Cancer du pancréas et médecine personnalisée

Où en est-on en 2025 ?

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institut Curie

UNIVERSITÉ DE VERSAILLES ST-QUENTIN-EN-YVELINES

université PARIS-SACLAY

Liens d’intérêts

- Honoraires / consulting : Amgen, AstraZeneca, Baxter, Bristol-Myers Squibb, Fresenius Kabi, GE Healthcare, Incyte Biosciences, Jazz, Merck, MSD, Mundipharma, Nestlé Health Science, Novartis, Nutricia, OncoSil, OSE Immunotherapeutics, Pierre Fabre, Roche, Sanofi, Servier, Tahio, Théradial, Viatris
- Financements recherche / essais cliniques : AstraZeneca, Bristol-Myers Squibb, Fresenius Kabi, Nutricia, OSE Immunotherapeutics, Roche, Servier, Viatris
- Board/shares : Cereus Biosciences

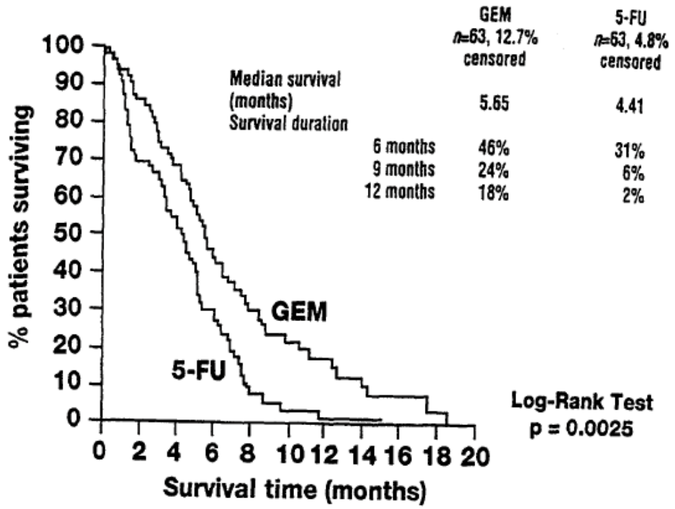
Les bases

Recommandations ESMO 2025

Les bases : 1ère ligne

1997: BURRIS
Gem > 5FU

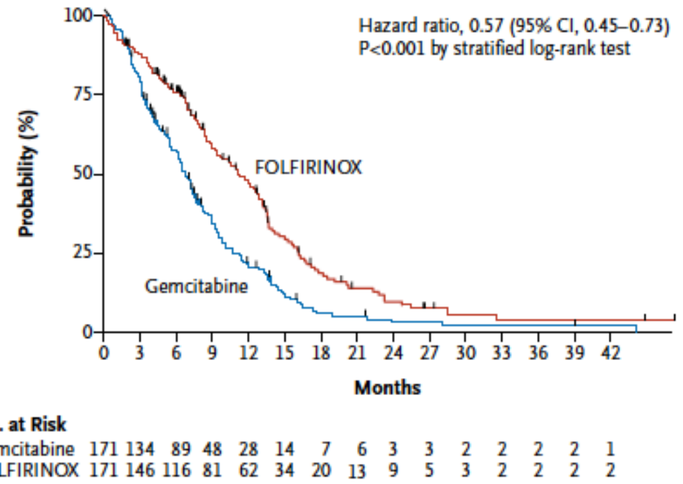
Gemcitabine 1,000 mg/m² weekly x 7/8 weeks, then weekly x 3, Q4W



Phase III - N=126 LA or M+ PDAC
Clinical benefit (pain, PS, weight): 23.8% vs 4.8%, p=0.0022

2011: PRODIGE 4
FOLFIRINOX > Gem

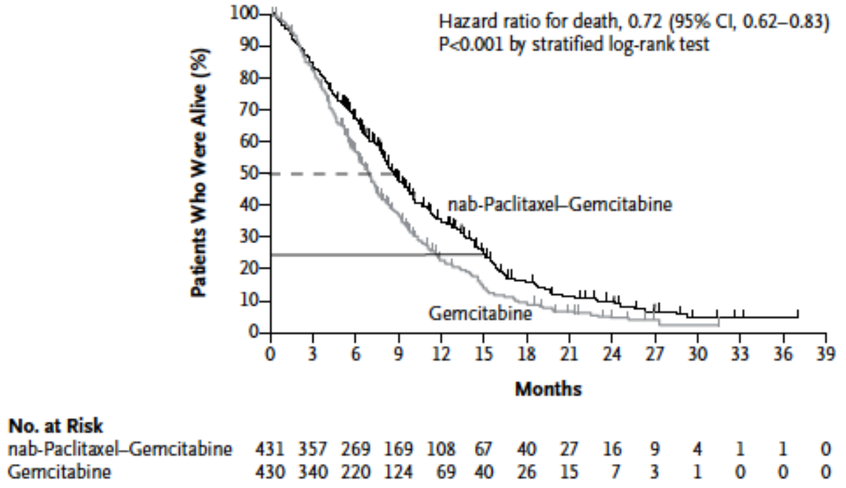
Oxaliplatin 85 mg/m², **irinotecan** 180 mg/m², **5FU** bolus 400 mg/m² then 2,400 mg/m² over 46h + **LV** 400 mg/m², Q2W



Phase III - N=342 M+ PDAC
mOS: 11.4 vs 6.8 months, p<0.001

2013: MPACT
Gem nab-paclitaxel > Gem

Nab-P 125 mg/m², **Gem** 1,000 mg/m², D1-D8-D15, Q4W



Phase III - N=861 M+ PDAC
mOS: 8.5 vs 6.7 months, p<0.001

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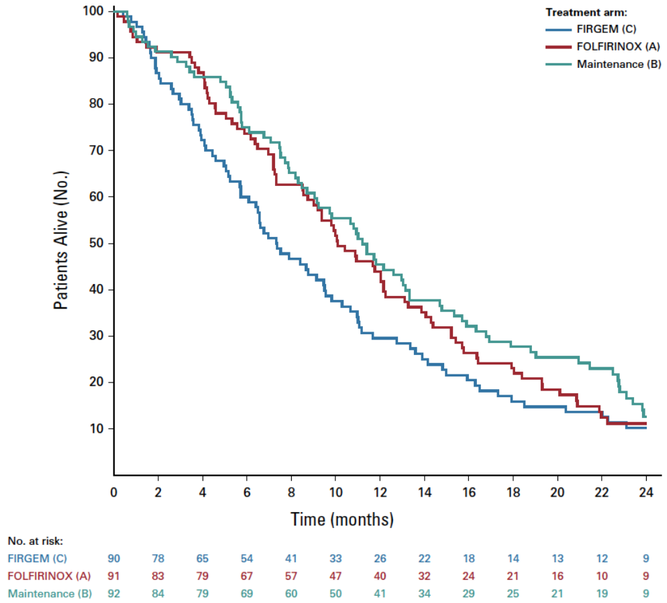
Burris et al, *J Clin Oncol* 1997; Conroy et al, *N Engl J Med* 2011; Von Hoff et al, *N Engl J Med* 2013

Traitement de maintenance

PRODIGE 35 PANOPTIMOX Phase II

LV5FU2 after FOLFIRINOX

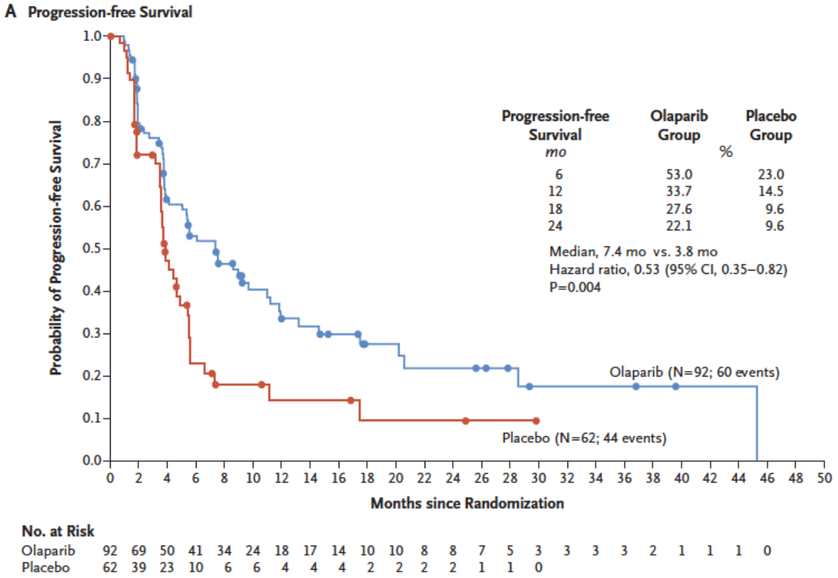


Dahan et al, *J Clin Oncol* 2021

POLO Phase III

Olaparib after platinum-based CTx

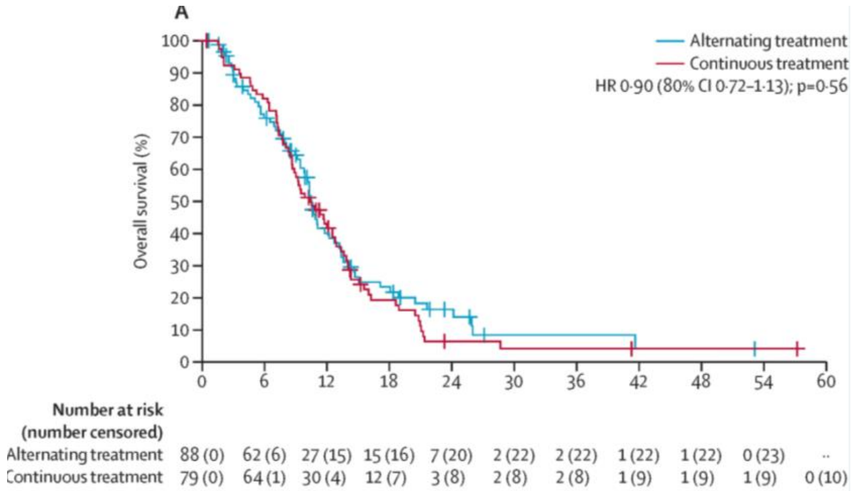
in germline *BRCA1* or *BRCA2* mut.



Golan et al, *N Engl J Med* 2019

ALPACA Phase II

Alternating Gem-NabP and Gem



Dorman et al,
Lancet Gastroenterol Hepatol 2024

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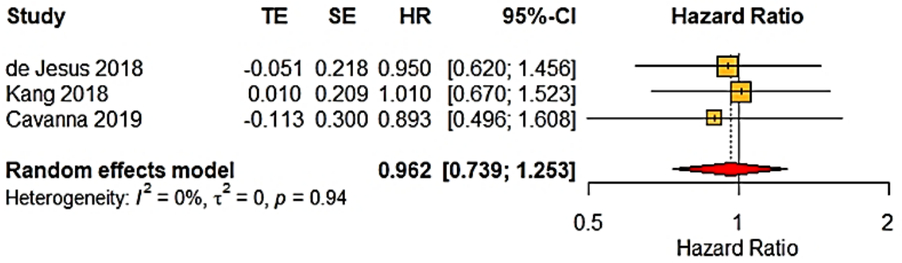
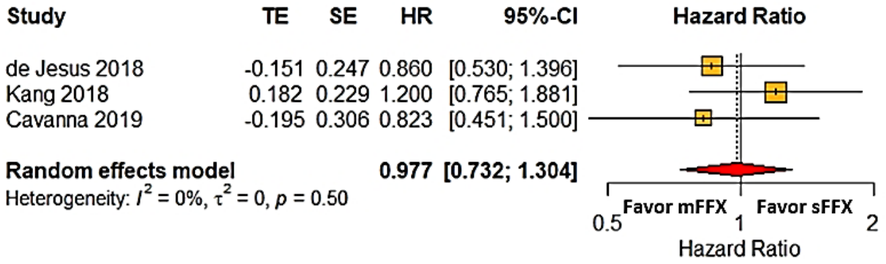
FOLFIRINOX modifié

37 studies, > 2000 patients, 12 regimens

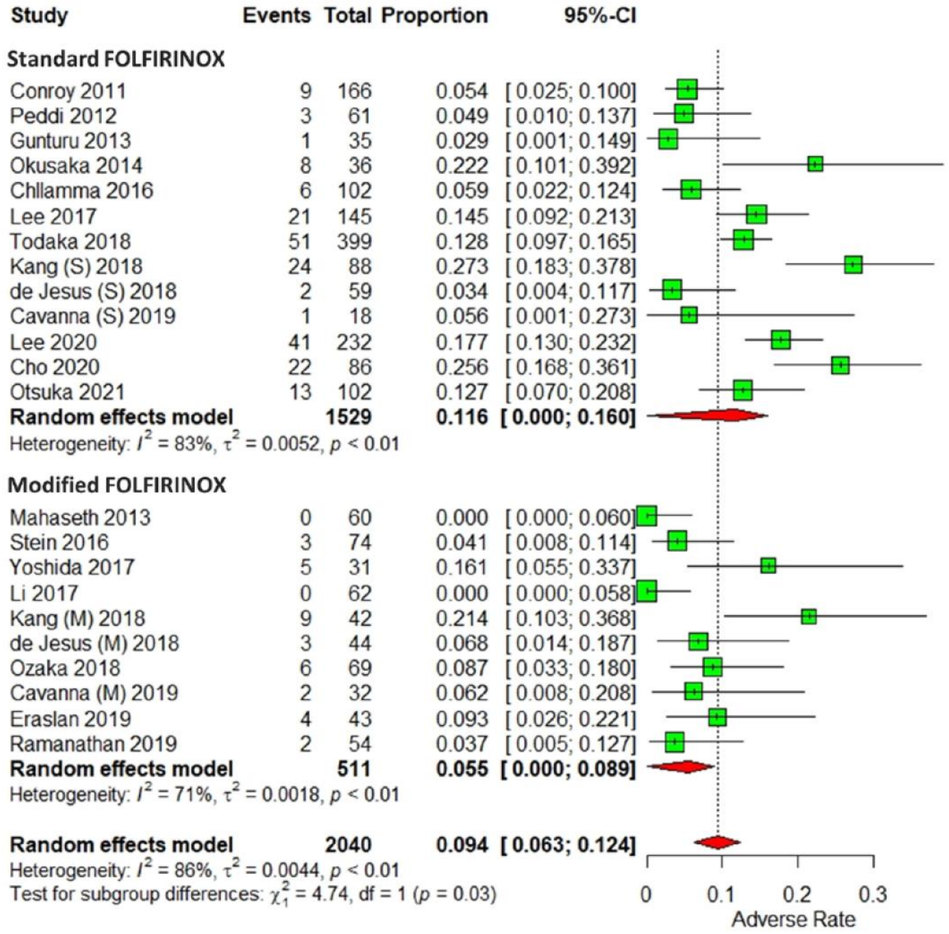
OS



PFS



Febrile neutropenia



Jung et al, *TAMO* 2023

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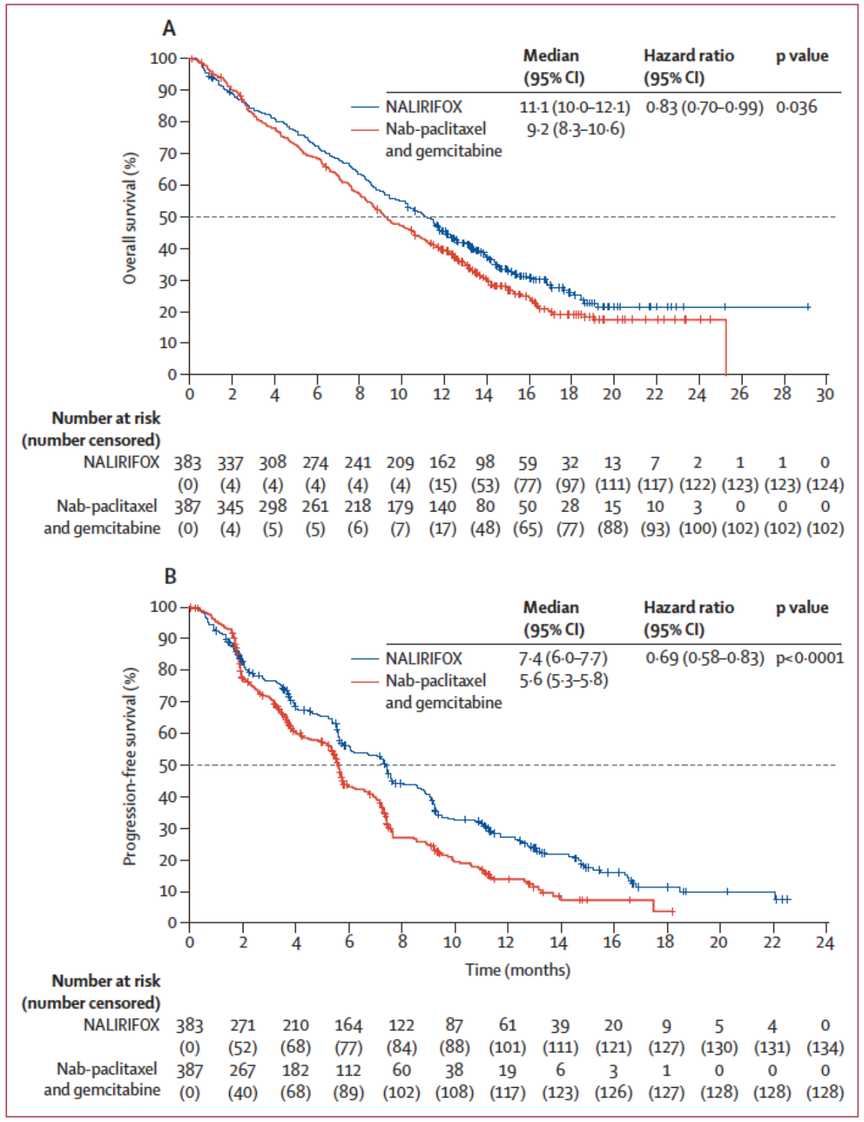
Nouveauté = NALIRIFOX, étude NAPOLI-3



