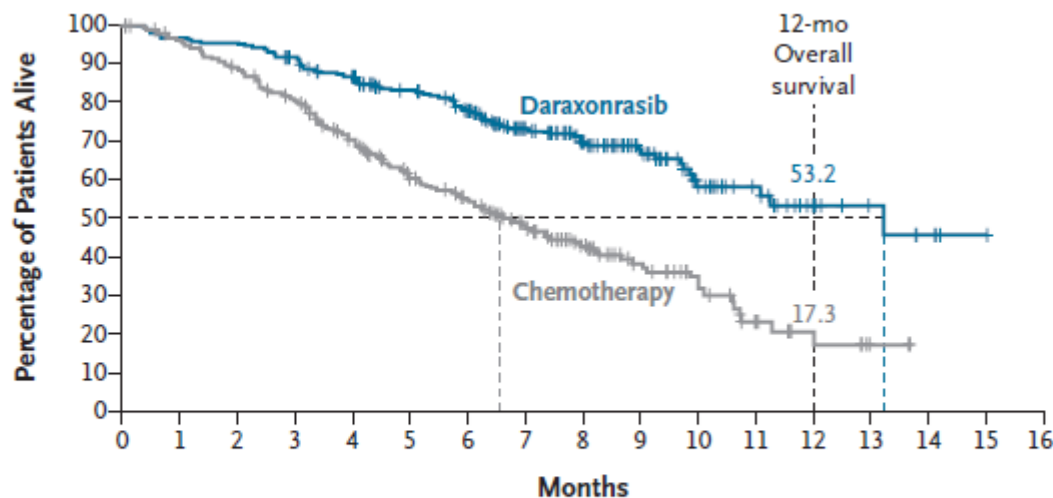
KRAS^{G12V}(ON) KRAS^{G12R}(ON) KRAS^{G12D}(ON)



KRAS^{Q61K}(ON) NRAS^{Q61R}(ON) KRAS^{WT}(ON)



Overall Survival in the Overall Population



No. at Risk

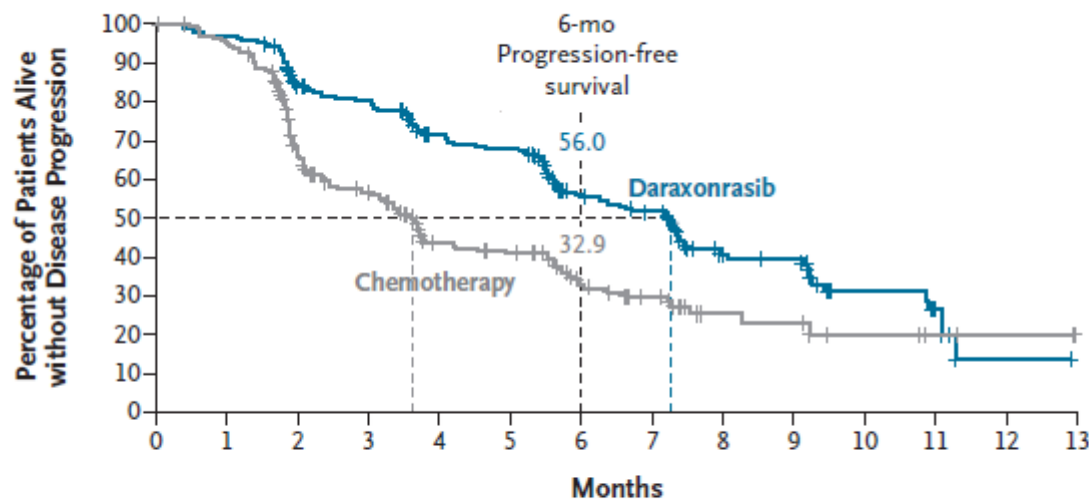
Daraxonrasib	248	240	237	225	208	188	165	125	90	62	37	24	11	7	4	1	0
Chemotherapy	252	235	217	193	161	126	108	78	53	35	21	10	5	2	0		

	No. of Patients	No. of Events (%)	Median Overall Survival (95% CI) mo
Daraxonrasib	248	79 (32)	13.2 (10.0–NR)
Chemotherapy	252	141 (56)	6.7 (5.8–8.0)

Hazard ratio for death, 0.40 (95% CI, 0.30–0.53)
P<0.001

O'Reilly, NEJM. 2026

Progression-free Survival in the Overall Population



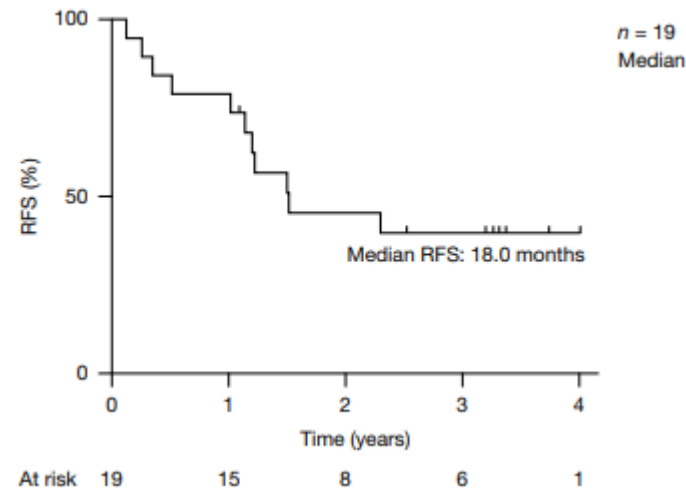
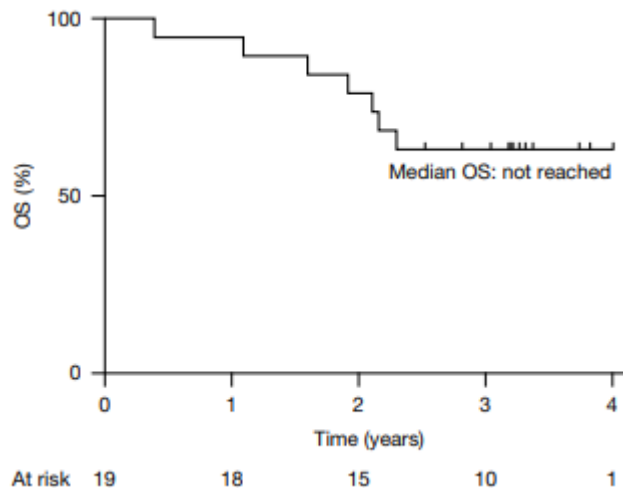
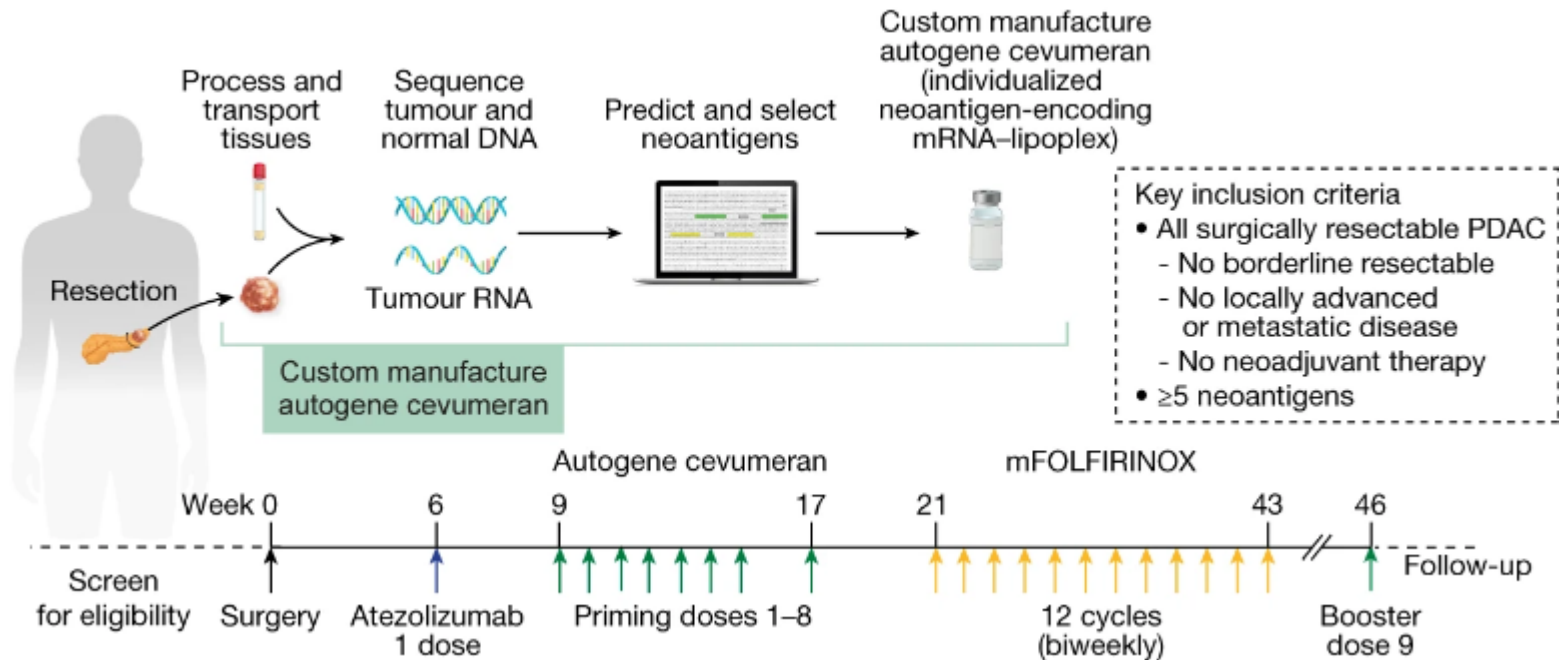
No. at Risk