Phase III - N=770 M+ PDAC

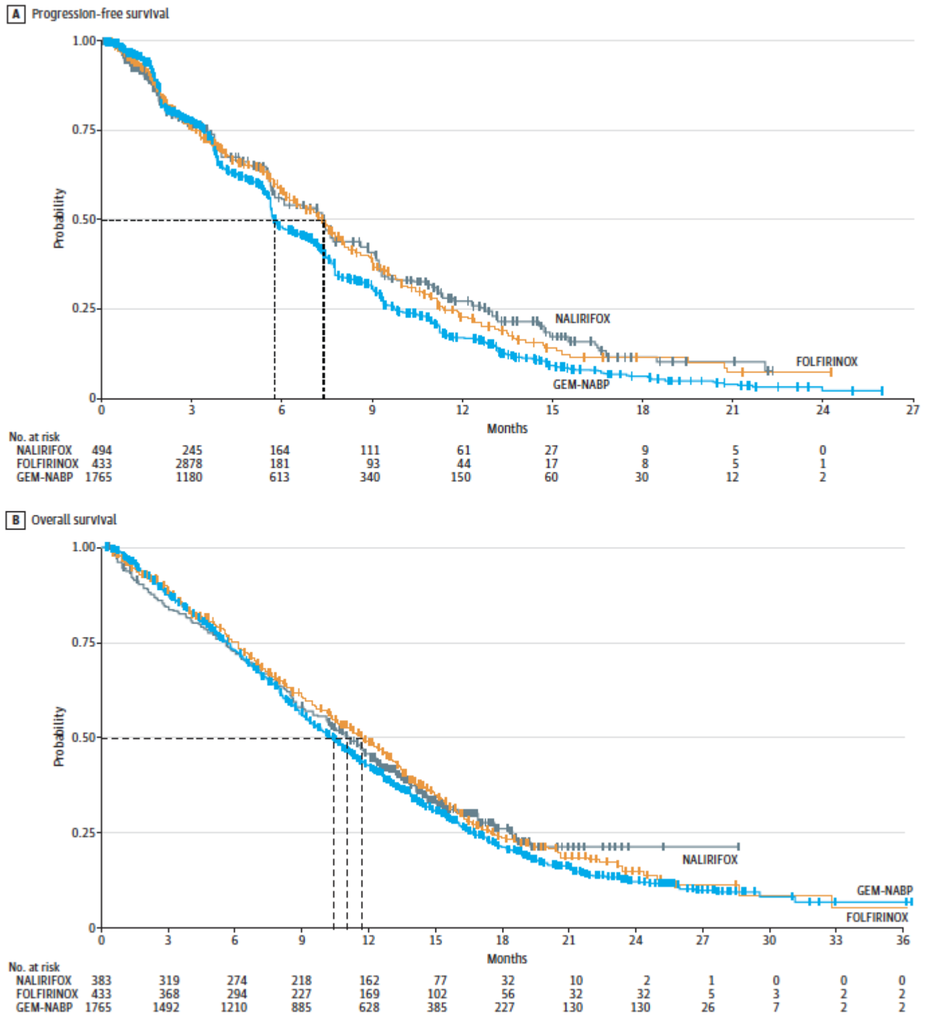
(**nal-iri** 50 mg/m^2, **oxaliplatin** 60 mg/m^2,
5FU 2,400 mg/m^2 over 46h + **LV** 400 mg/m^2, Q2W)

	NALIRIFOX (n=370)	Nab-paclitaxel and gemcitabine (n=379)
Median duration of treatment, weeks	24·3 (0·4–100·9; 8·4–42·1)	17·6 (0·7–81·7; 8·1–30·1)
Median number of treatment cycles	5·0 (1–24; 2–10)	4·0 (1–20; 2–7)
Any dose reductions	220 (60%)	204 (54%)
TEAEs of grade 3–4 occurring in ≥5% of patients in either treatment arm		
Diarrhoea	75 (20%)	17 (5%)
Nausea	44 (12%)	10 (3%)
Vomiting	26 (7%)	8 (2%)
Decreased appetite	32 (9%)	10 (3%)
Hypokalaemia	56 (15%)	15 (4%)
Fatigue	23 (6%)	20 (5%)
Asthenia	33 (9%)	19 (5%)
Neutropenia	52 (14%)	93 (25%)
Neutrophil count decreased	36 (10%)	51 (14%)
Anaemia	39 (11%)	66 (17%)
Peripheral neuropathy	12 (3%)	22 (6%)
Increased γ-glutamyltransferase	23 (6%)	21 (6%)

Wainberg et al, *Lancet* 2023

1ère ligne : méta-analyse

Figure 2. Reconstructed Kaplan-Meier Plots for Progression-Free Survival and Overall Survival According to First-Line Regimen



FOLFIRINOX indicates irinotecan, oxaliplatin, folinic acid, and fluoruracil; GEM-NABP, gemcitabine and nab-paclitaxel; NALIRIFOX, liposomal irinotecan, oxaliplatin, folinic acid, and fluoruracil. Dotted lines indicate median survival.

Figure 1. Study Selection Flowchart

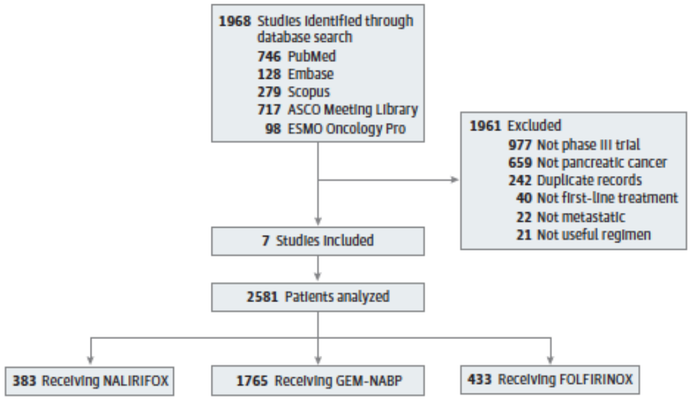
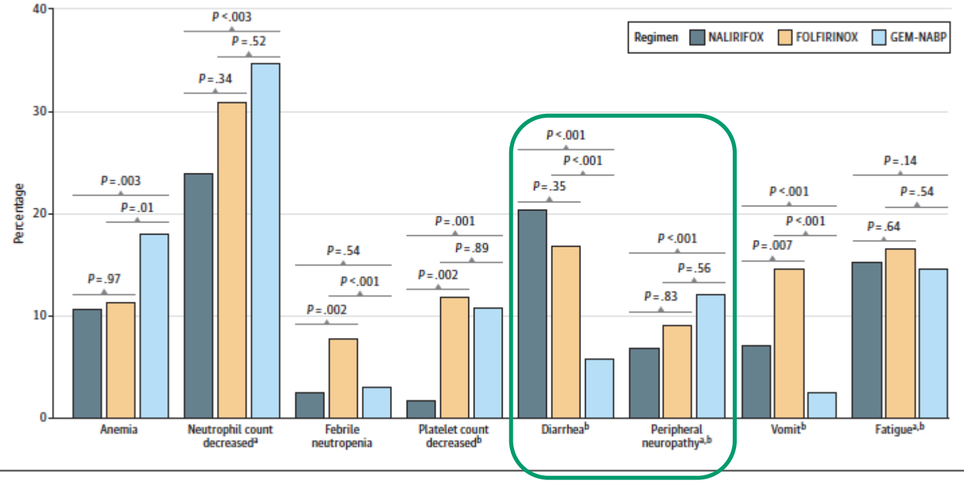
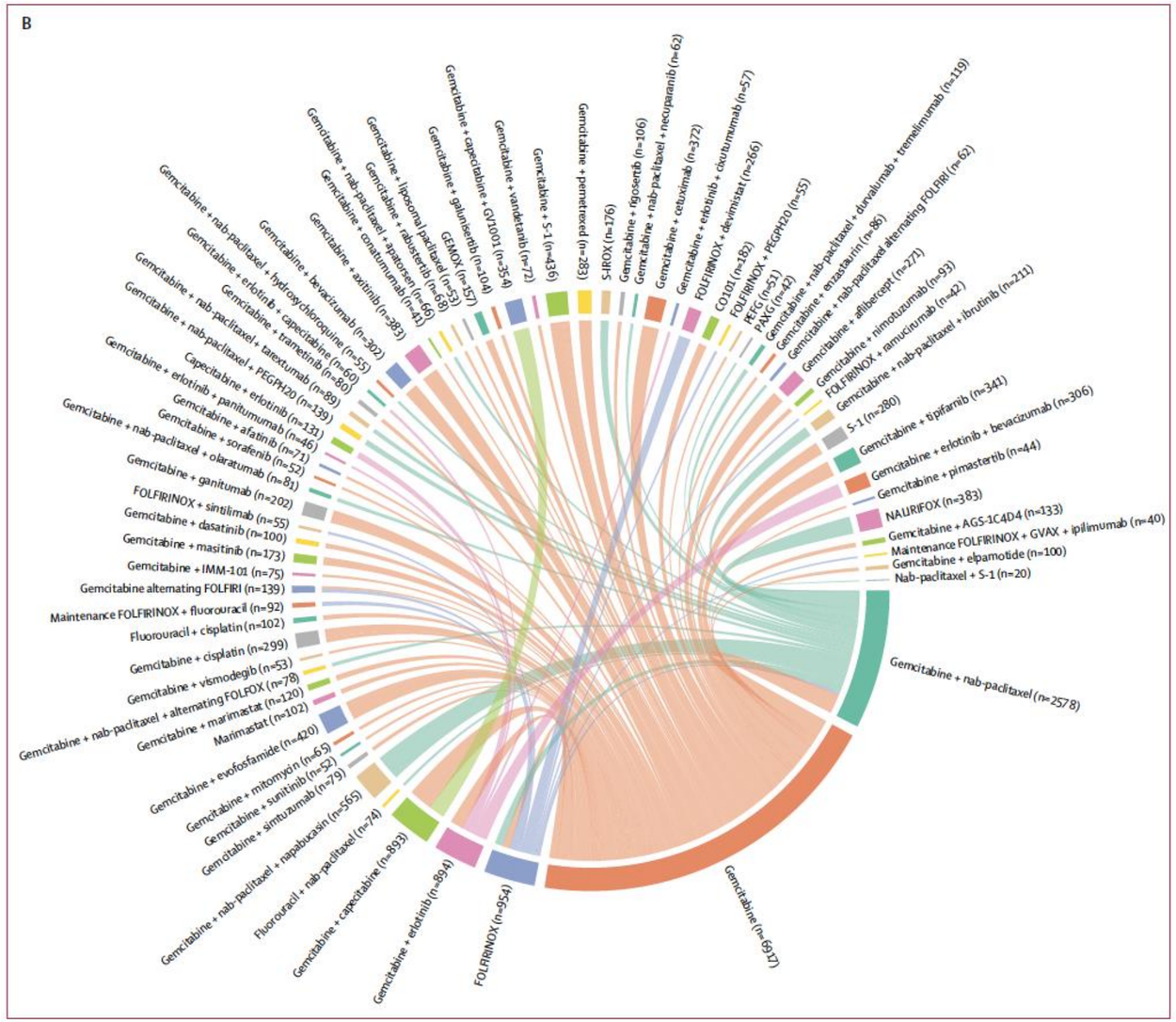


Figure 3. Reporting Incidence of Grade 3 or Higher Toxic Effects According to the Pooled Treatment Regimens



Nichetti et al, *JAMA Netw* 2024

1ère ligne : méta-analyse



Comparison of first-line chemotherapy regimens in unresectable locally advanced or metastatic pancreatic cancer: a systematic review and Bayesian network meta-analysis

Luca Mastrantoni, Marta Chiaravalli*, Alexia Spring, Viria Beccia, Armando Di Bello, Cinzia Bagalà, Maria Bensi, Diletta Barone, Giovanni Trovato, Giulia Caira, Giulia Giordano, Emilio Bria, Giampaolo Tortora†, Lisa Salvatore†*

Comparison | PFS | OS

Gemcitabine (PFS=5652, OS=6917 patients)	0·67* (0·59–0·77)	0·66* (0·56–0·78)	0·56† (0·45–0·70)	0·40† (0·25–0·65)	0·46† (0·32–0·66)
0·62* (0·54–0·72)	Gemcitabine plus nab-paclitaxel (PFS=2553, OS=2578 patients)	0·98‡ (0·83–1·16)	0·83§ (0·70–0·98)	0·60* (0·38–0·94)	0·68* (0·48–0·95)
0·55* (0·47–0·65)	0·88‡ (0·75–1·04)	FOLFIRINOX (PFS and OS=954 patients)	0·85‡ (0·66–1·08)	0·61‡ (0·38–0·99)	0·69‡ (0·47–1·01)
0·43* (0·34–0·54)	0·69§ (0·58–0·83)	0·78‡ (0·61–1·00)	NALIRIFOX (PFS and OS=383 patients)	0·72‡ (0·45–1·16)	0·82‡ (0·56–1·20)
0·35† (0·22–0·55)	0·56* (0·36–0·87)	0·63‡ (0·39–1·02)	0·81‡ (0·50–1·30)	PAXG (PFS and OS=42 patients)	1·14‡ (0·65–2·00)
0·32† (0·22–0·47)	0·52* (0·36–0·74)	0·59‡ (0·40–0·87)	0·75‡ (0·51–1·12)	0·93‡ (0·52–1·64)	Gemcitabine plus nab-paclitaxel alternating FOLFOX (PFS and OS=78 patients)

Mastrantoni et al, *Lancet Oncol* 2024

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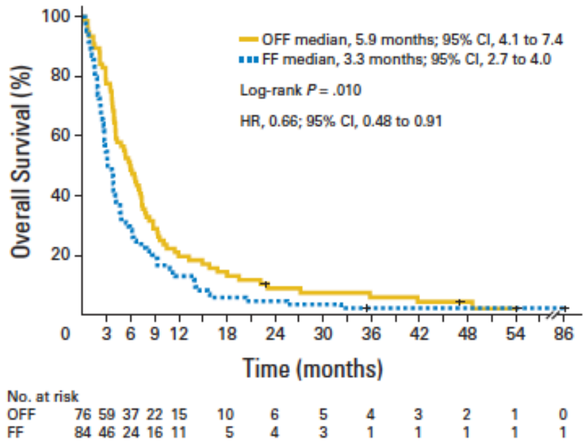
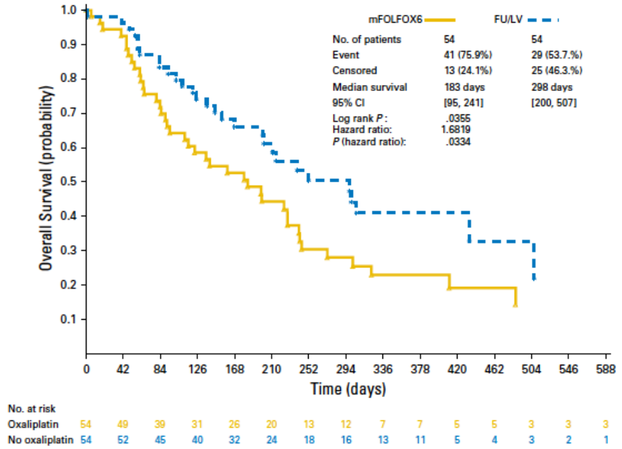
Les bases : 2ème ligne

2014: CONKO-003
OFF
(**FF** + **oxaliplatin** 85 mg/m^2, D8-D22)
> FF
(**5FU** 2,000 mg/m^2 + **FA** 200 mg/m^2, D1-D8-D15-D22, D1=D43)



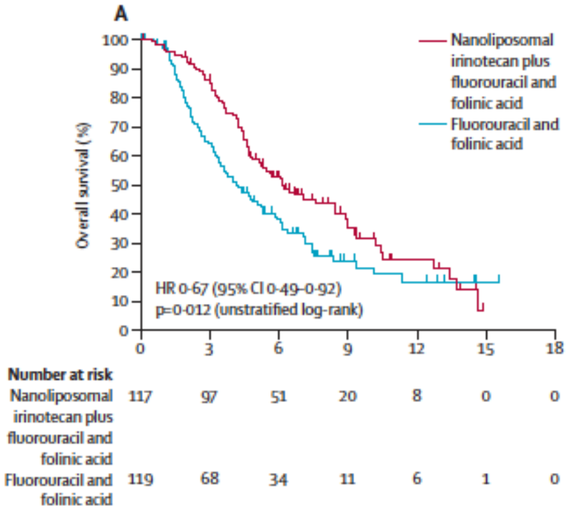
Phase III – N=168, post-Gem
mOS: 5.9 vs 3.3 months, p=0.010