Daraxonrasib	248	238	198	184	147	139	86	76	32	30	14	10	1	0
Chemotherapy	252	203	129	102	64	58	32	24	10	9	5	3	2	0

	No. of Patients	No. of Events (%)	Median Progression-free Survival (95% CI)
Daraxonrasib	248	127 (51)	7.2 (5.7–7.5)
Chemotherapy	252	130 (52)	3.6 (2.9–4.2)

Hazard ratio for disease progression or death, 0.49 (95% CI, 0.38–0.64)
P<0.001

mRNA vaccine

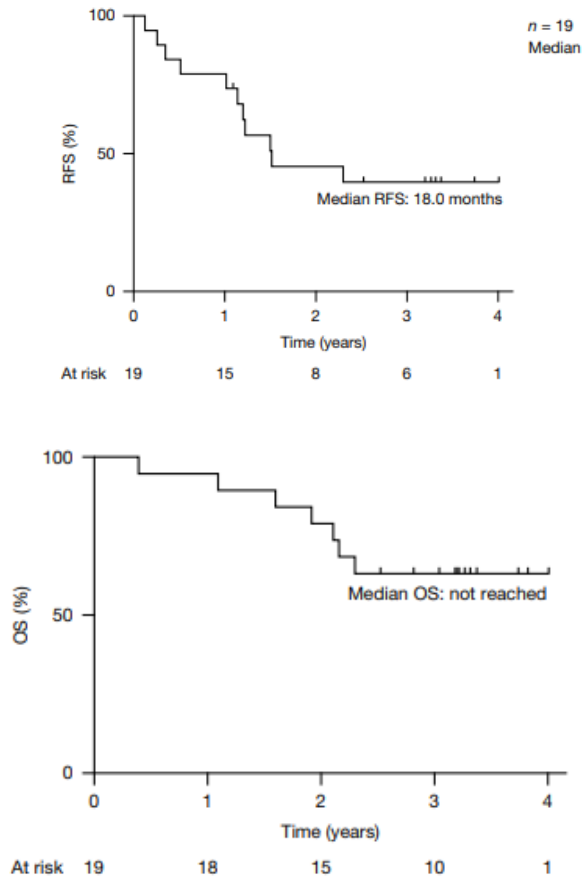


Cancers 2021
Nature 2023
Nature 2025

mRNA Vaccine

RFS

18 months

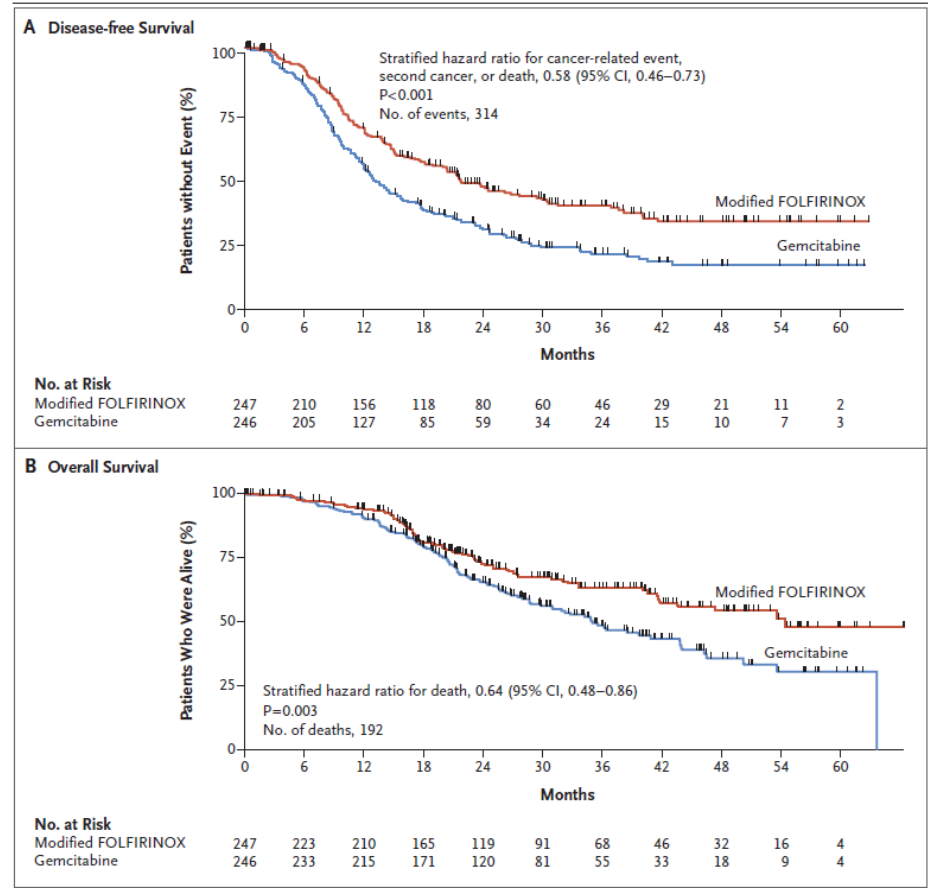


OS

Not reached

mFOLFIRINOX

22 months



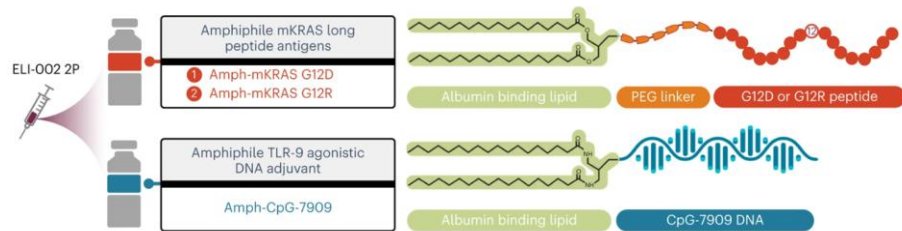
4.5 years

Phase 3 INTerpath-001 trial: Melanoma

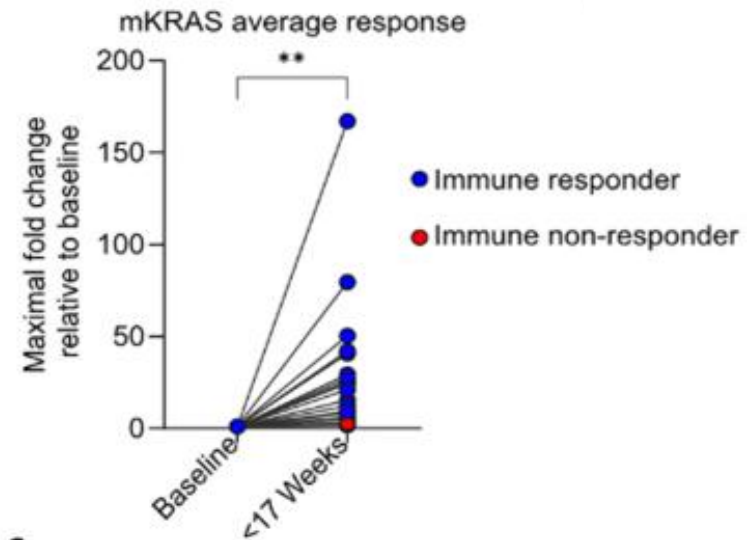
intismeran autogene + pembrolizumab (KEYTRUDA) vs.
KEYTRUDA

- Phase III trial
- Completely resected stage IIB, IIC, III or IV cutaneous melanoma
- Improved RFS
- Improved DMFS

Peptide Vaccine for PDAC prevention

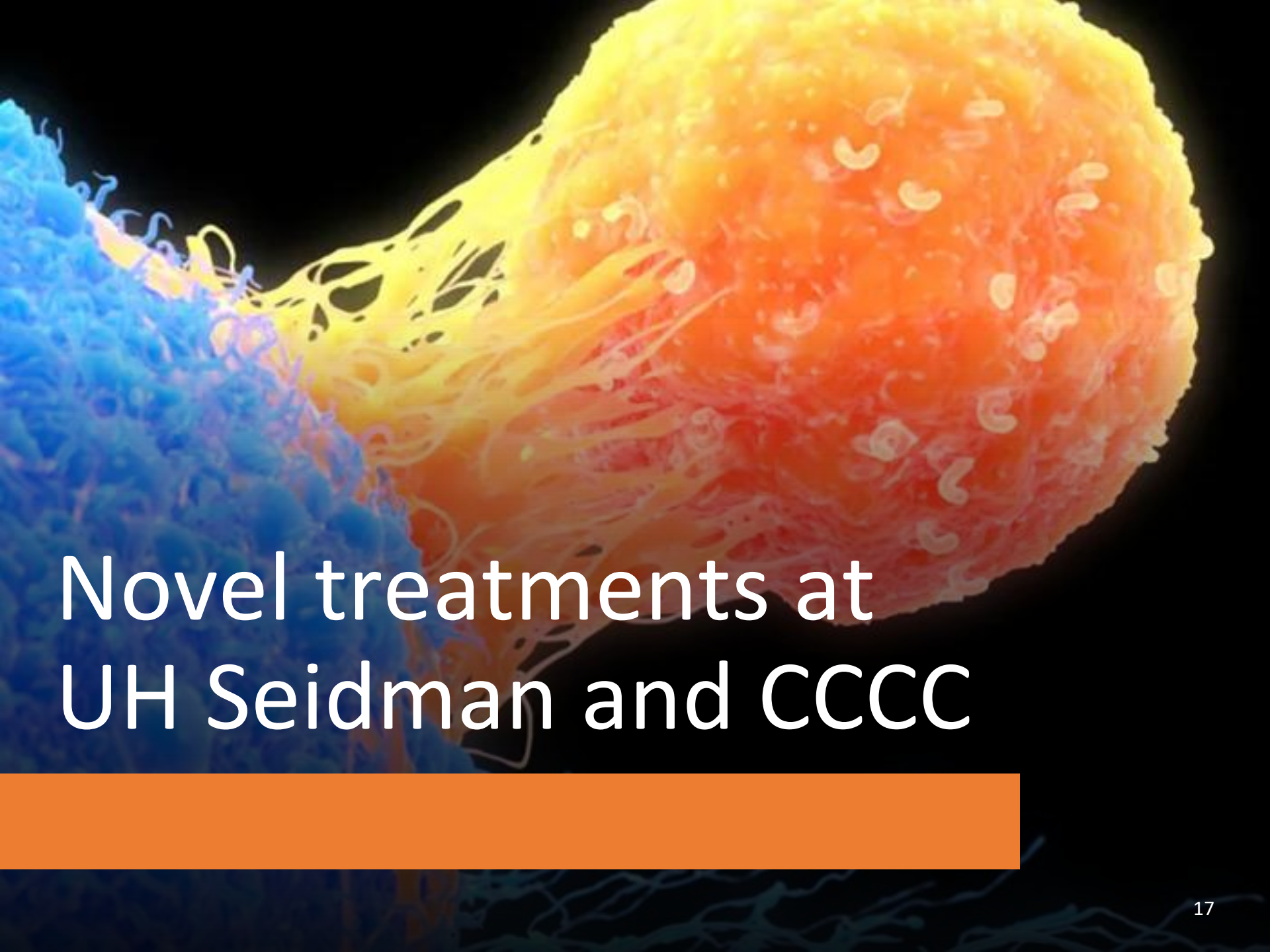


	Vaccinated Cohort (n=16)	Unvaccinated Cohort (n=44)
Stable	10/16 (62.5%)	31/44 (70.5%)
Increase	0/16 (0%)	10/44 (22.7%)
Decrease	3/16 (19%)	2/44 (4.54%)
Resolution	3/16 (19%)	1/44 (2.27%)