2016: PANCREOX
FU/LV
(**5FU** bolus 400 mg/m^2 then 2,400 mg/m^2 + **LV** 400 mg/m^2, D1=D15)
> mFOLFOX6
(**FU/LV** + **oxaliplatin** 85 mg/m^2)



Phase III – N=108, post-Gem
mPFS: NS
mOS: shorter with FOLFOX, p=0.02
Grade 3-4 tox.: 63% vs 11%

2016: NAPOLI-1
5FU/FA + Nal-IRI
(80 mg/m^2=70 mg/m^2 of irinotecan base)
> 5FU/FA



Phase III – N=417, post-Gem
mOS: 6.1 vs 4.2 months, p=0.012

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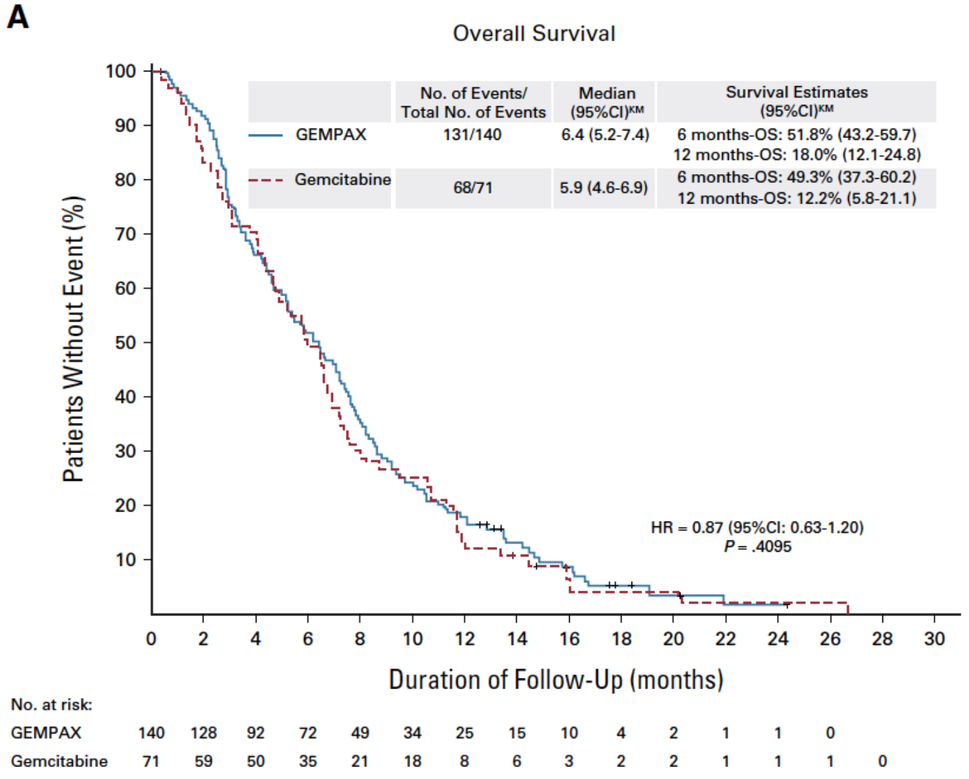
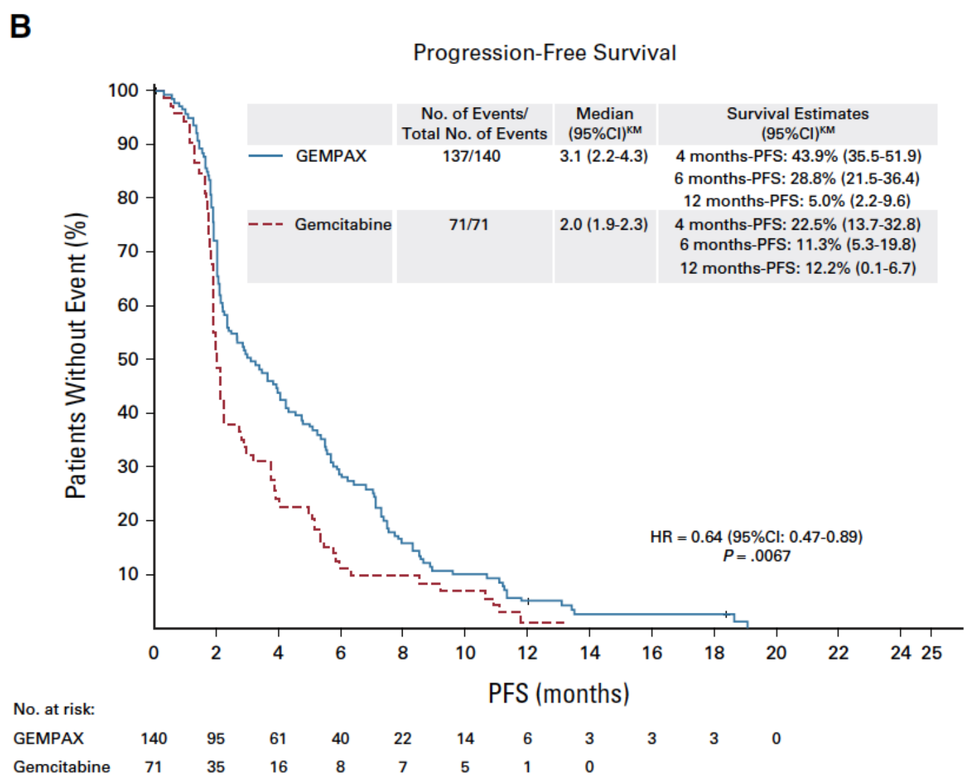
Oettle et al, *J Clin Oncol* 2014; Gill et al, *J Clin Oncol* 2016; Wang-Gillam et al, *Lancet* 2016

Nouveauté = GEMPAX (post-FFX)





ORR and Duration of Follow-Up	Random Assignment Arm: GEMPAX (arm A; n = 140)	Random Assignment Arm: Gemcitabine (arm B; n = 71)	Randomly Assigned Patients (n = 211)
Objective response,[a] n/N (%)	24/140 (17.1)	3/71 (4.2)	27/211 (12.8)
95% CI	11.3 to 24.4	0.9 to 11.9	8.6 to 18.1 Chi-2 *P* = .008

de la Fouchardière et al, *J Clin Oncol* 2024

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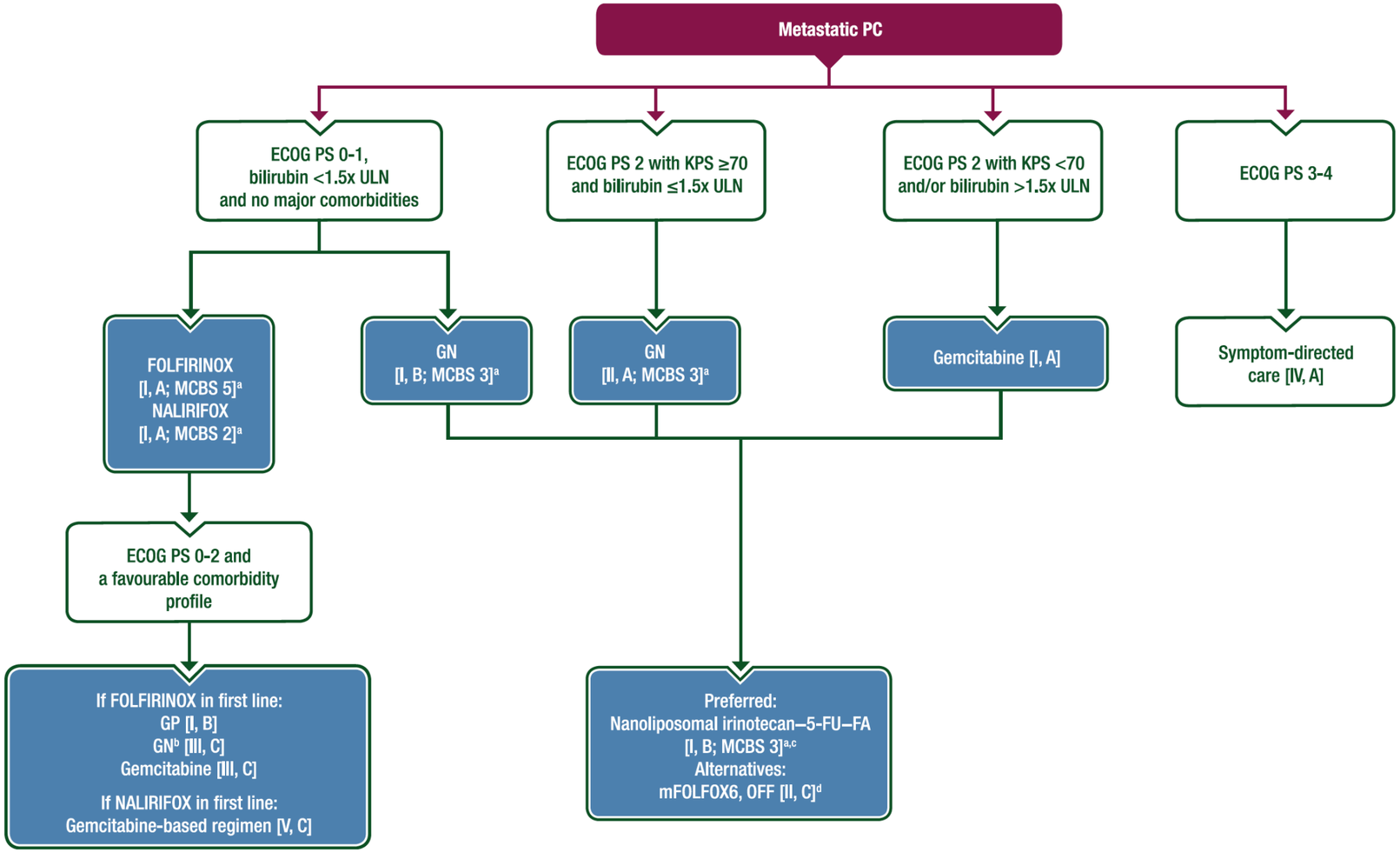
Recommandations ESMO 2025



Conroy et al., *Ann Oncol* 2025

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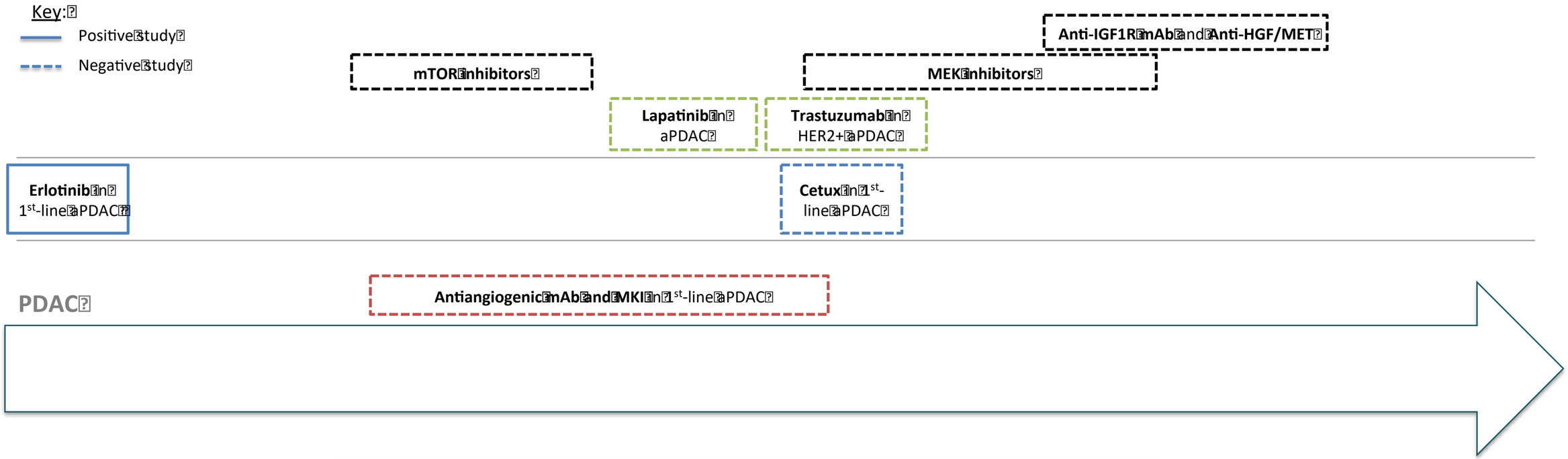
Médecine personnalisée ?

Place dans les recommandations ESMO 2025

Les leçons du passé…



Échec de toutes les thérapies ciblées testées dans des populations « tout venant » non sélectionnées

(sauf **erlotinib** mais gain de mSG= 10 jours…)

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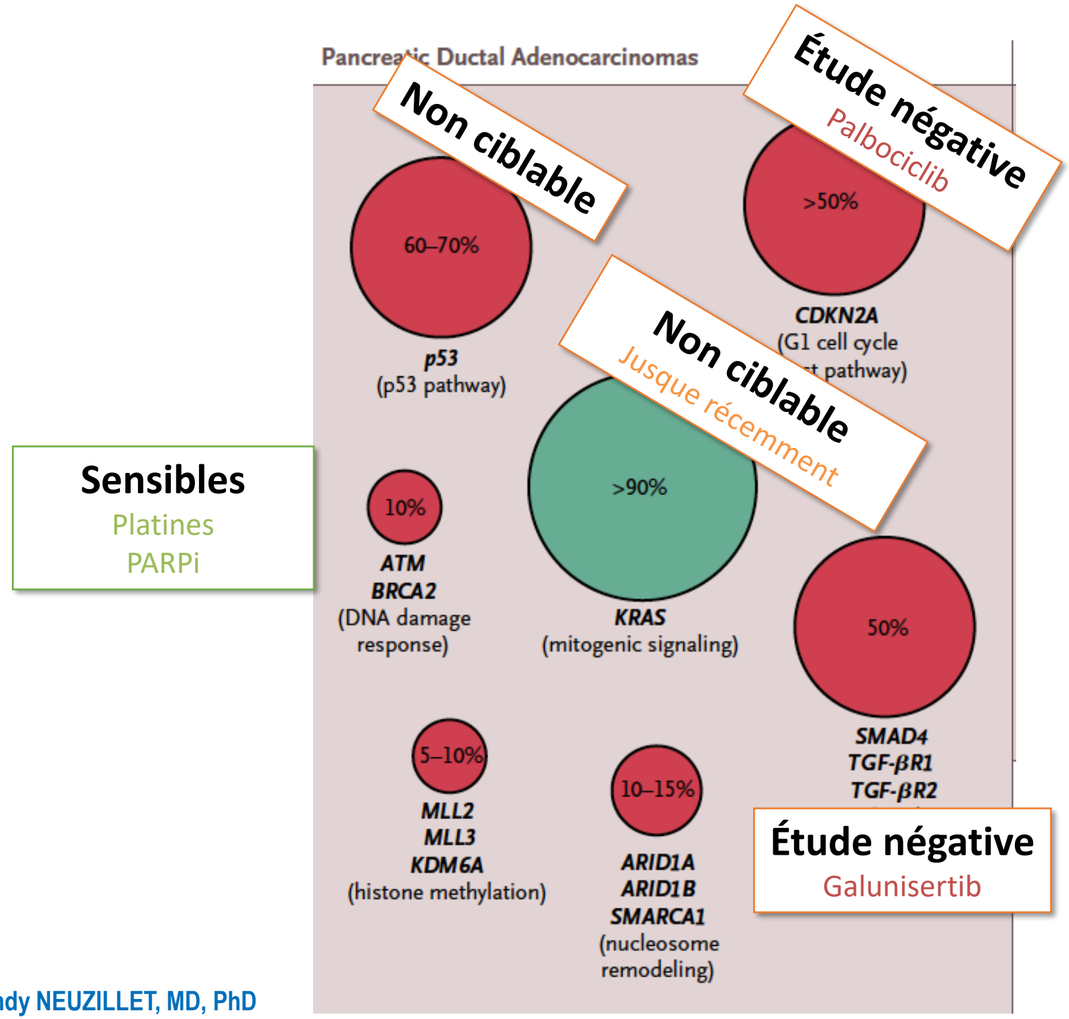
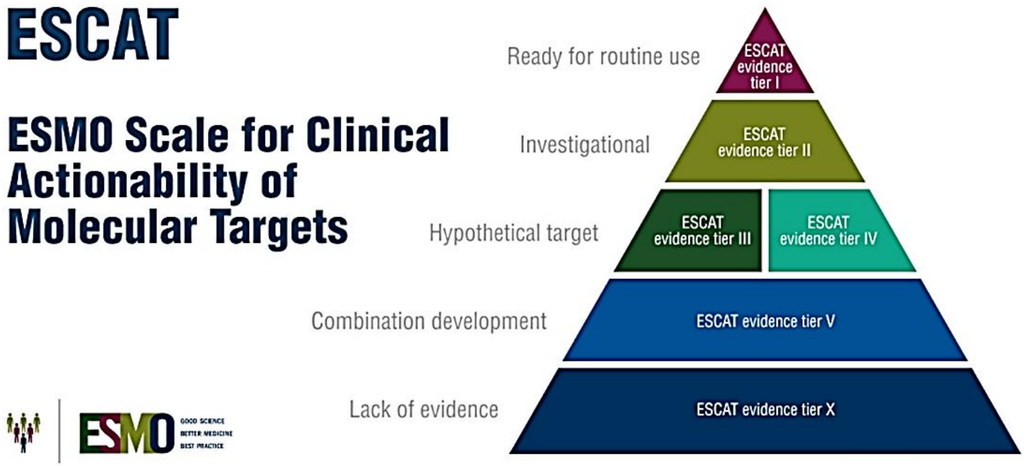
Lowery et al., Clin Cancer Res 2017

Neuzillet et al., Pharmacol Ther 2017

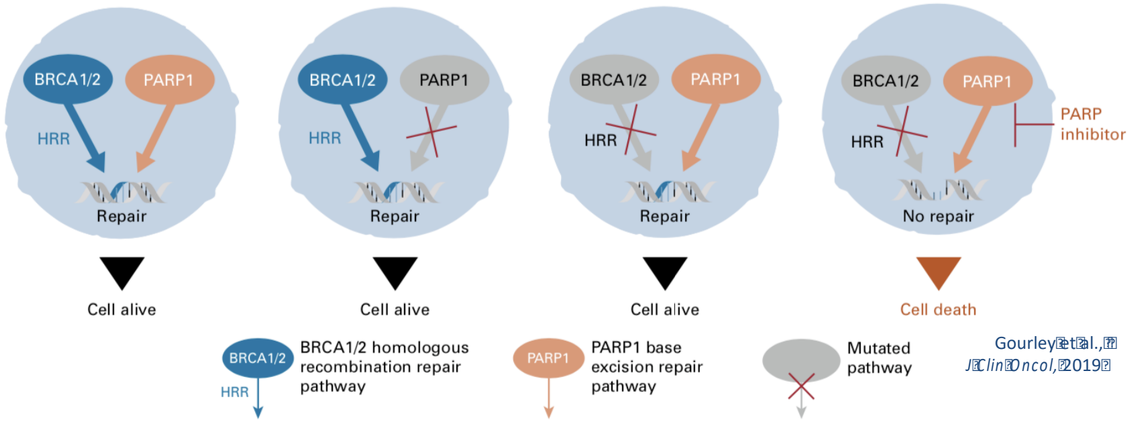
Les leçons du passé…



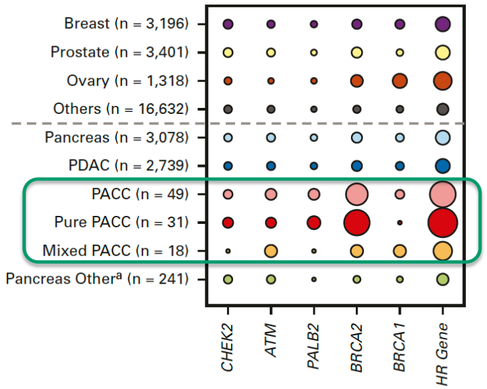


Ryan et al., *N Engl J Med* 2014

Mutations germinales BRCA1/BRCA2 (5%-7%)

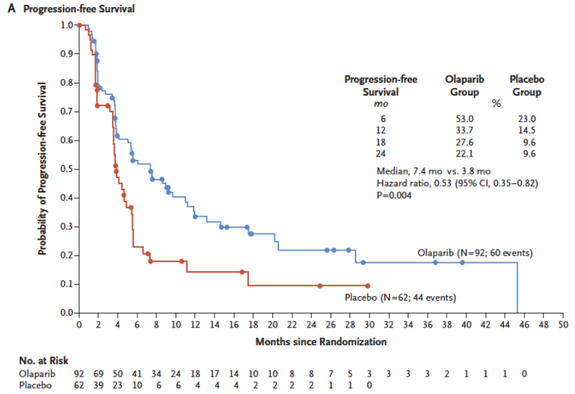


Gourley et al., *J Clin Oncol*, 2019



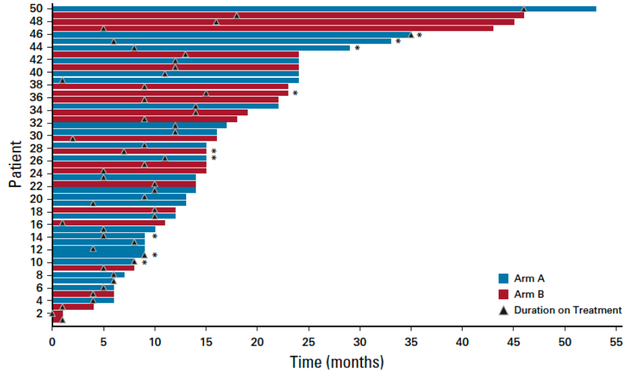
Mandelker et al., J Clin Oncol 2023

Olaparib maintenance POSITIVE



POLO Ph. III trial: Golan et al., *N Engl J Med* 2019; Kindler et al., *J Clin Oncol* 2022

CisGem + Veliparib NEGATIVE



O'Reilly et al., *J Clin Oncol* 2020

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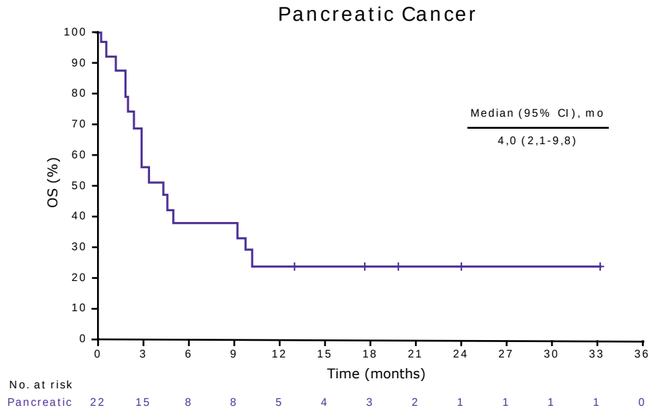
MSI/dMMR (1%-2%)

The NEW ENGLAND JOURNAL of MEDICINE

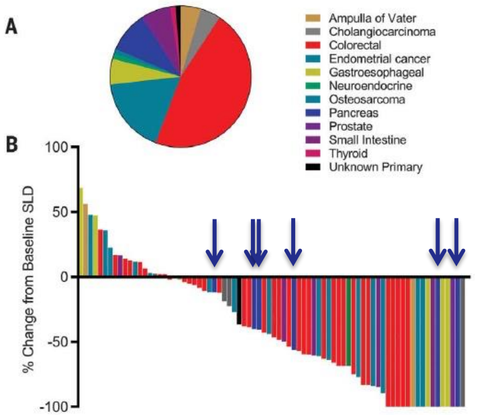
ORIGINAL ARTICLE

PD-1 Blockade in Tumors with Mismatch-Repair Deficiency

Le et al., N Engl J Med 2015; Science 2017



Tumor Type	No.	CR, No.	PR, No.	ORR, % (95% CI)	Median PFS, Months (95% CI)	Median OS, Months (95% CI)
Endometrial	49	8	20	57.1 (42.2 to 71.2)	25.7 (4.9 to NR)	NR (27.2 to NR)
Gastric	24	4	7	45.8 (25.6 to 67.2)	11.0 (2.1 to NR)	NR (7.2 to NR)
Cholangiocarcinoma	22	2	7	40.9 (20.7 to 63.6)	4.2 (2.1 to NR)	24.3 (6.5 to NR)
Pancreatic	22	1	3	18.2 (5.2 to 40.3)	2.1 (1.9 to 3.4)	4.0 (2.1 to 9.8)



Efficacy of immune checkpoint inhibitors in microsatellite unstable/mismatch repair-deficient advanced pancreatic adenocarcinoma: an AGEO European Cohort

Julien Taïeb, MD-PhD • Lina Sayah, MD • Kathrin Heinrich, MD • ... C. Benedikt Westphalen, MD • Edouard Auclin, MD • Lorenzo Pilla, MD • Show all authors • Show footnotes

Published: April 22, 2023 • DOI: https://doi.org/10.1016/j.ejca.2023.04.012

ORR: 48.4% and DCR: 67.7%
mPFS: 26.7 months and mOS: not reached

KEYNOTE 158 et 164
Diaz et al., ESMO 2019, abs 1174O
Marabelle et al., *J Clin Oncol* 2020
Taieb et al., Eur J Cancer 2023
Wang et al., *JNCCN* 2021
Philip et al., Clin Cancer Res 2022

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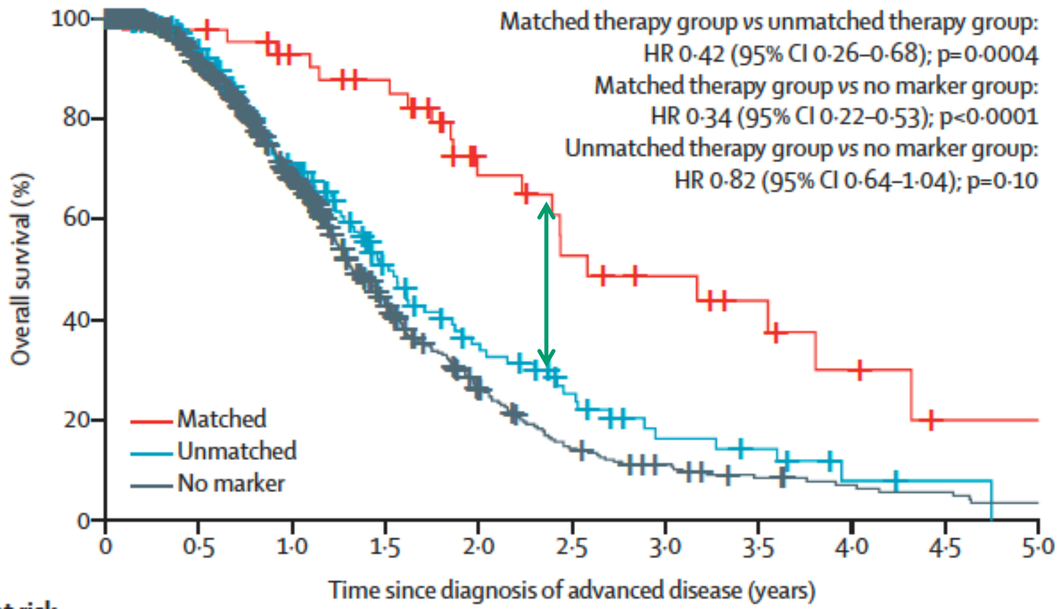
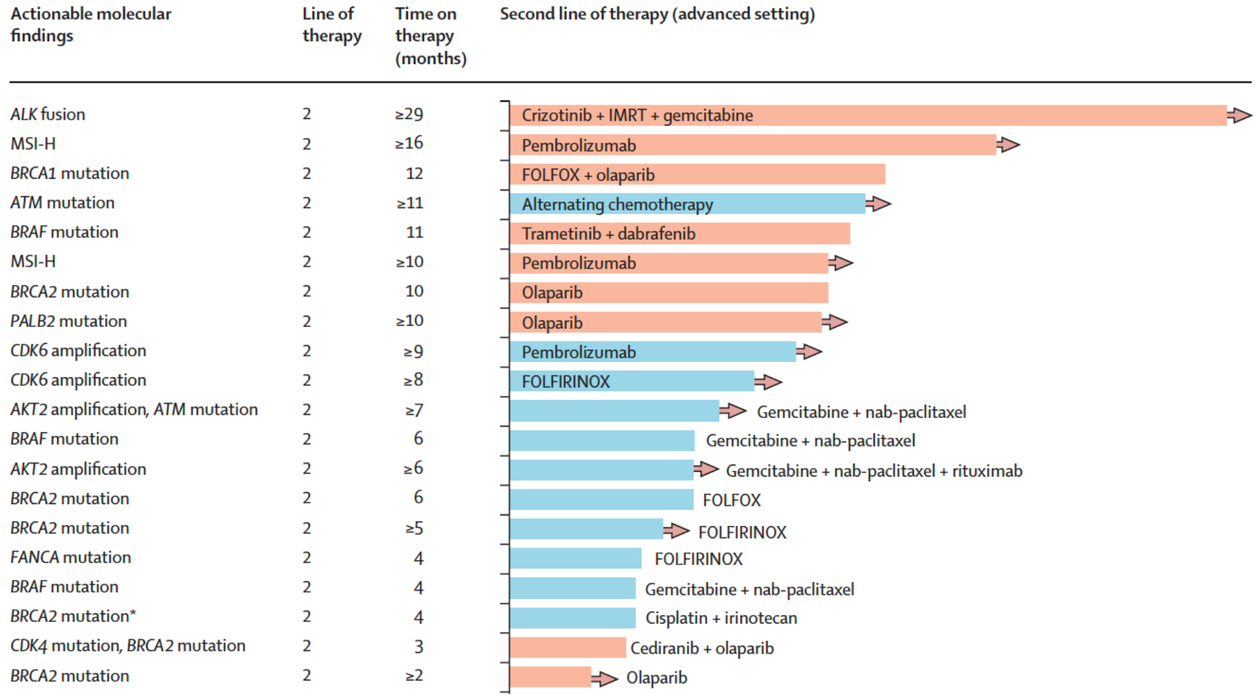
Thérapie ciblée : utilité clinique ?



Number at risk (number censored)											
Matched therapy	46	42	36	32	18	13	10	7	4	1	1
	(0)	(3)	(4)	(2)	(8)	(1)	(2)	(2)	(1)	(2)	(0)
Unmatched therapy	143	116	78	44	27	16	8	6	2	1	0
	(0)	(19)	(11)	(15)	(4)	(4)	(3)	(1)	(2)	(1)	(0)
No marker	488	384	241	124	63	33	22	14	10	8	5
	(0)	(66)	(55)	(39)	(15)	(4)	(4)	(3)	(2)	(0)	(0)



MSI, BRCAness, gènes de fusions
(< 10% des patients)

Pishvaian et al., *Lancet Oncol* 2020

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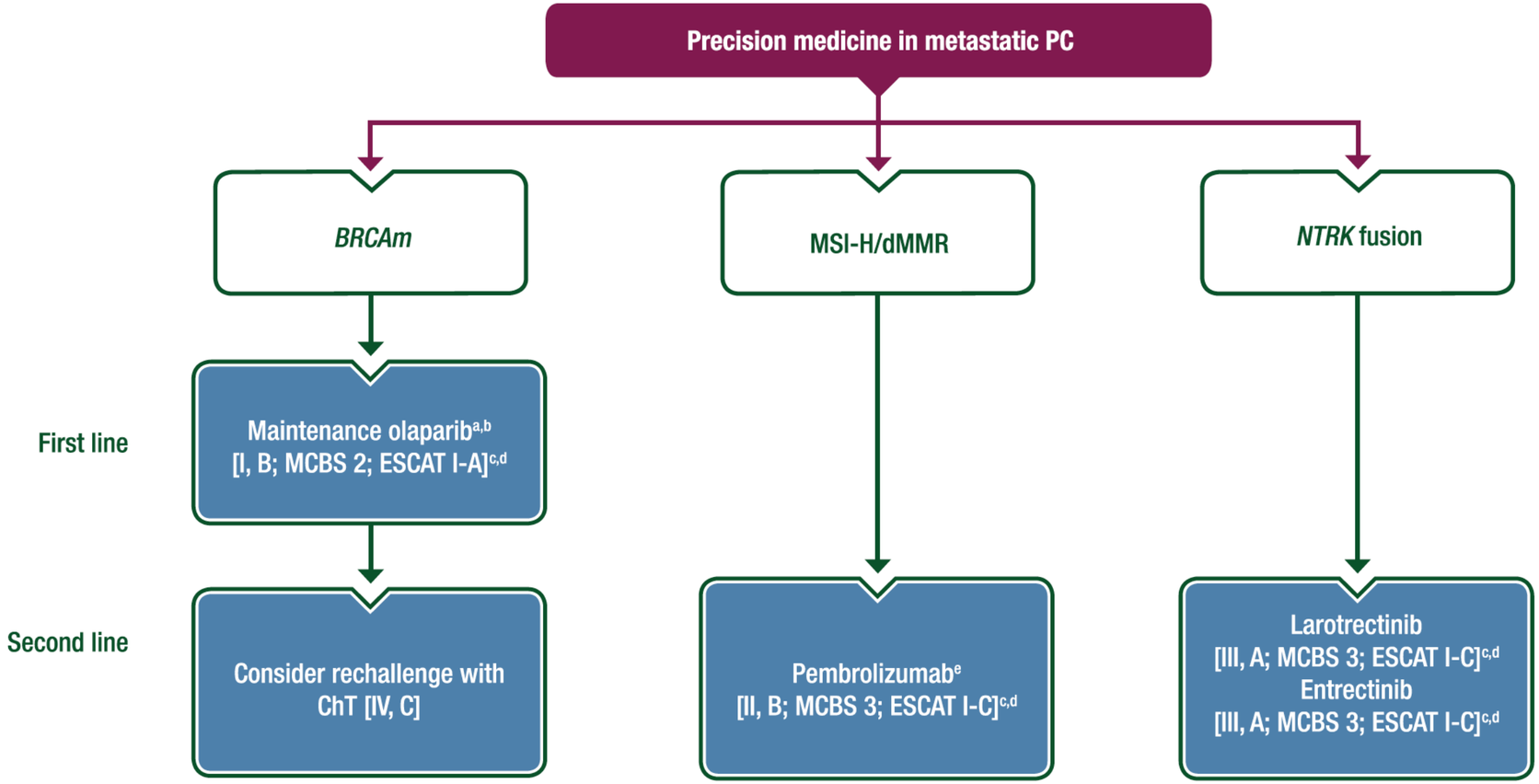
Recommandations ESMO



Conroy et al., *Ann Oncol* 2023

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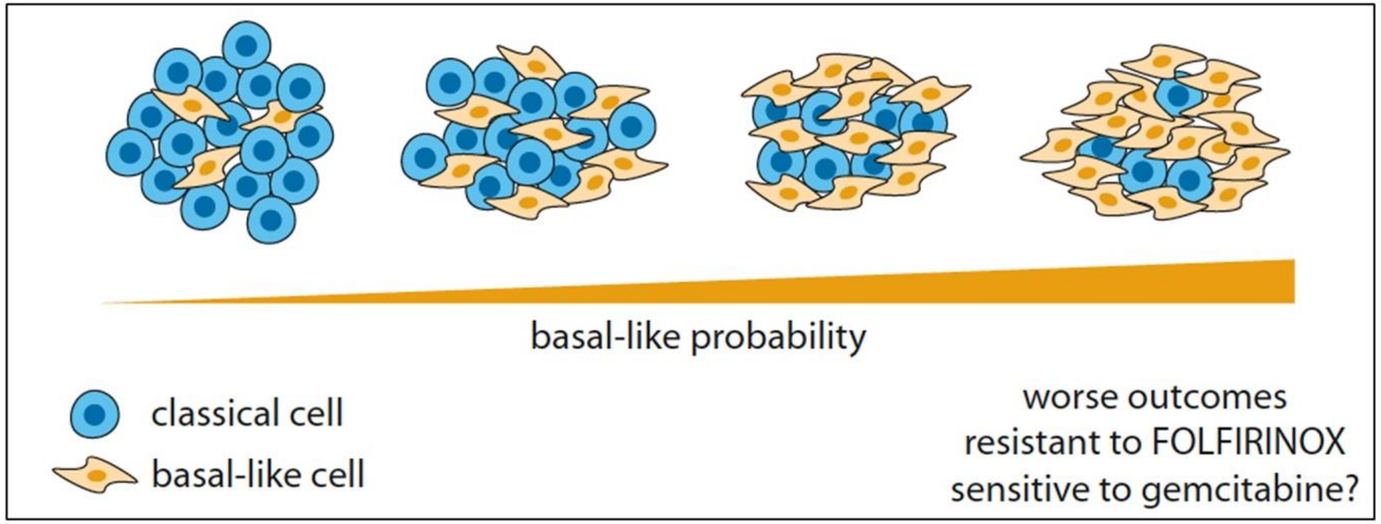
Mais ça bouge !