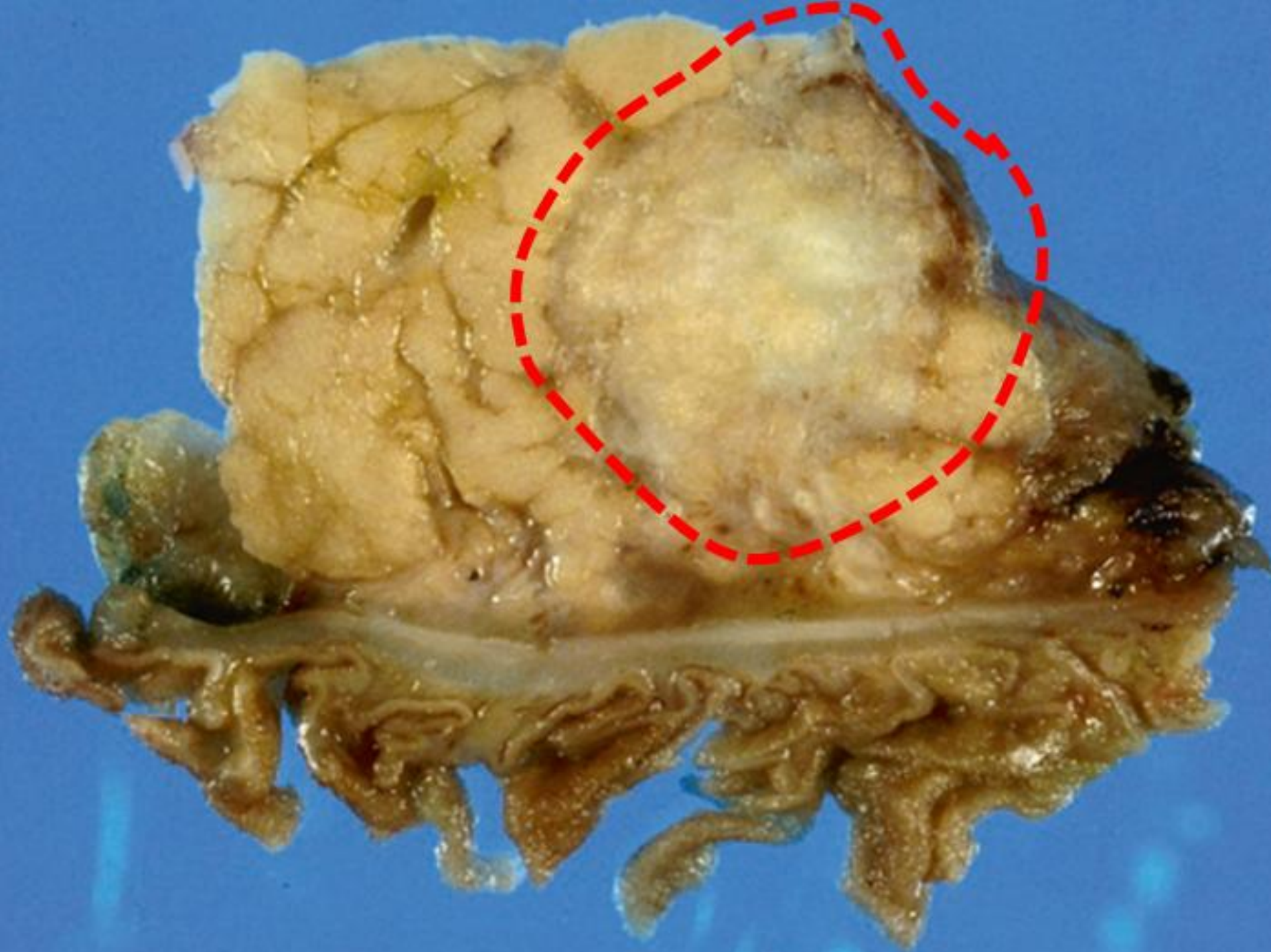


Haldar, Can Disc. 2026

Pant, Nat Med. 2024

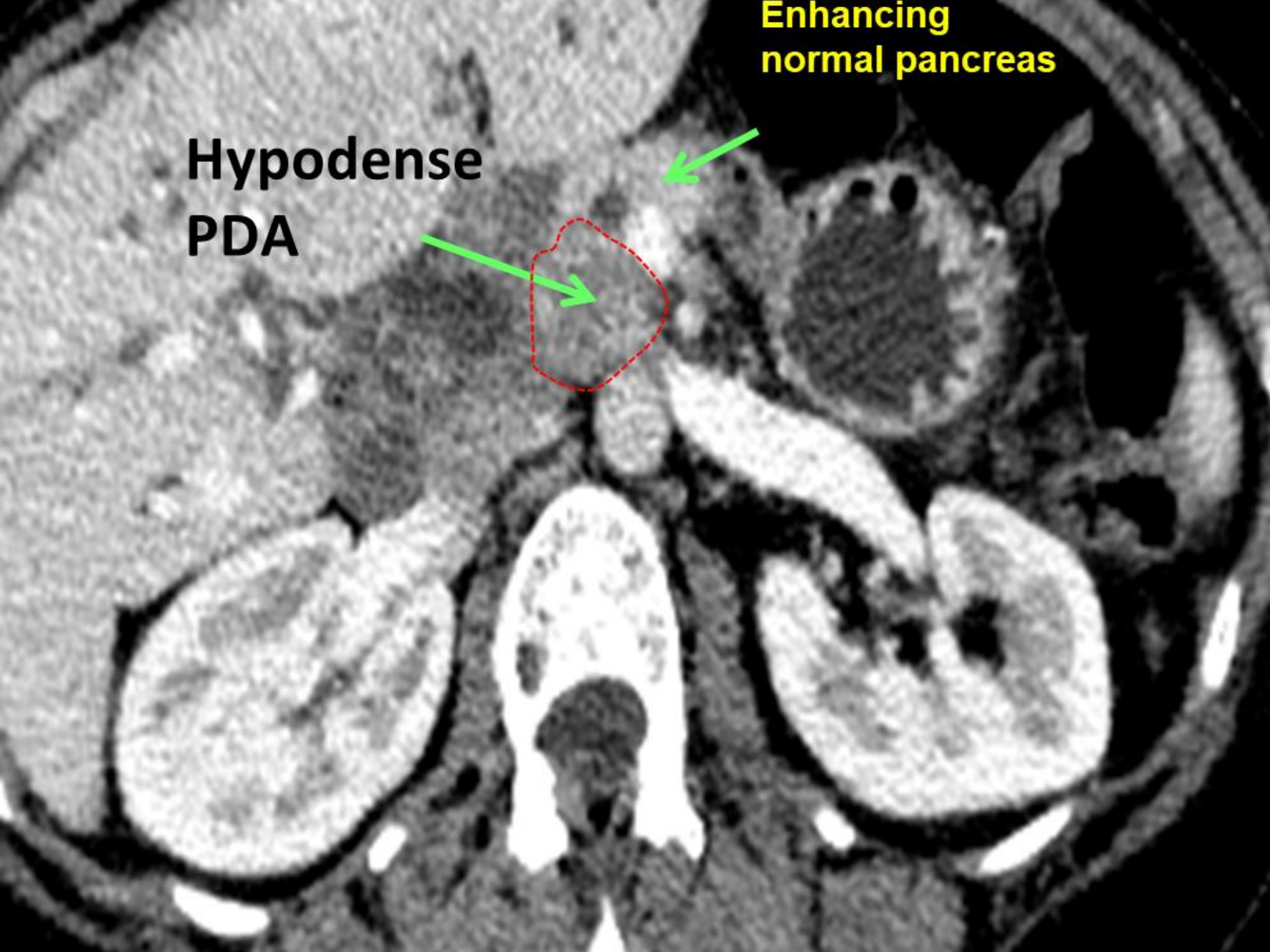


Novel treatments at UH Seidman and CCCC



**Enhancing
normal pancreas**