Perspectives en 2025

PISTE #1 : Mieux utiliser les molécules déjà disponibles



Trial	CTx	Classical	Basal	P-value
COMPASS Investigator choice (N=195)	**FOLFIRINOX,** mOS (months)	10.62	6.54	HR 0.33 p=0.0001
	Gem nabP, mOS (months)	8.19	8.12	NS
PASS-01 Randomized (N=103)	**FOLFIRINOX,** mPFS (months)	5.7	2.7	
	Gem nabP, mPFS (months)	5.7	5.7	

Cindy NEUZILL

Lee et al., *Surg Clin N Am* 2024; O'Kane et al., *Clin Cancer Res* 2024; Knox et al., ASCO® Annual Meeting 2024

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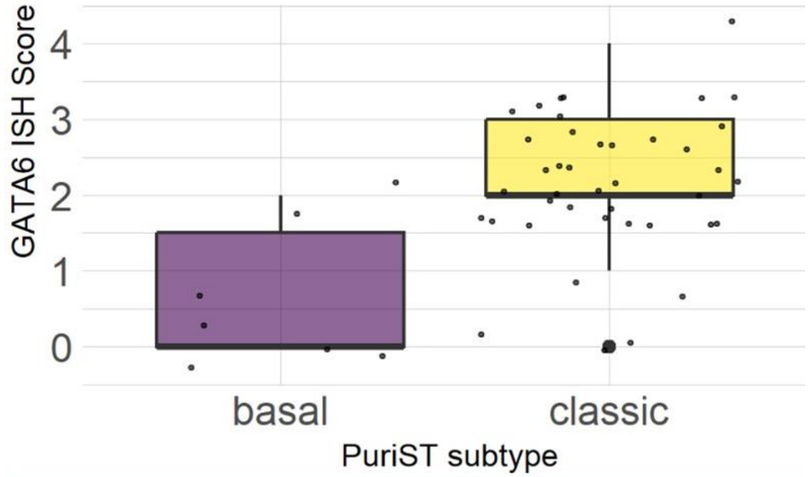
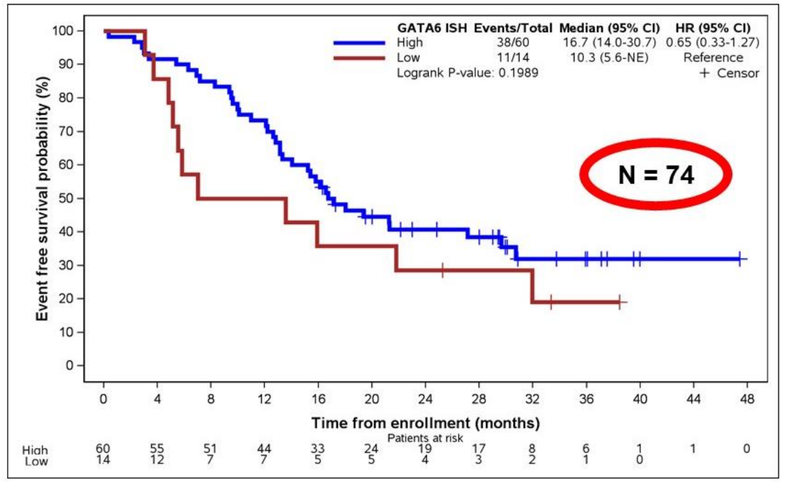
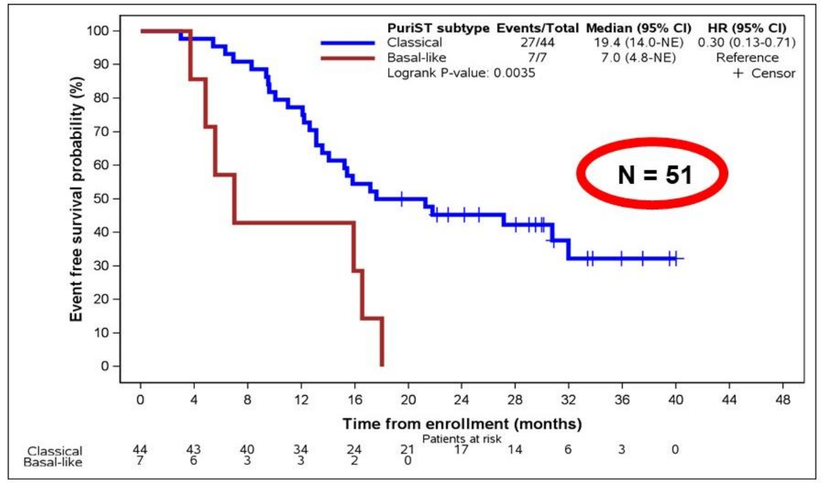




1 year EFS: **88% in high** vs **71% for low** GATA6-ISH
HR: 0.65 (0.33 – 1.27)
Logrank **P-value = 0.1989**



1 year EFS: **77% in Classical** vs **43% in Basal-like**
HR: 0.30 (0.13 – 0.71)
Logrank **P-value = 0.0035**

<u>Études en cours</u> :
Néoadjuvant - **PANCREAS PurIST** (NCT04683315)
Adjuvant - **ESPAC-6** (NCT05314998)

Mclaughlin et al., ASCO® Annual Meeting 2025

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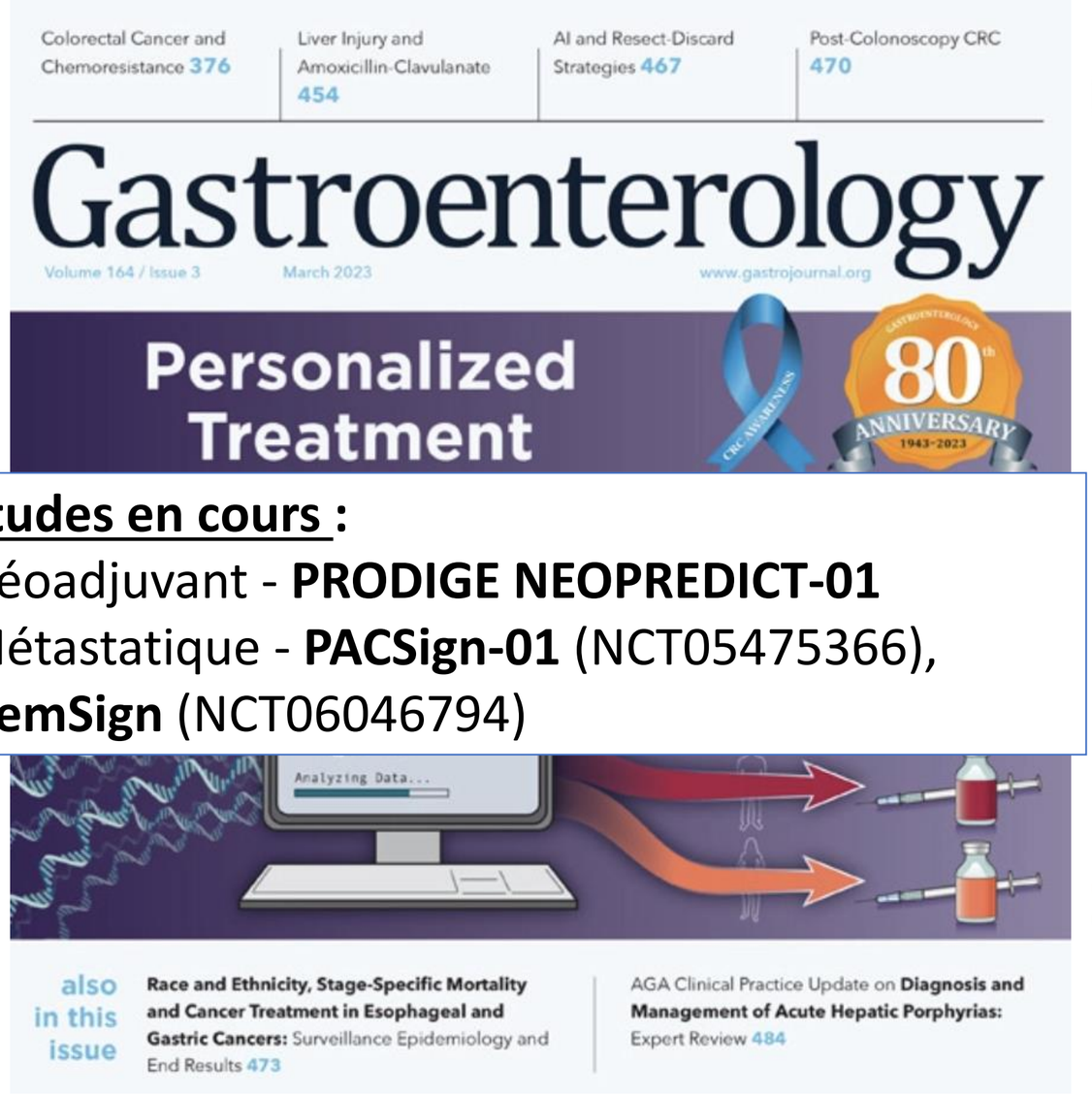
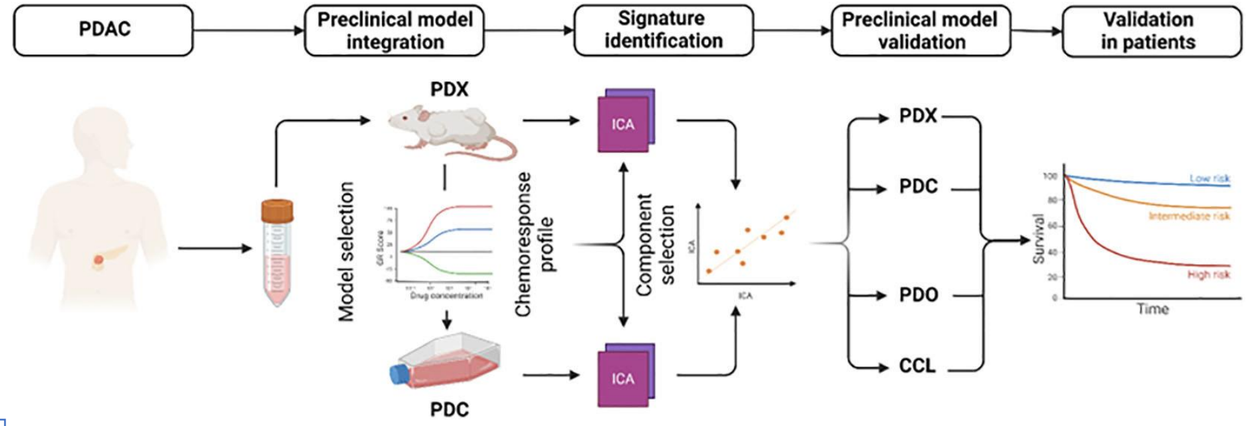
PISTE #1 : Mieux utiliser les molécules déjà disponibles

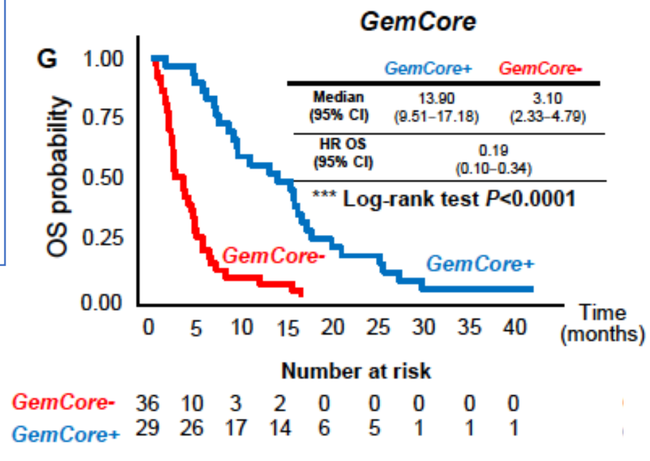


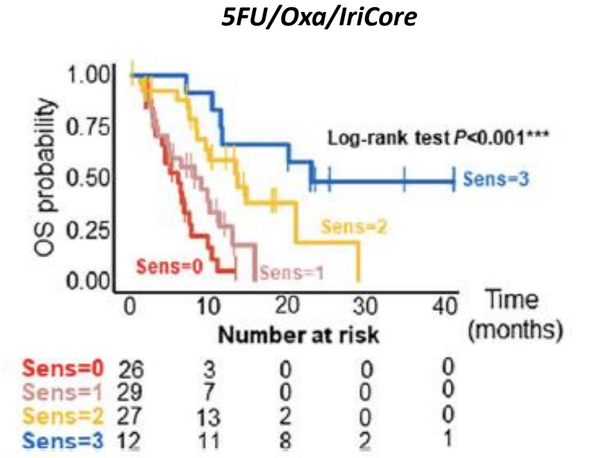
Études en cours :

Néoadjuvant - **PRODIGE NEOPREDICT-01**

Métastatique - **PACSign-01** (NCT05475366), **GemSign** (NCT06046794)





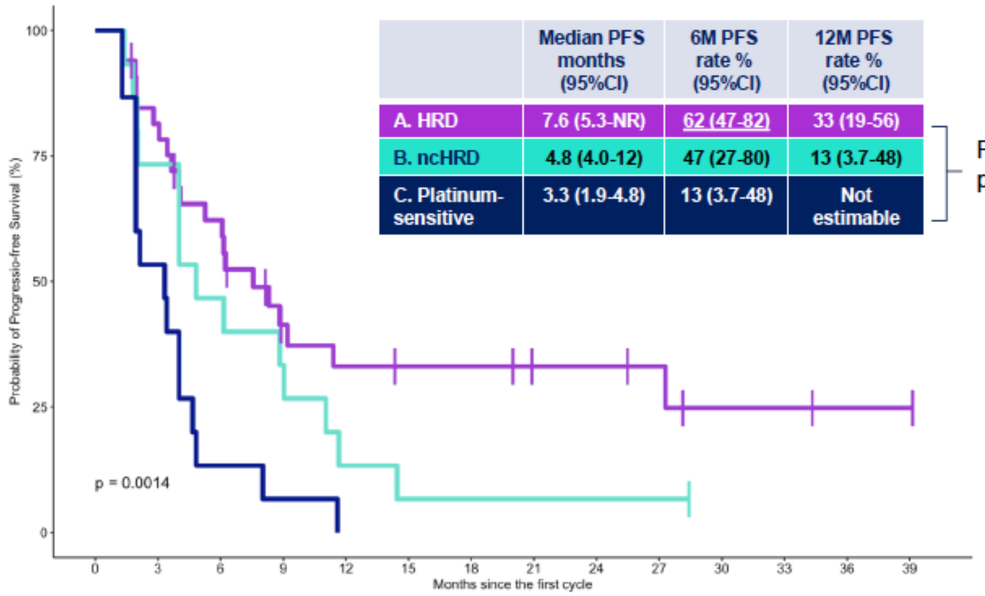


Fraunhoffer et al., *Gastroenterology* 2023

Fraunhoffer et al., *Front Oncol* 2024

PISTE #2 : Nouvelles cibles thérapeutiques - HRD

POLAR study
Maintenance
avec olaparib + pembrolizumab



	Median PFS months (95%CI)	6M PFS rate % (95%CI)	12M PFS rate % (95%CI)
A. HRD	7.6 (5.3-NR)	62 (47-82)	33 (19-56)
B. ncHRD	4.8 (4.0-12)	47 (27-80)	13 (3.7-48)
C. Platinum-sensitive	3.3 (1.9-4.8)	13 (3.7-48)	Not estimable