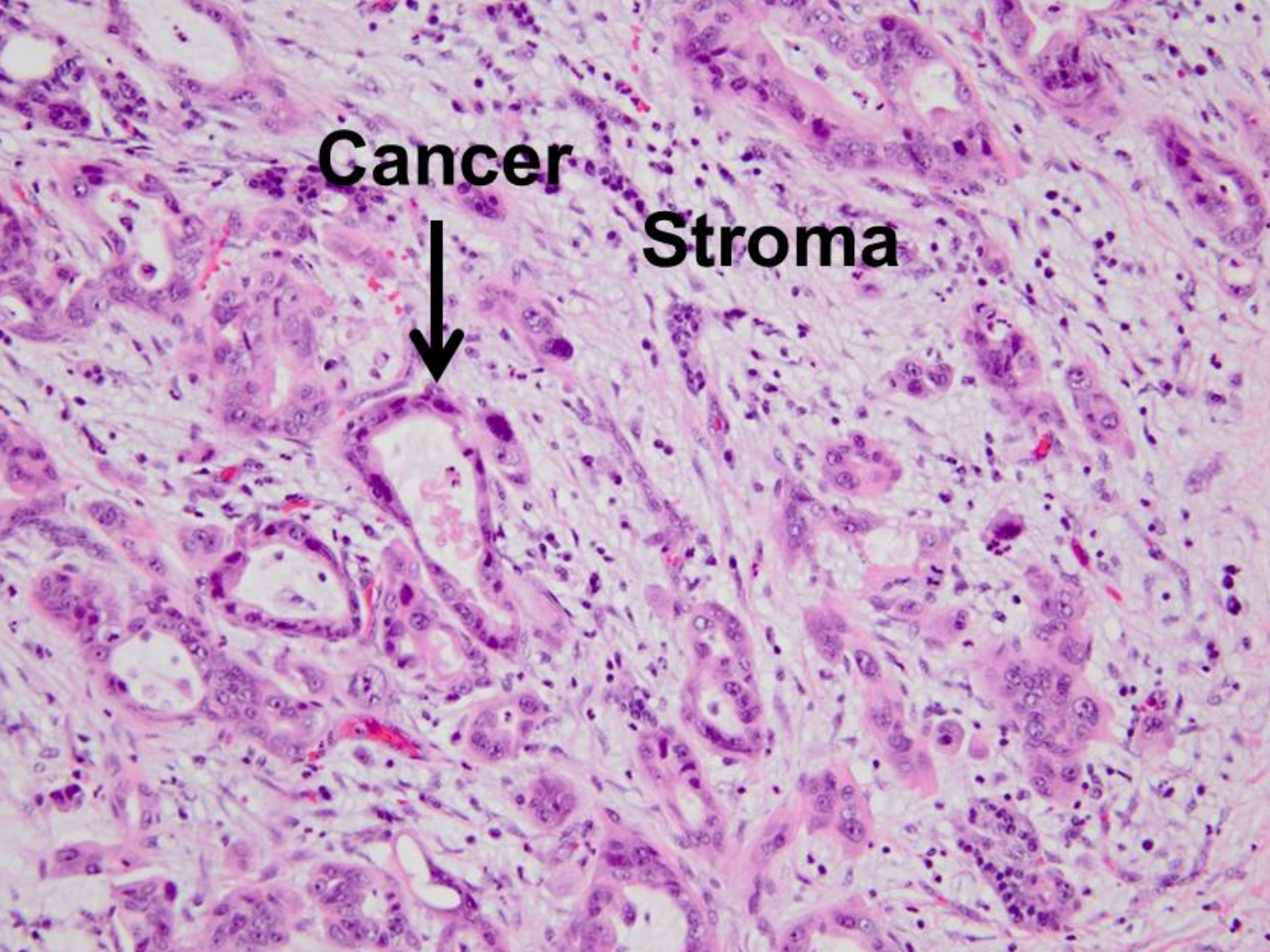
**Hypodense
PDA**



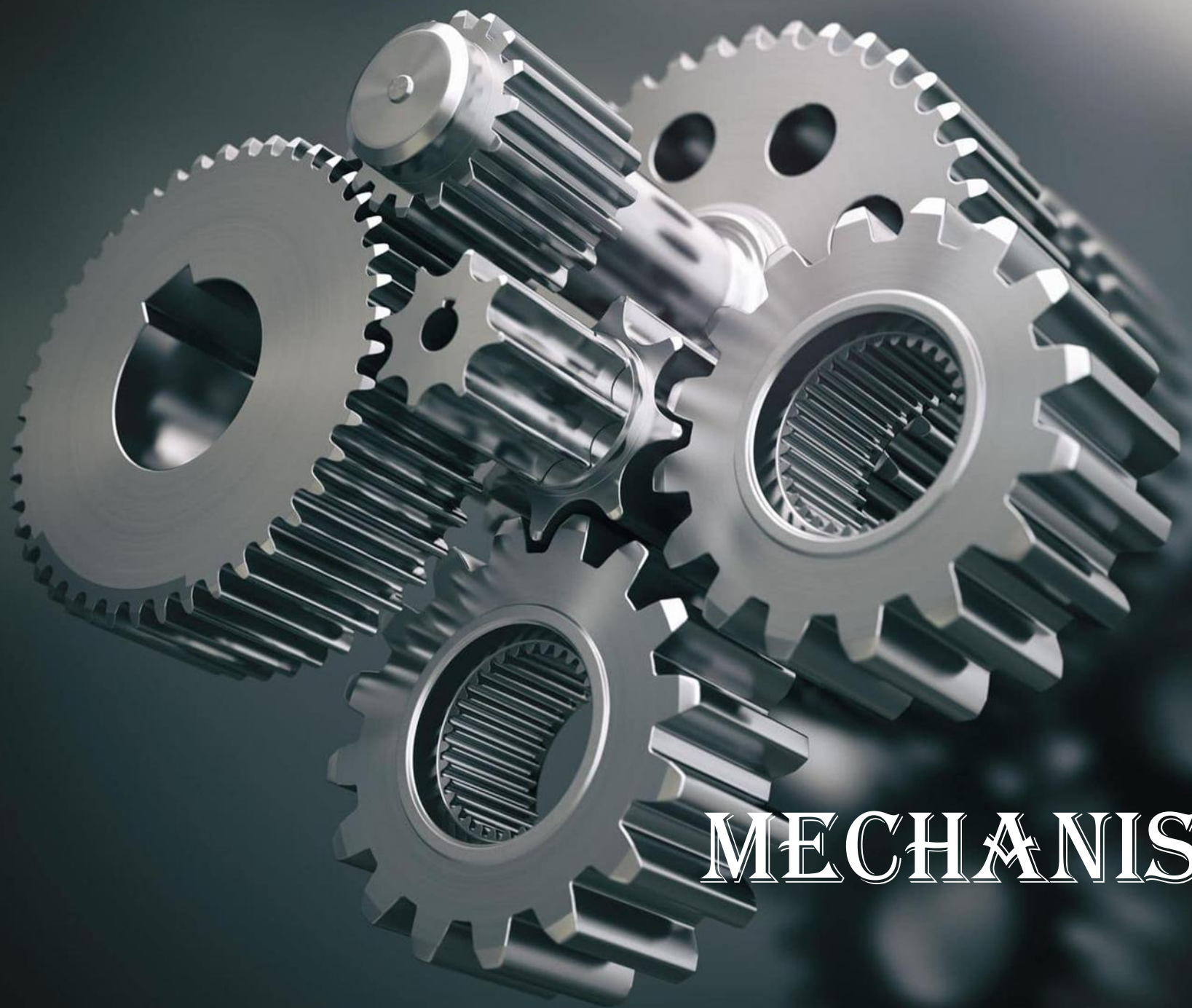
Cancer



Stroma







MECHANISM

A

Isocitrate

α KG

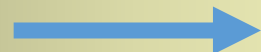
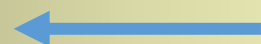
+