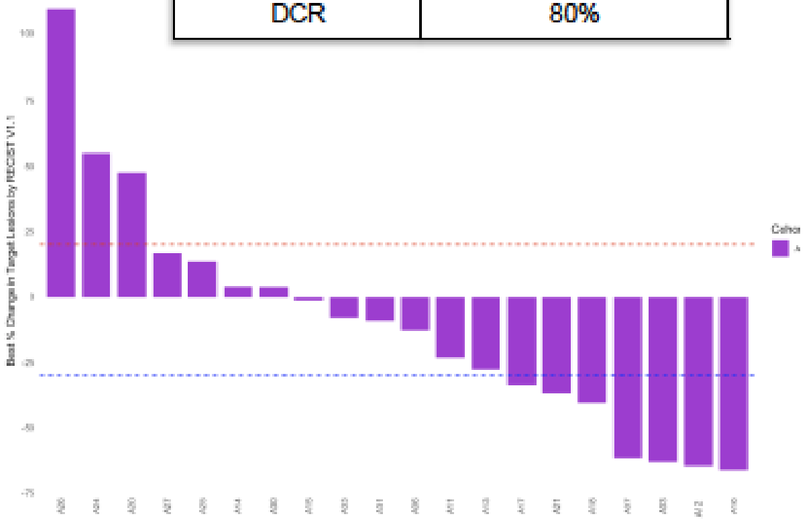
Post-hoc
p=0.0014

Cohort A. HRD
Homologous Recombination Deficiency (germline or somatic *BRCA2, PALB2, BRCA1* mutation) + SD/PR > 4M on platinum

Cohort B. ncHRD:
Non-Core HRD Mutation + SD/PR > 4M on platinum

Cohort C. Platinum Sensitive:
Platinum-sensitive without HRD mutation + PR/CR > 6M on platinum

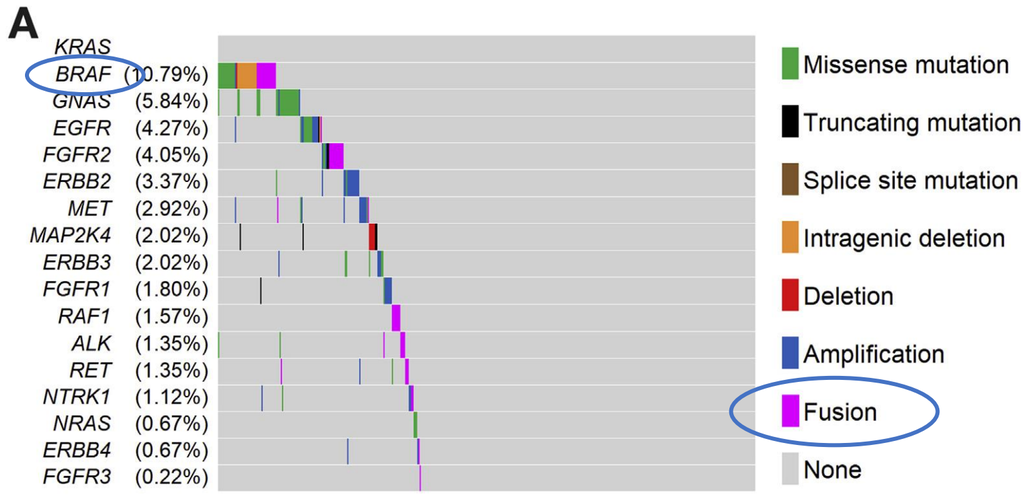
Primary endpoint	Cohort A. HRD
Total	N=20
ORR	35%
DCR	80%



Cohort A had only 20 out of 33 (60%) participants had measurable disease.
Cohort B had 12 (80%) and Cohort C had 14 (93%) measurable disease.

Park et al., ESMO® Annual Meeting 2024

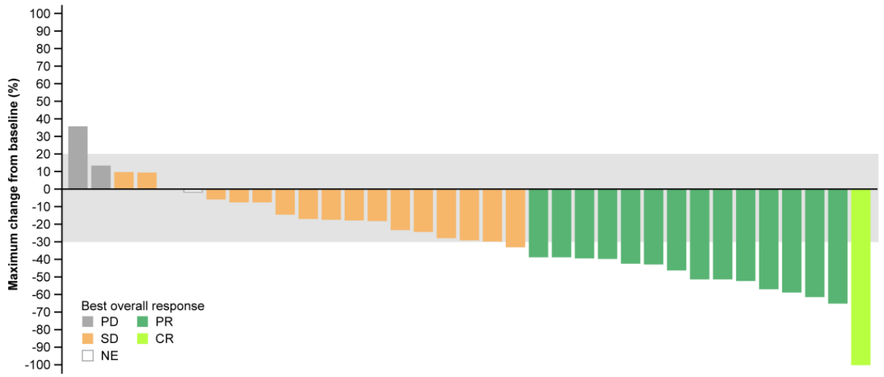
PISTE #2 : Nouvelles cibles thérapeutiques - KRAS^{WT} (5-10%)



Singhi et al., *Gastroenterology* 2019

ORIGINAL ARTICLE

Efficacy of Zenocutuzumab in NRG1 Fusion–Positive Cancer



Schram et al., *N Engl J Med* 2025

- **Plus fréquent dans les acineux (env. 90%)**

Philip et al., *Clin Cancer Res* 2022

- **Early Onset PDAC - âge ≤ 50 ans (n=450)**

Enrichis en *KRAS^{WT}* (15,9%)

Varghese et al., *JNCI* 2021

- **Sensibilité aux anti-EGFR**

Schultheis et al., *Ann Oncol* 2017

Phase III NOTABLE (N=82) Qin et al., *J Clin Oncol* 2023

- **KRAS^{WT} (n=266/2,483)**

Enrichis en altérations ciblables

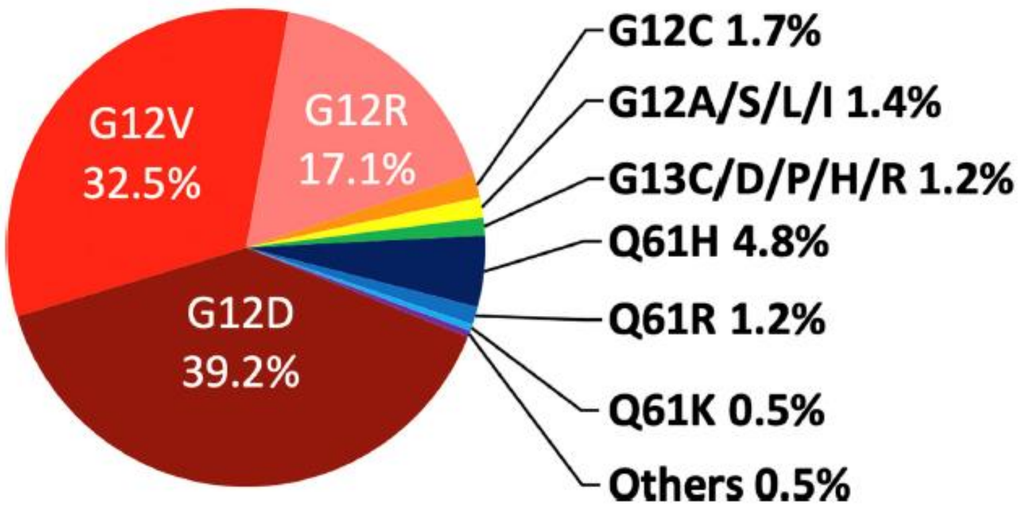
  - ***BRAF* :** mutation (13.0%), fusion (6.6%)
  - **Fusions** (mutuellement exclusives avec mut *KRAS/BRAF*)**:** *NTRK, NRG1, ALK, RET…*
  - **MSI:** 4,7% vs 0,7%

Philip et al., *Clin Cancer Res* 2022

Cindy NEUZILLET, MD, PhD

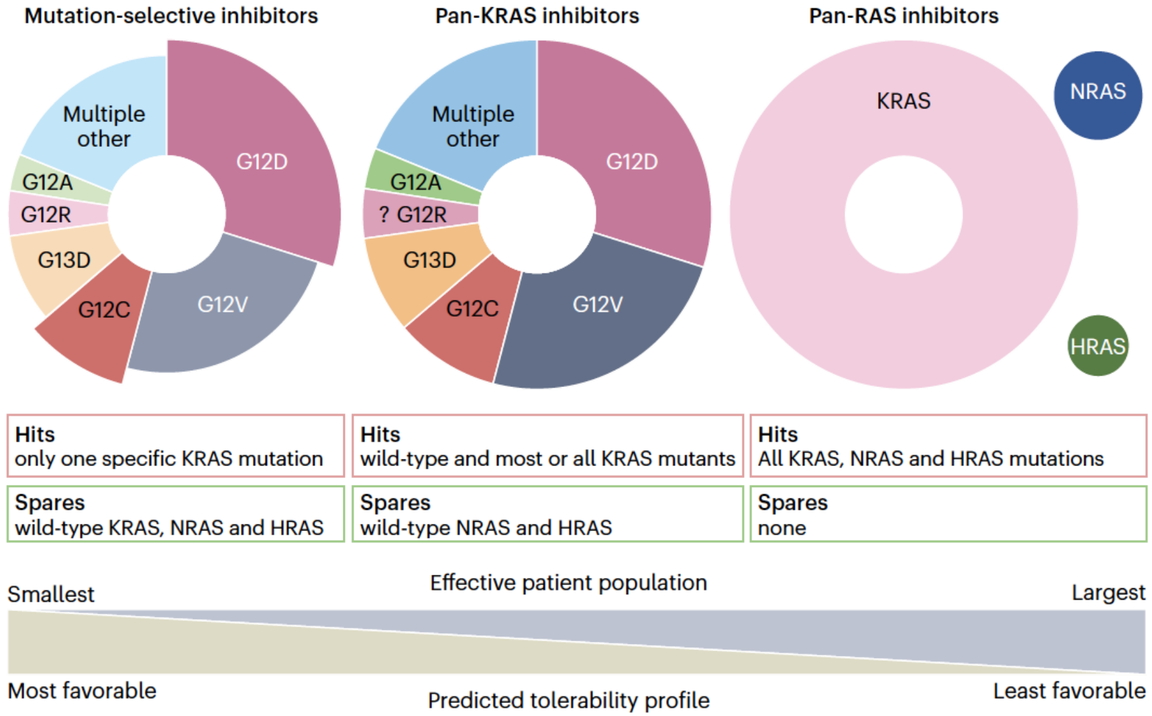
PISTE #2 : Nouvelles cibles thérapeutiques - KRAS^{MUT} (90%)

Type de mut. *KRAS* dans l'ADKP



cBioPortal - Luo et al., *Semin Oncol* 2021

Échec des inhibiteurs de Farnesyl transferase, MEK / RAF



Corcoran, *Nature Cancer* 2023

Agent	Target	ORR	DCR	PFS (months)
Adagrasib	KRAS G12C	33%	81%	5.4
Sotorasib	KRAS G12C	21%	75%	4.0
Daraxonrasib	Pan-KRAS	36% (G12X)	87% (G12X)	8.1
Zoldonrasib	KRAS G12D	30%	80%	-

Bekaii-Saab et al., *J Clin Oncol* 2023; Strickler et al., *N Engl J Med* 2022; Arbour et al., *Ann Oncol* 2023; Spira et al., *J Clin Oncol* 2025

Cindy NEUZILLET, MD, PhD

PISTE #2 : Nouvelles cibles thérapeutiques - $KRAS^{MUT}$ (90%)

Description	Compound (Company)	Target	Phase	Tumor Type
RASolute: Daraxonrasib in patients with previously treated mPDAC	RMC6236 (Revolution Medicine)	Pan-RAS	III	PDAC
RAS(ON) inhibitors +/- chemotherapy in patients with gastrointestinal solid tumors	RMC6236 RMC9805 (RevMed)	Pan-RAS KRAS G12D	Platform	PDAC, CRC
TSN1611 in KRAS G12D mutated advanced solid tumors	TSN1611 (Tyligand Therapeutics)	KRAS G12D	I/II	I: Solid tumors II: NSCLC, PDAC, NSCLC
AZD0022 as monotherapy and in combination with anti-cancer agents in KRAS G12D mutated tumors	AZD0022 (AstraZeneca)	KRAS G12D	I/Iia	Solid tumors
BGB53038 alone or in combinations	BGB53038 (Beigene)	Pan-KRAS	Ia/Ib	Solid tumors
LY4066434 in KRAS mutated advanced solid tumors	LY40664343 (Lilly)	Pan-KRAS	I	Solid tumors
LY3962673 in KRAS G12D mutated solid tumors	LY3962673 (Lilly)	KRAS G12D	I	Solid tumors
RMC9805 KRAS G12D mutated solid tumors	RMC9805 (RevMed)	KRAS G12D	I	Solid tumors
INCB1161734 in advanced KRAS G12D mutated solid tumors	INCB171734 (Incyte)	KRAS G12D	I	Solid tumors

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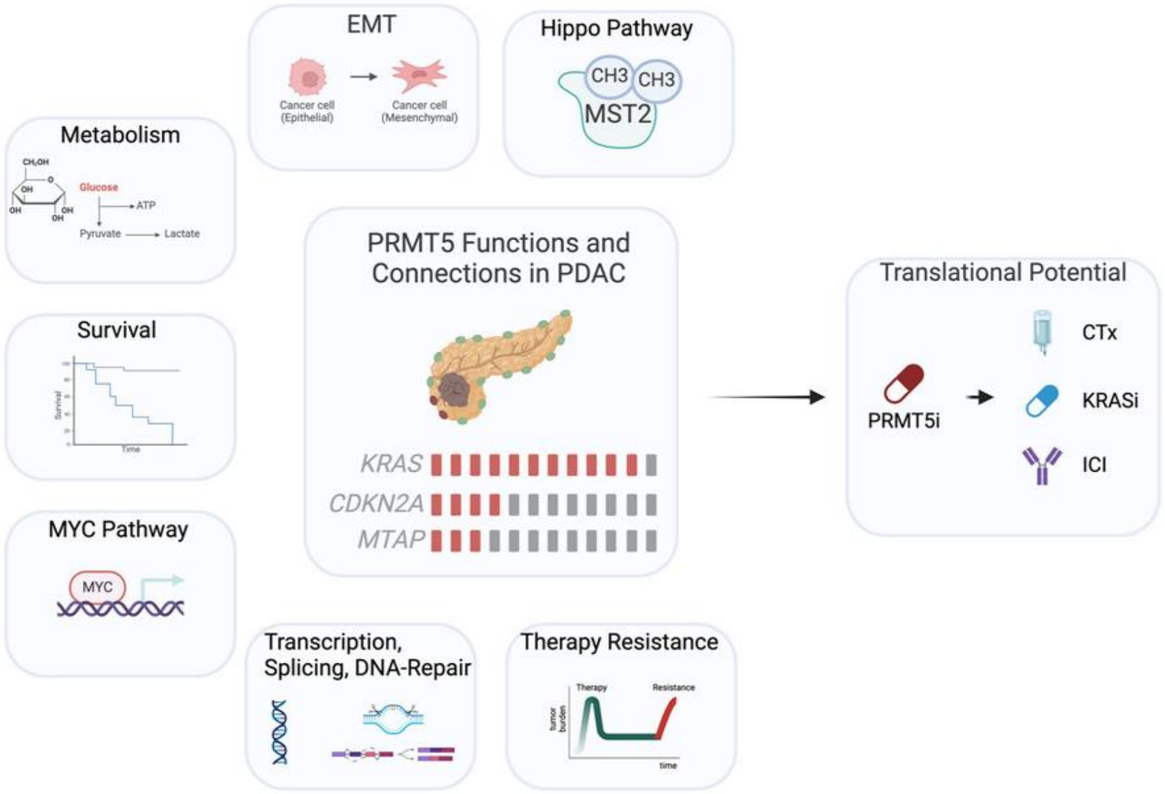
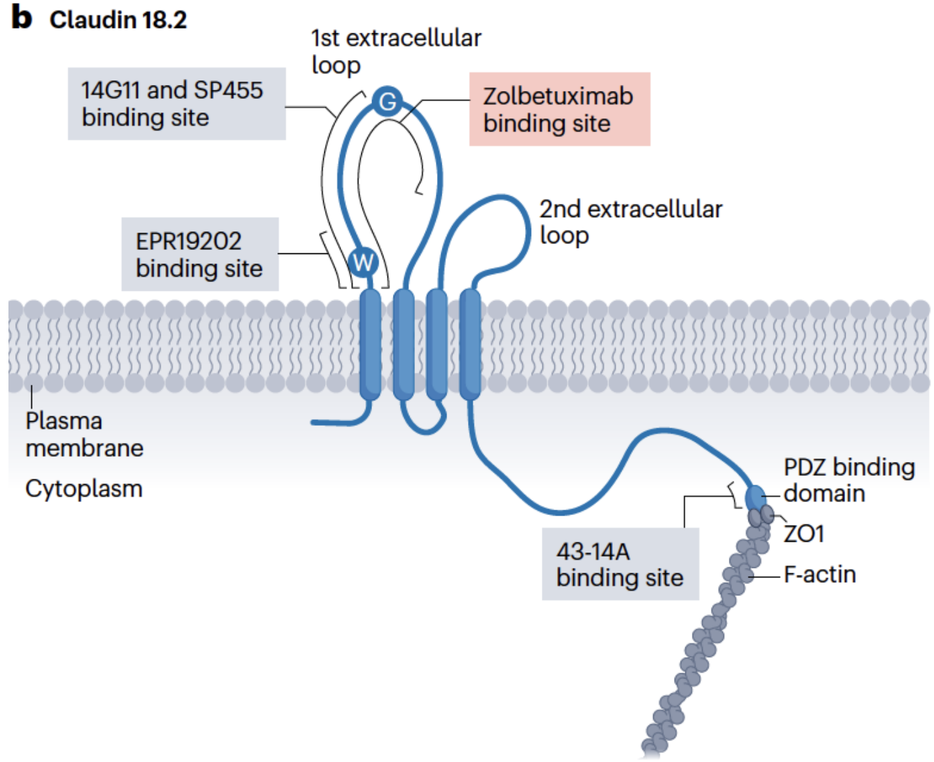
PISTE #2 : Nouvelles cibles thérapeutiques