IDH1

+

NADP⁺

NADPH



B



mitochondria

function

~~ROS • O₂⁻~~

antioxidant

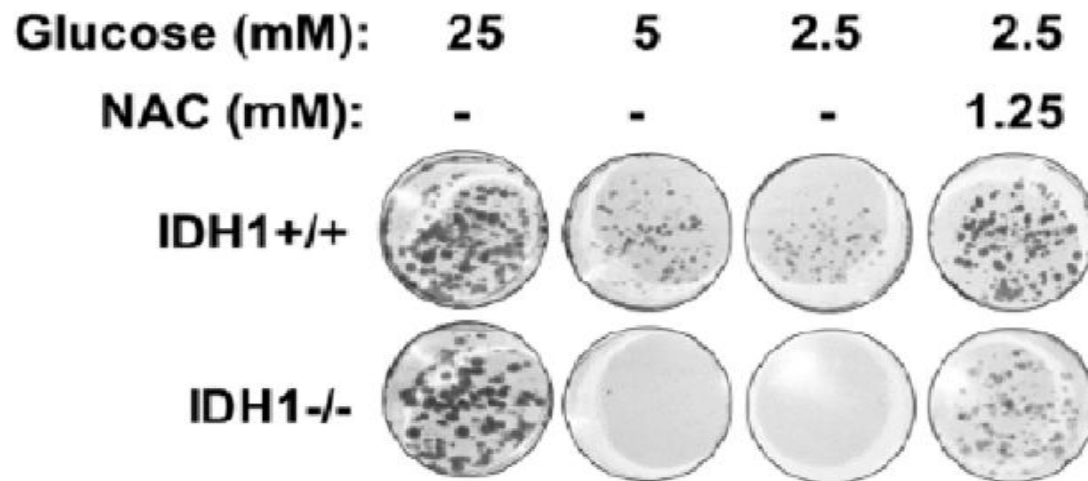
defense



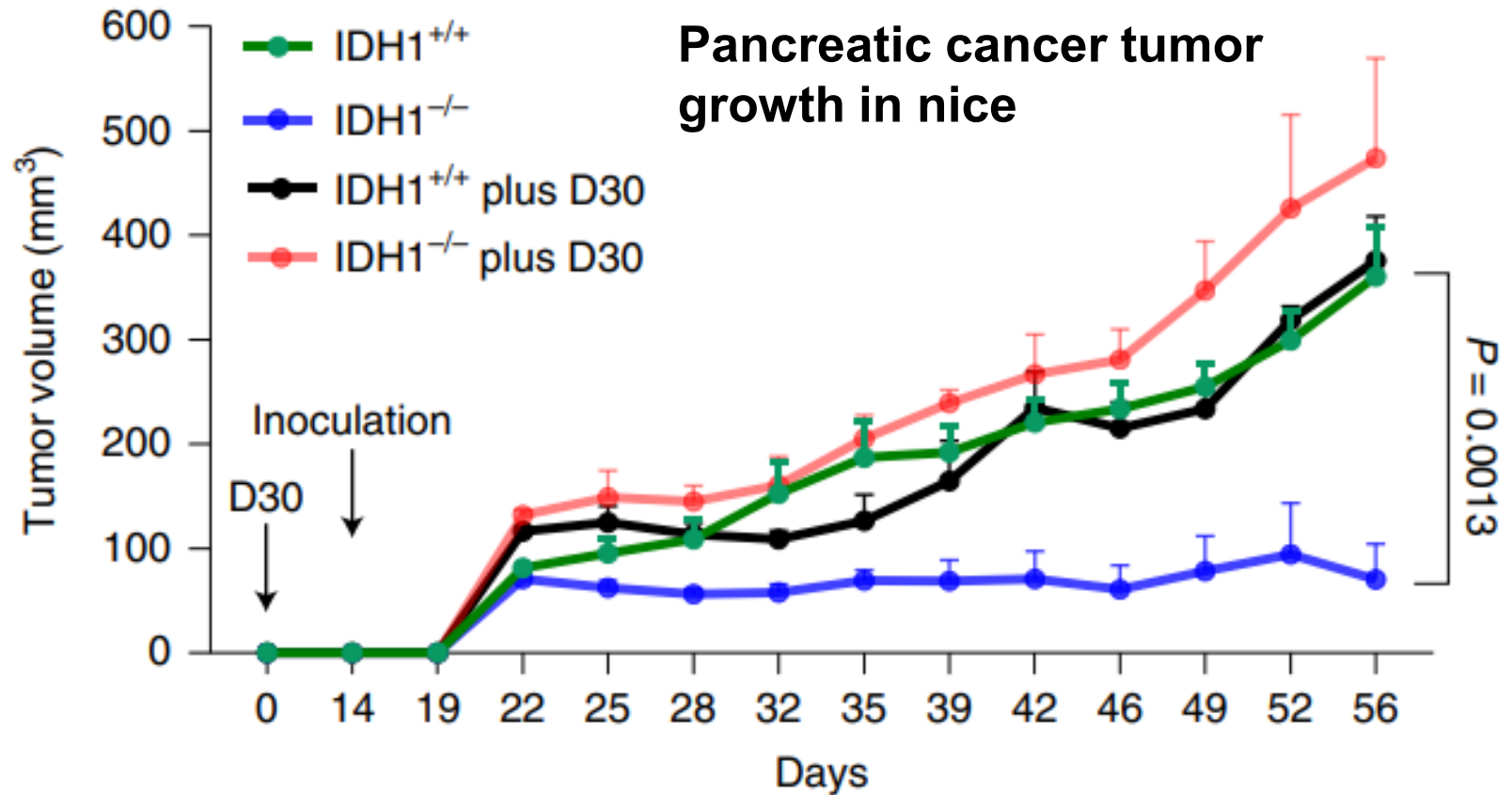
TARGET VALIDATION

IDH1 KO grow poorly under tumor conditions

Pancreatic cancer cell line



IDH1 KO grow poorly under tumor conditions

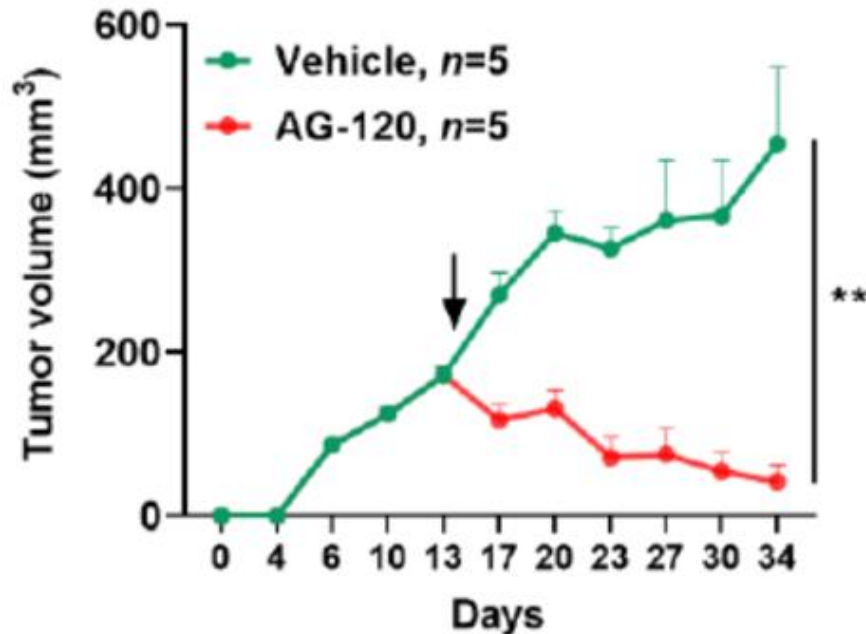


The image features a complex, glowing green molecular structure, possibly a protein or a large organic molecule, set against a dark green background. The molecule is composed of numerous spheres (atoms) connected by lines (bonds), with some spheres appearing larger than others. The overall effect is a high-tech, scientific aesthetic. In the upper right quadrant, the words "DRUG" and "DISCOVERY" are stacked vertically in a bold, yellow, serif font. The text is slightly shadowed, giving it a three-dimensional appearance as if it's floating or attached to the molecular structure.

DRUG DISCOVERY

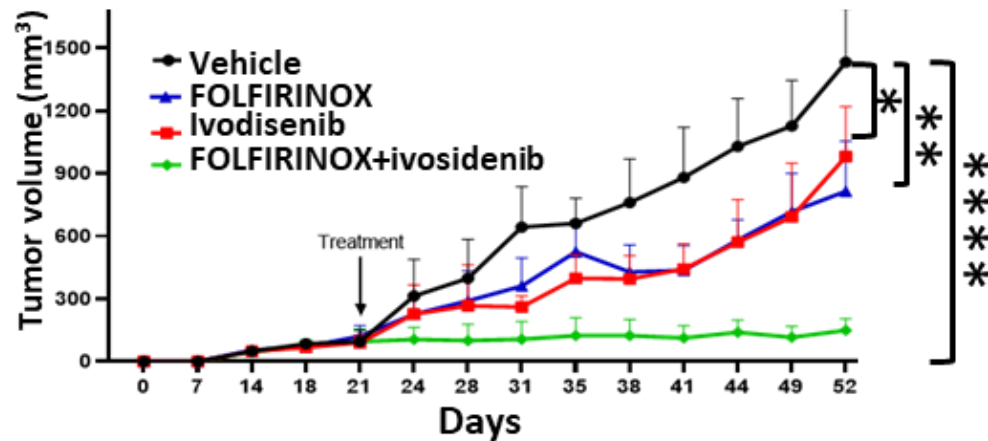
IDH1 inhibition treats pancreatic cancer in mice using a repurposed drug

Pancreatic cancer tumor growth in mice



IDH1 inhibition is additive with FOLFIRINOX

Pancreatic cancer tumor growth in mice

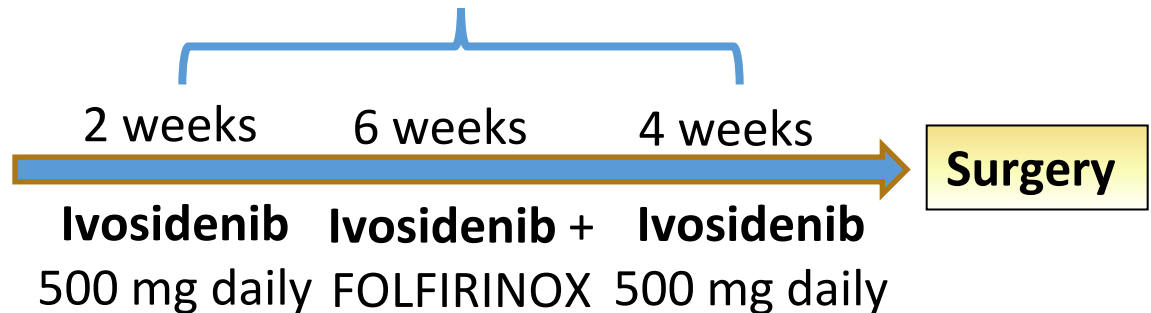




Phase 1b

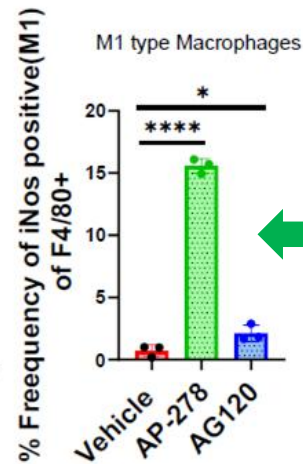
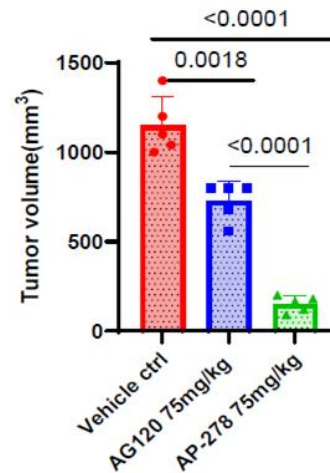
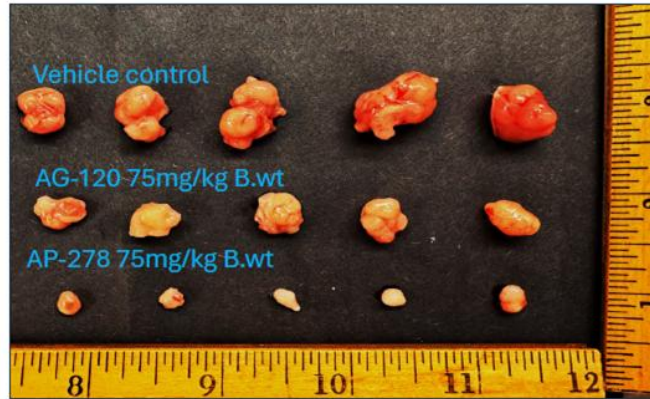
3 months neoadjuvant

Resectable pancreatic cancer, neoadjuvant, n=16 patients undergoing resection*

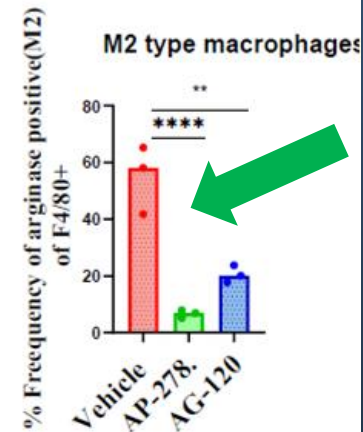


- **Primary Objective: Safety Secondary Objective: Efficacy** (path, CA 19-9, imaging)