MTAP



Schneider et al., *Transl Oncol* 2025; Nakayama et al., *Nature Rev Clin Oncol* 2024

Claudin 18.2



- **Monoclonal antibodies**
- **ADC**
- **Bispecific antibodies or T cell engagers**
- **CAR-T**

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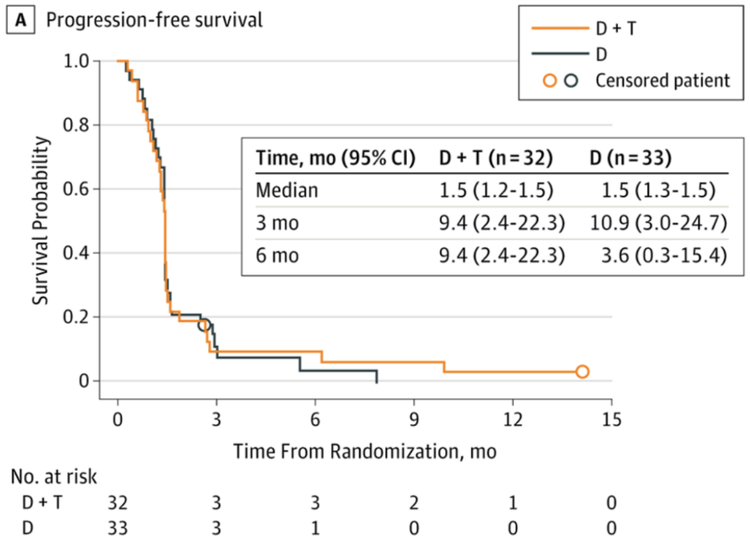
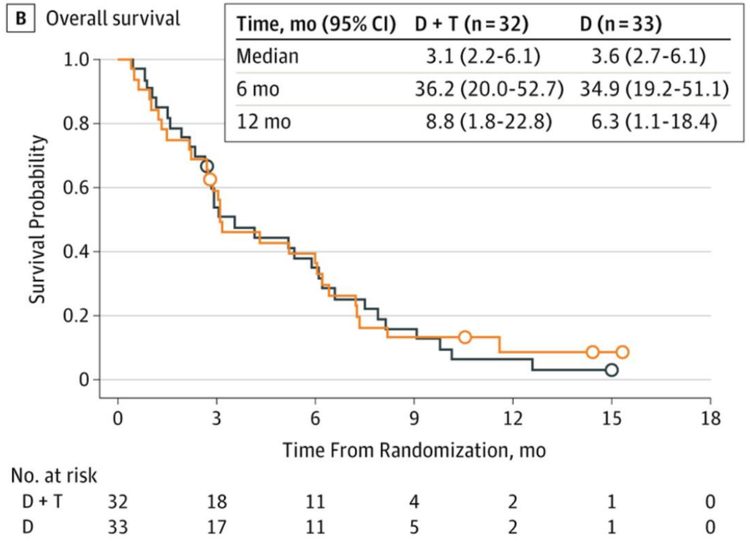
PISTE #3 : Revisiter l'immunothérapie

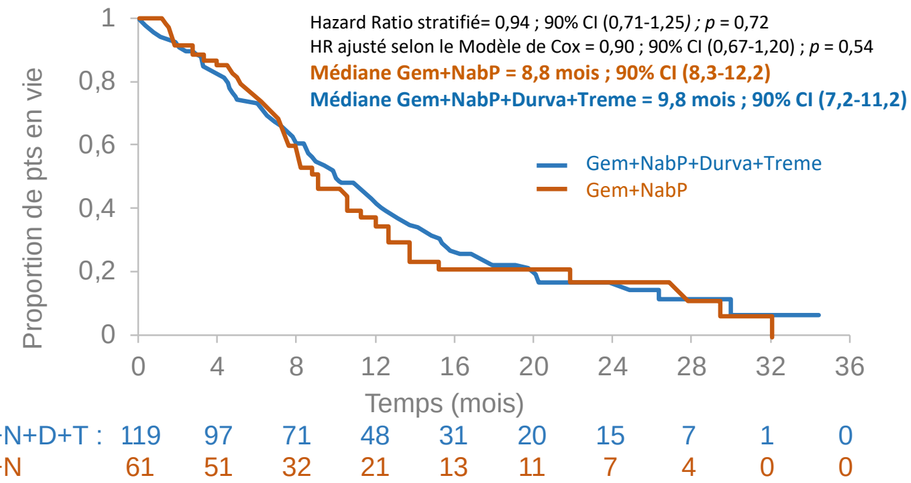
Durvalumab ± tremelimumab
Phase IIR
O'Reilly et al., *JAMA Oncol* 2019



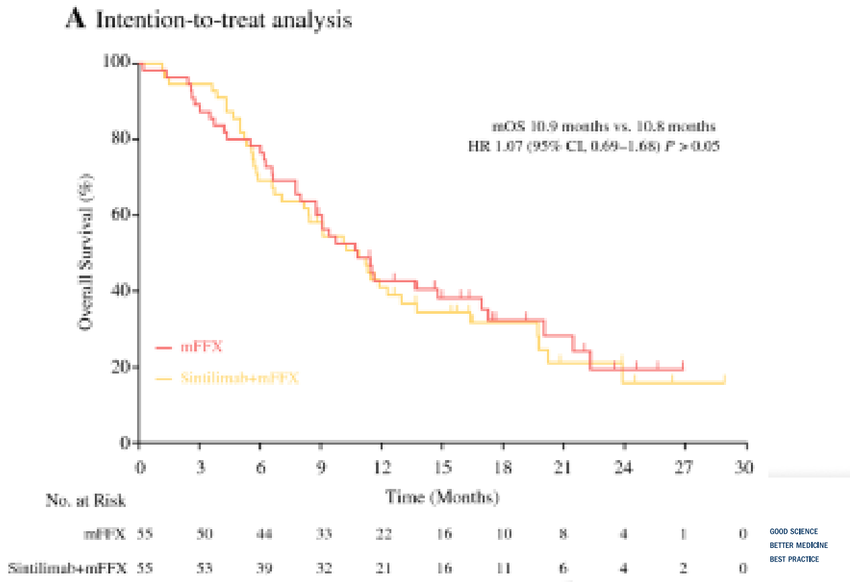


Résultats "prometteurs" puis décevants
JAK inhibiteur
TGFB inhibiteur
MEK inhibiteur…

Gem-nabP ± durvalumab + tremelimumab
Phase III PA.7
Renouf et al., ESMO 2020, Abs #LBA65

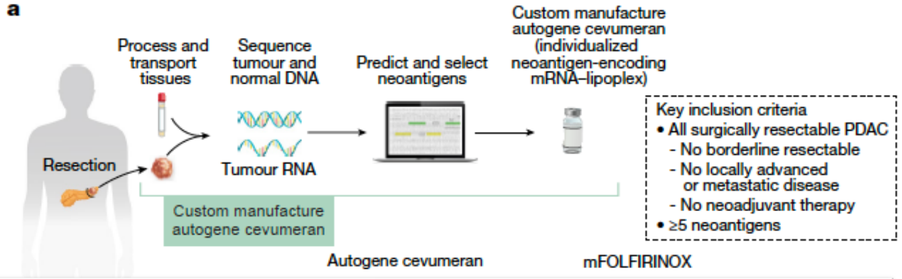


mFOLFIRINOX ± sintilimab
Phase IIR CISPD3
Fu et al., *Ann Surg Oncol* 2023



PISTE #3 : Revisiter l'immunothérapie

Vaccine trials



Recruiting

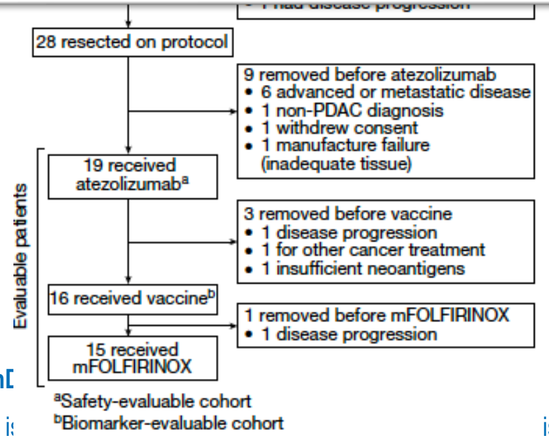
A Study of the Efficacy and Safety of Adjuvant Autogene Cevumeran Plus Atezolizumab and mFOLFIRINOX Versus mFOLFIRINOX Alone in Participants With Resected PDAC (IMCODE003)

ClinicalTrials.gov ID NCT05968326

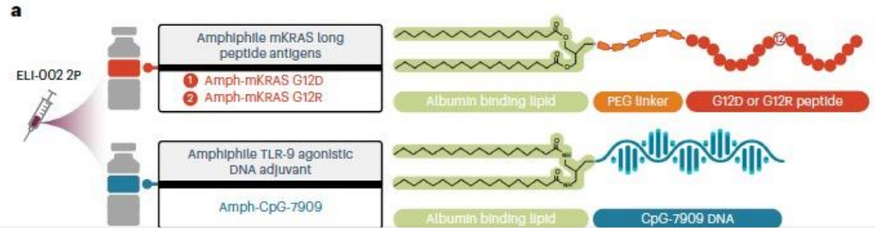
Sponsor Genentech, Inc.

Information provided by Genentech, Inc. (Responsible Party)

Last Update Posted 2024-12-05



Rojas et al., *Nature* 2023



Recruiting

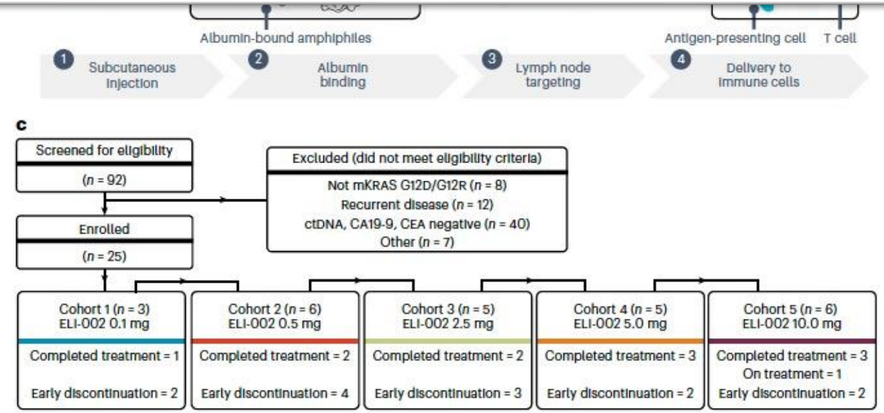
A Study of ELI-002 7P in Subjects With KRAS/NRAS Mutated Solid Tumors (AMPLIFY-7P)

ClinicalTrials.gov ID NCT05726864

Sponsor Elicio Therapeutics

Information provided by Elicio Therapeutics (Responsible Party)

Last Update Posted 2024-10-08



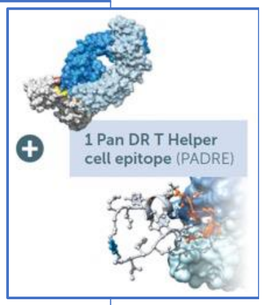
Pant et al, *Nature* 2024

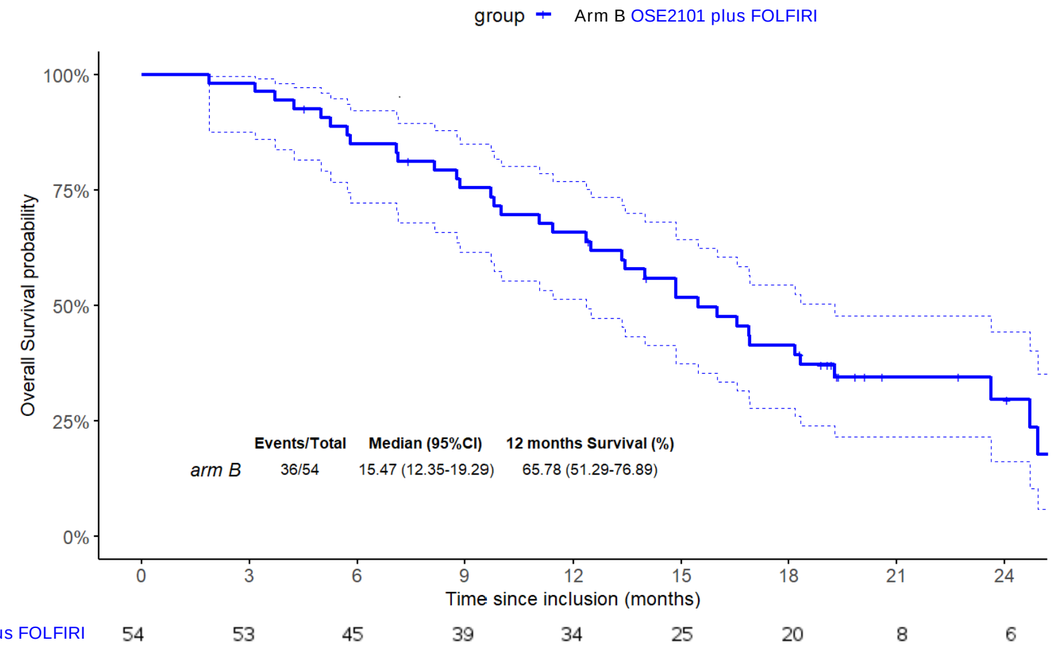
PISTE #3 : Revisiter l'immunothérapie

OSE2101 COMPOSITION

9 epitopes targeting 5 TAAs

Tumor associated antigens (TAAs) [expression in PDAC]	Wild-type and neo-epitopes
CEA [39-75%] P53 [47-70%] HER2 [11-45%] MAGE-2 [30%] MAGE-3 [40%]	





Main inclusion criteria
- Age ≥ 18
- ECOG PS 0-1
- HLA-A2 genotype (DNA screening)
- Histologically proven PDAC
- Advanced or recurrent disease
- Controlled disease after 4 months (8 cycles) of CTx with (modified) FOLFIRINOX
- Measurable/evaluable lesion (RECISTv1.1)

R 1:1

Arm A – Reference arm (n=53)

FOLFIRI*

Arm B – Experimental arm (n=53)

FOLFIRI* + OSE2101**
Subcutaneous injection on D1, D15, Q4W/6 doses then Q8W to M12 then Q12W up to M24

Phase II non comparative

H_1: M12-OS = 50%

M12-OS: 65.4%
95%CI 50.9-78.0

→ Objectif principal atteint

Neuzillet et al., ASCO® Annual Meeting 2025

Cindy NEUZILLET, MD, PhD

PISTE #3 : Revisiter l'immunothérapie

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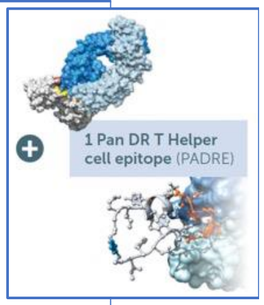