Novel IDH1 inhibitor AP-278 is superior to AG-120



Good immune cells increased

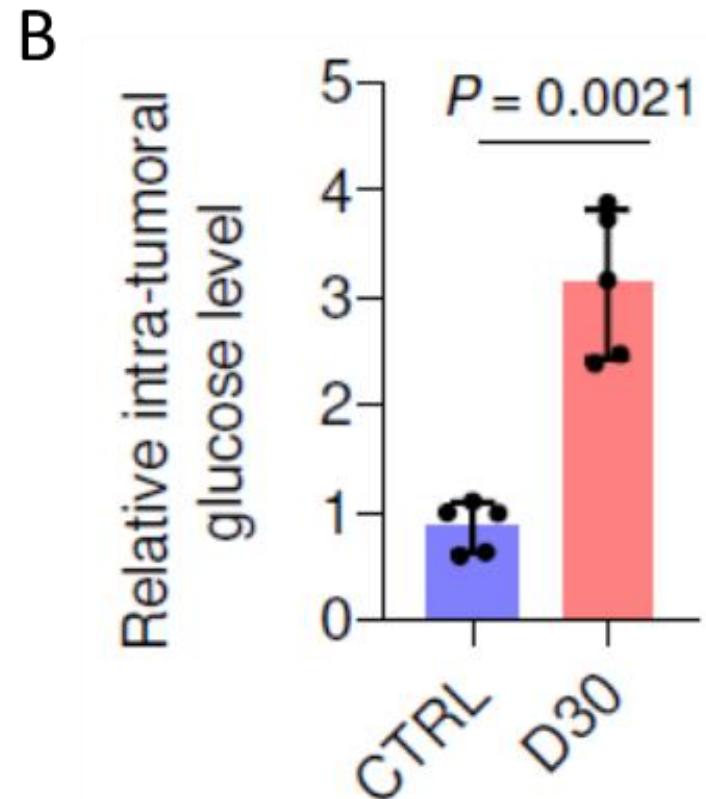
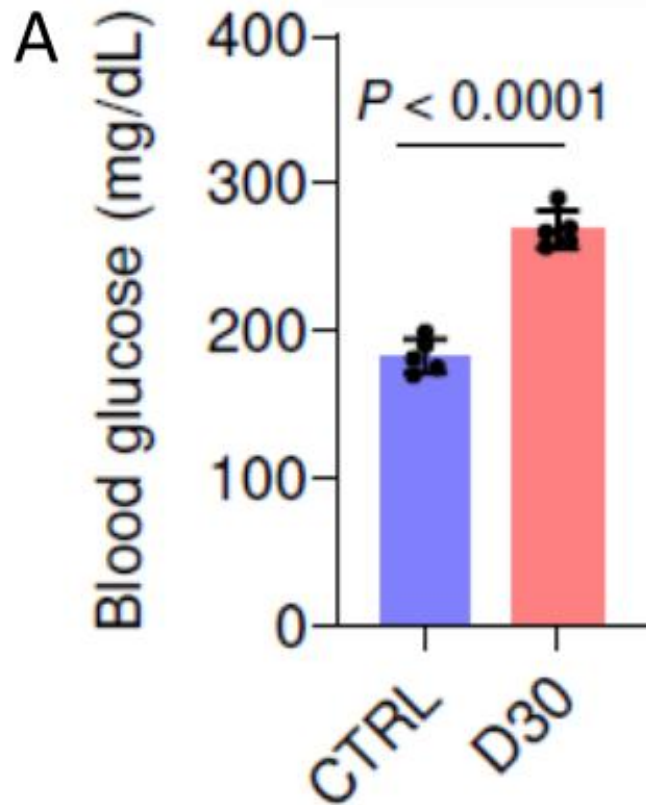
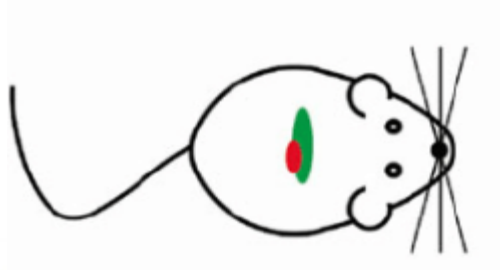


Bad immune cells decreased

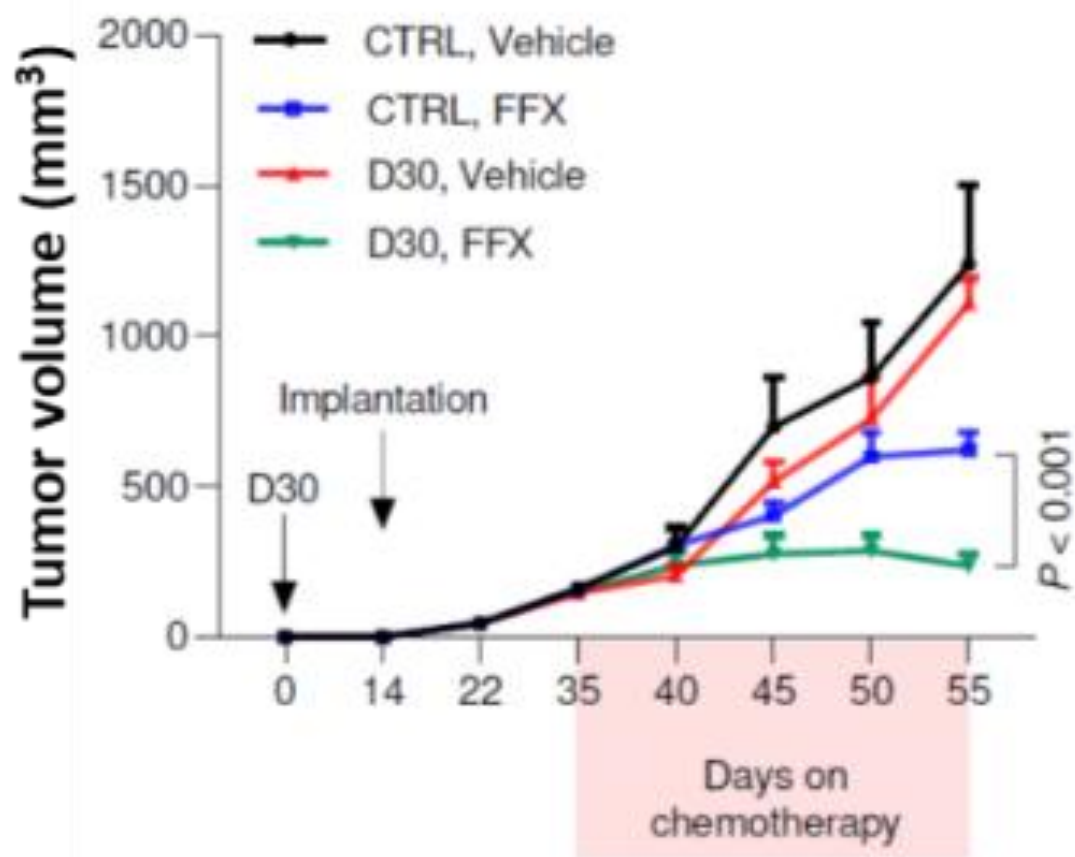
EXPLOITING
CANCER'S
SWEET TOOTH



Induce high glucose with sugar water



PDX (TM01212)



HgbA1C $\geq$ 7.0%

R
A
N
D
O
M
I
Z
E



Permissive hyperglycemia
(glucose, 175 mg/dL – 250
mg/dL)

1° Objective: progression
free survival

2° Objectives:

- OS
- Response rate
- Correlatives

Standard care (glucose, <154
mg/dL)

Phase II trial design. Diabetics with stage IV
PDAC, N=57.



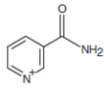
- Pancreatic cancer prevention

Restoring NAD⁺ delays pancreatic cancer progression in a KRAS^{G12D} model

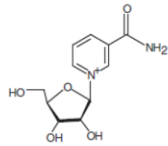
Vitamin B3, NAD⁺ and derivatives



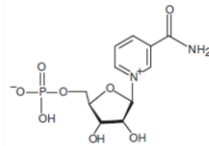
Nicotinic acid (NA)
Vitamin B3
(niacin)



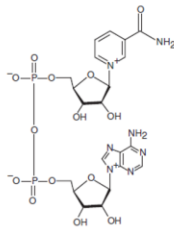
Nicotinamide (NAM)



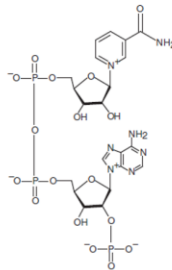
NAM riboside (NR)



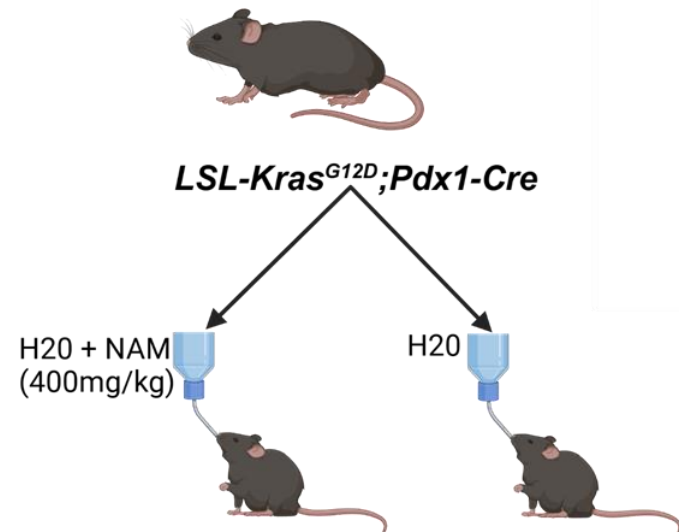
NAM mononucleotide (NMN)



Nicotinamide adenine dinucleotide (NAD⁺)



Phosphorylated NAD⁺ (NADP⁺)



NAD⁺ is protective to cells: KC Mice

LSL-Pdx-cre ; KRAS^{G12D/+}

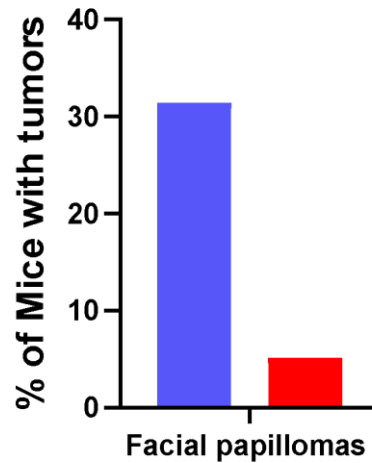


Anal
SCC

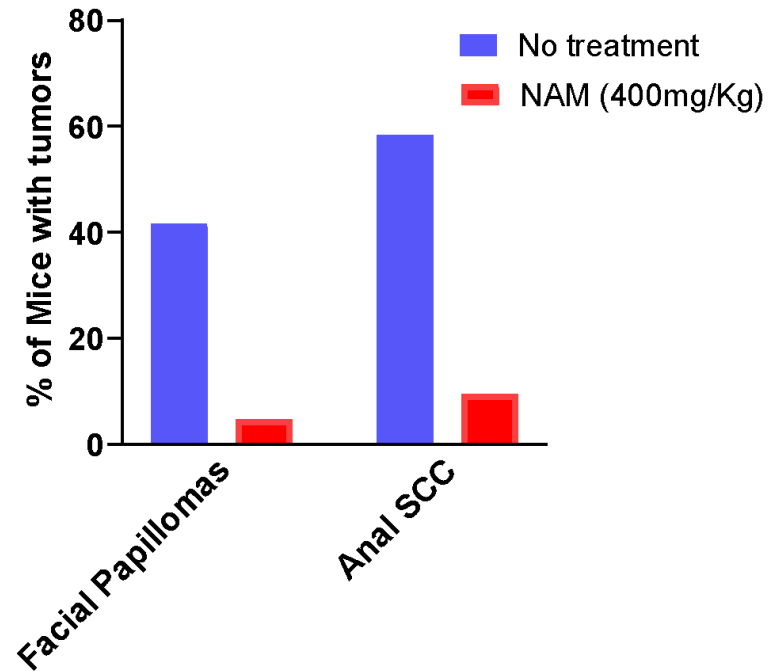


Facial papilloma

Male mice (≤ 20 weeks)



Female Mice (≤ 20 weeks)

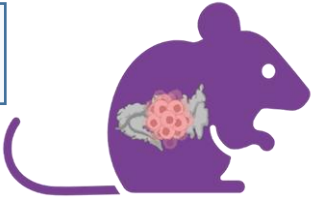


Restoring NAD+ delays pancreatic cancer progression

Percentage						
		<i>PanINs</i>				<i>Total</i>
	PDAC	Diffuse	Patchy	Focal	None	
<i>Vehicle</i>	2.9	65.7	31.4	0	0	100
<i>NAM</i>	0	18.4	44.7	31.6	5.3	100

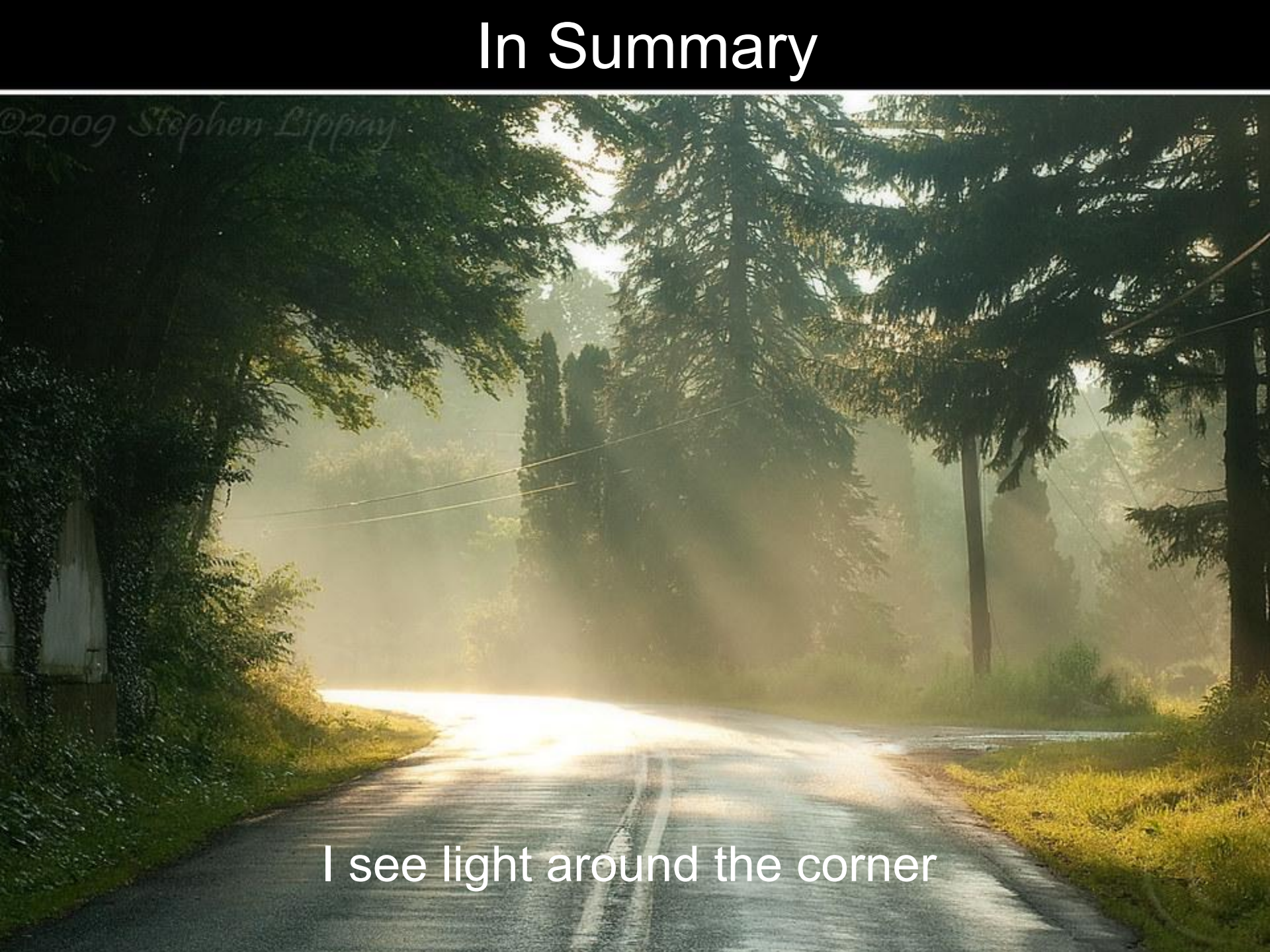


The development of pancreatic cancer



In Summary

©2009 Stephen Lippay



I see light around the corner



Philanthropy
Garson Family
Novak Family
Weinberger Family
DiSanto Family
Hieronymous Family