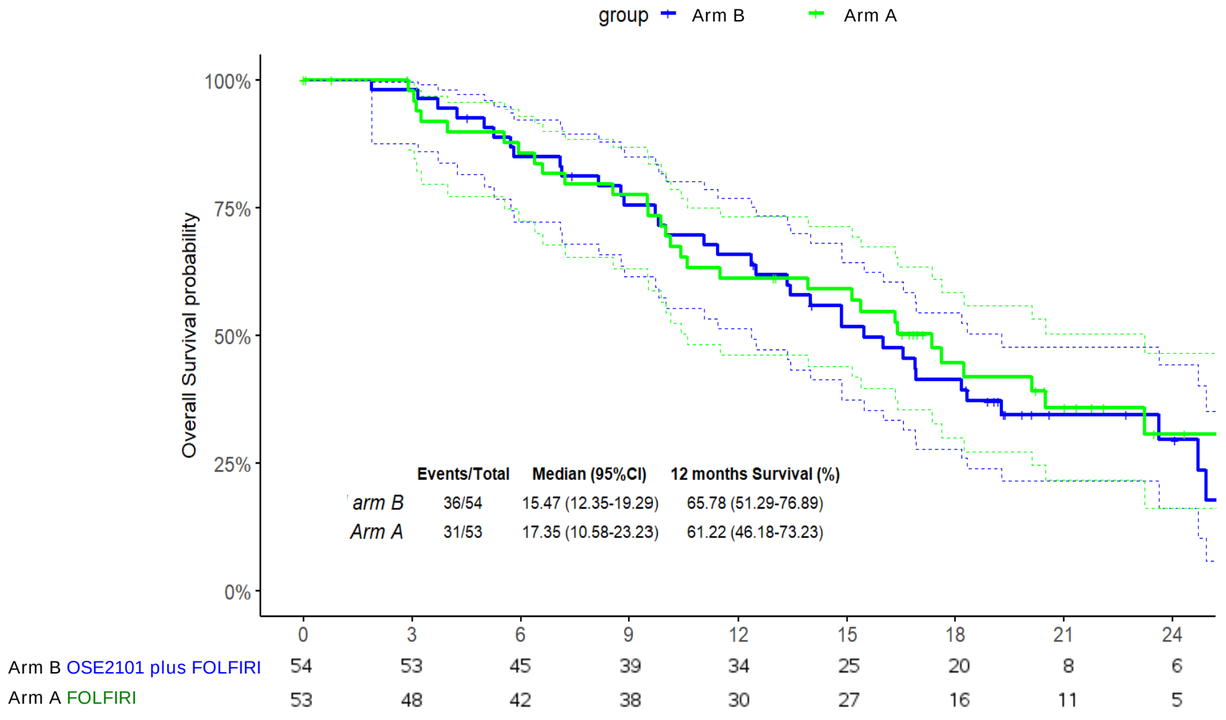

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Phase II non comparative

H_1: M12-OS = 50%

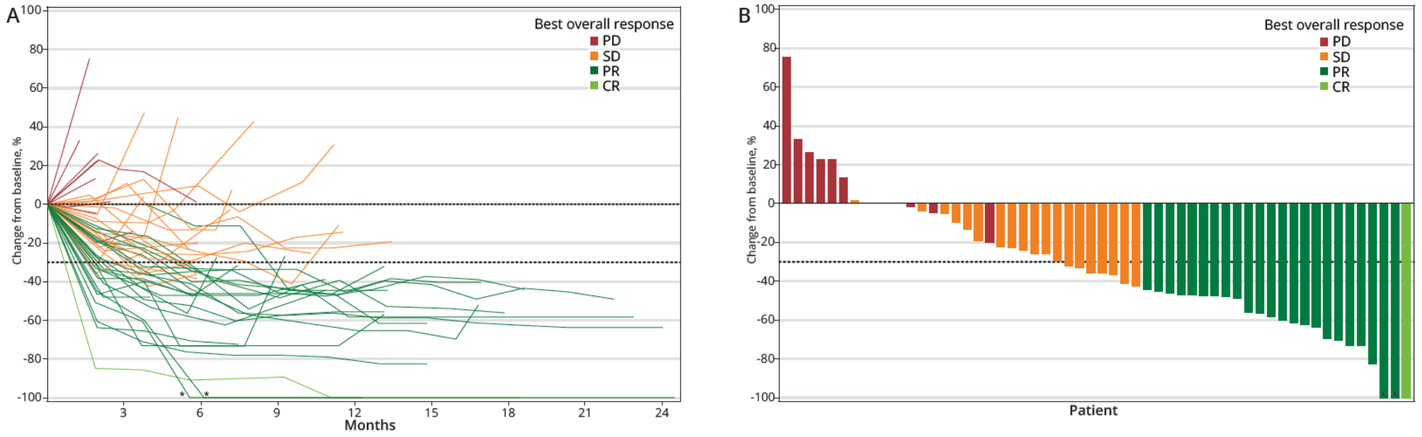
Utilité du bras contrôle +++

Cindy NEUZILLET, MD, PhD

Neuzillet et al., ASCO® Annual Meeting 2025

PISTE #3 : Revisiter l'immunothérapie

CD40 agonist (mitazalimab)

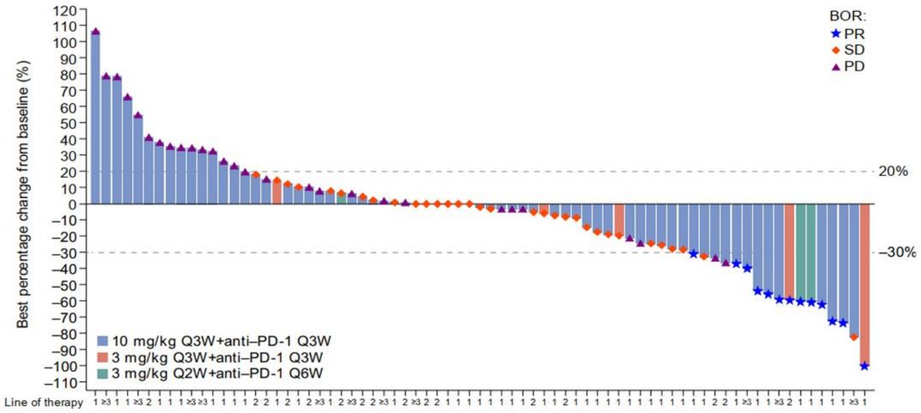


	N=57
Median follow-up, months	18.2
Best Overall Response, n (%)	
CR	1 (1.8%)
PR	23 (40.4%)
SD	21 (36.8%)
PD	12 (21.1%)
Disease Control Rate	45 (78.9%)
Objective response	
Number of patients with objective response (unconfirmed)	31
ORR (unconfirmed), % (90% CI)	54.4 (42.7 - 65.7)
Number of patients with objective response (confirmed)	24
ORR (confirmed), % (90% CI)	42.1(31.0 - 53.9)

Median DoR, months (95% CI)	12.6 (7.5 - NE)
Progression Free Survival	
Median PFS, months (95% CI)	7.7 (5.8 - 11.3)
6-month PFS rate, % (95% CI)	60.9 (46.9 - 72.3)
12-month PFS rate, % (95% CI)	35.1 (22.8 - 47.6)
Overall Survival	
Median OS, months (95% CI)	14.9 (10.0 - 17.3)
12-month OS rate, % (95% CI)	57.8 (43.9 - 69.4)
18-month OS rate, % (95% CI)	36.2 (23.0 - 49.5)

Anti-CCR8 (cafelkibart)

- **Cible les Tregs intra-tumoraux**
- **Association avec anti-PD1**



Besoin de marqueurs compagnons +++

Cindy NEUZILLET, MD, PhD

Van Laethem et al., *Lancet Oncol* 2024; Geboes et al., SITC® Annual Meeting 2024; Gong et al., ASCO® Annual Meeting 2025

PISTE #4 : Aussi pour les soins de support !!

APACaP – study design

Main inclusion criteria
- Unresectable advanced PDAC
- Eligible for chemotherapy
- ECOG PS ≤2
- Age ≥18
- ≥1 measurable lesion (RECIST 1.1)
- Availability of a Physical Activity Partner

Main exclusion criteria
- Any medical condition contraindicating exercise practice

R 1:1

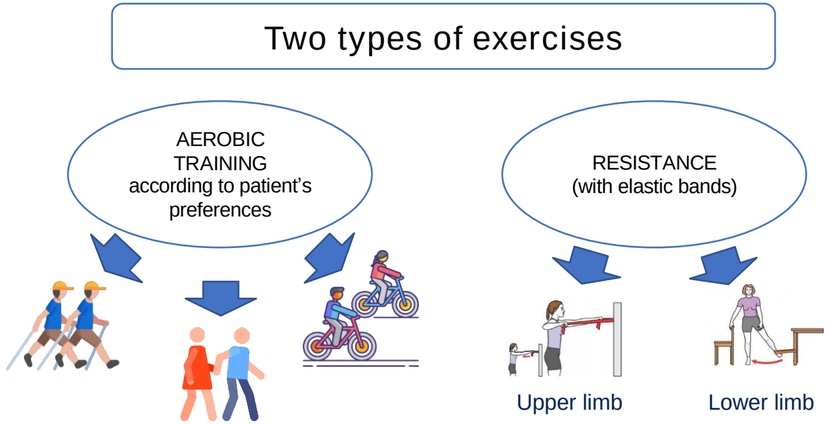
Standard Arm

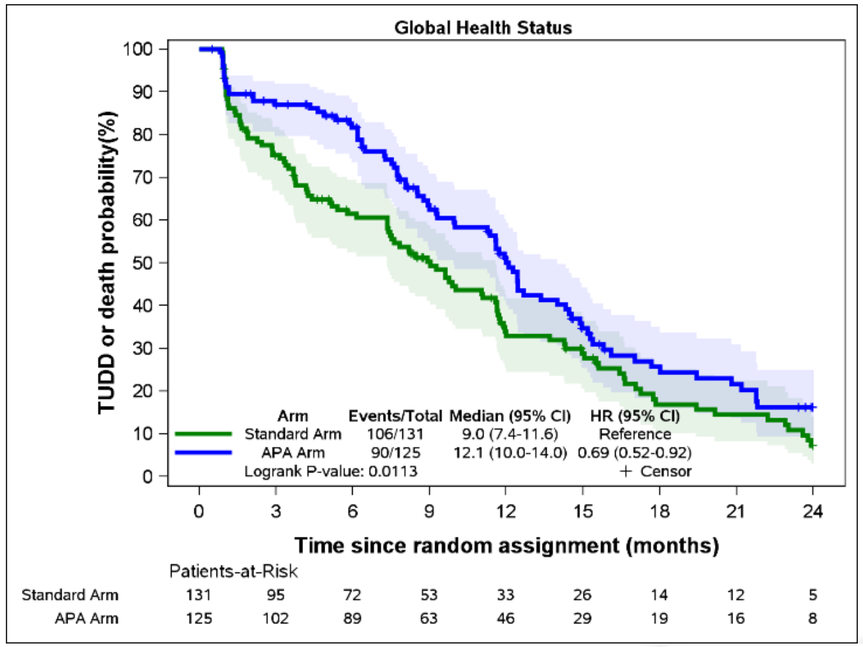
Usual care
- Chemotherapy at the investigator's choice
- Nutritional support (SFNEP guidelines)
- Tumor evaluation Q8W: TAP-CT scan & CA19-9

APA Arm

Usual care
+ APA (a 16-week program)

ClinicalTrials registration: NCT02184663





Recruiting

Preoperative Optimisation of Modifiable Risk Factors in Surgery of the Pancreas (PROMISE-P)

ClinicalTrials.gov ID NCT05851534

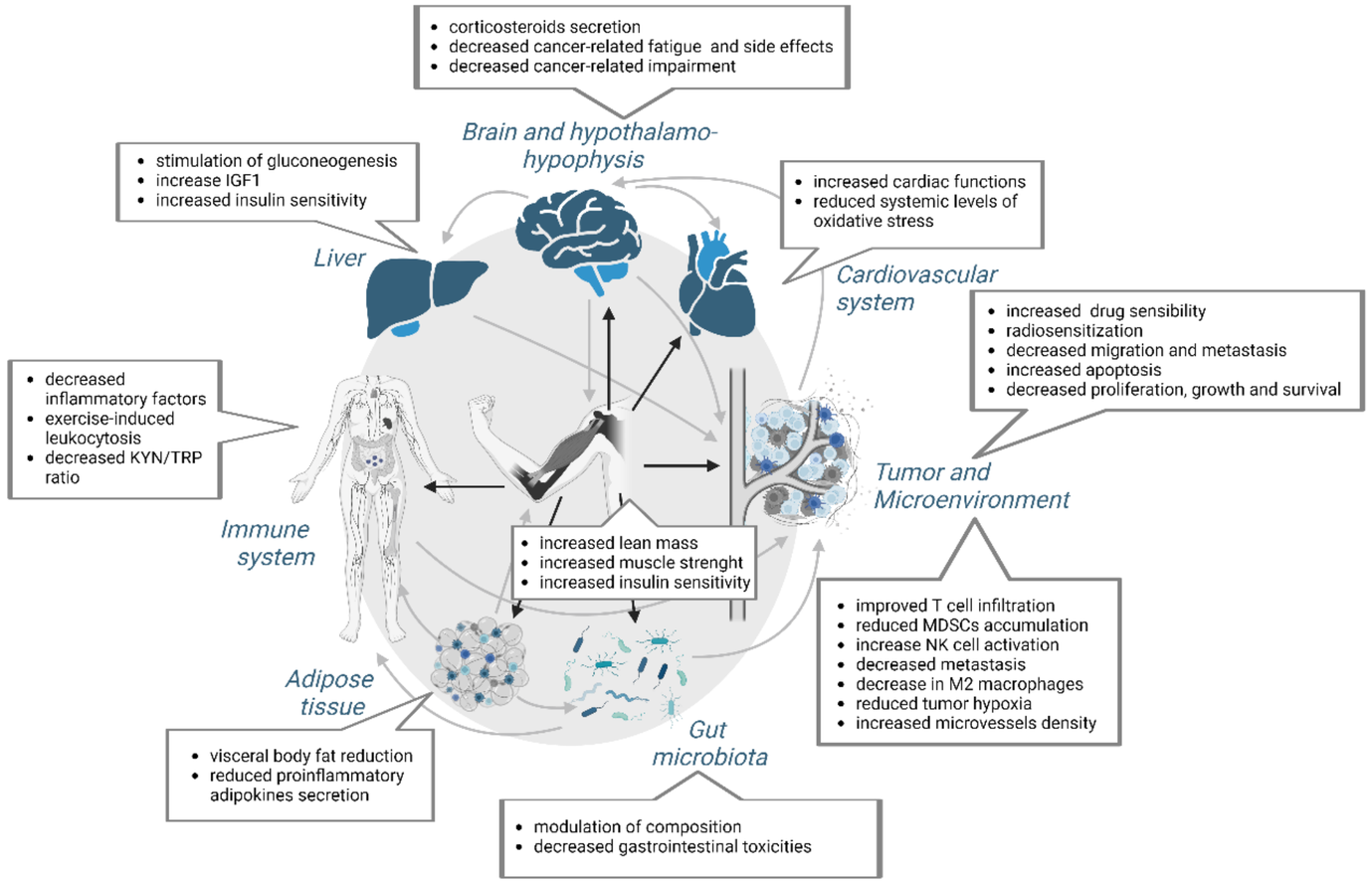
Sponsor Maastricht University Medical Center

Information provided by Maastricht University Medical Center (Responsible Party)

Last Update Posted 2024-10-26

Neuzillet et al., *J Natl Compr Canc Netw* 2023

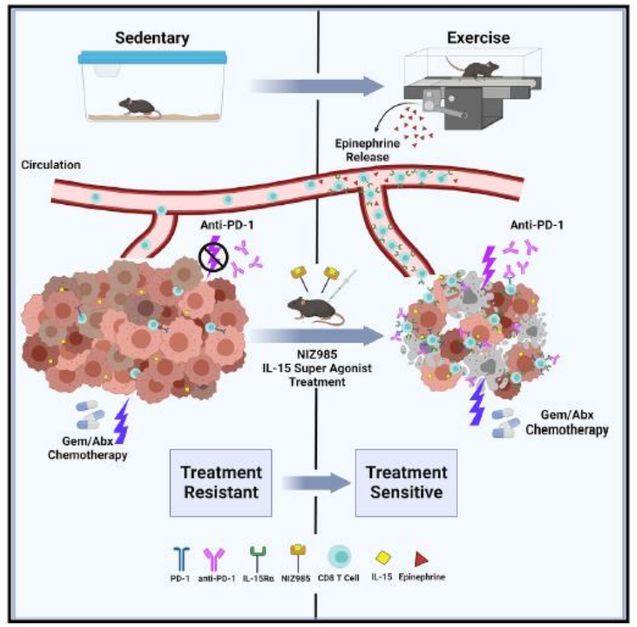
PISTE #4 : Aussi pour les soins de support !!



Torregrosa et al., *Cancers* 2022

Exercise-induced engagement of the IL-15/IL-15Rα axis promotes anti-tumor immunity in pancreatic cancer

Graphical abstract



Authors

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In brief

Kurz. et al. discover that aerobic exercise slows pancreatic cancer growth in mice through activation of the immune system, particularly CD8⁺ T cells. The beneficial effects of exercise can be mimicked by treatment with an IL-15 super-agonist, NIZ985. Exercise or NIZ985 both improve the responsiveness of murine pancreatic tumors to immune- and non-immune-based therapeutics.

Cancer Cell 2022

Agents ciblants les cytokines de la cachexie (e.g. GDF-15/Ponsegromab)

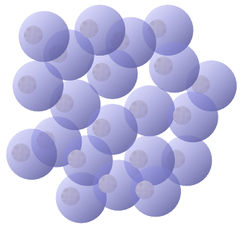
Groarke et al., *N Engl J Med* 2024

Cindy NEUZILLET, MD, PhD

CONCLUSION : APPROCHE THÉRAPEUTIQUE MULTI-ÉCHELLE POUR LE CANCER DU PANCRÉAS

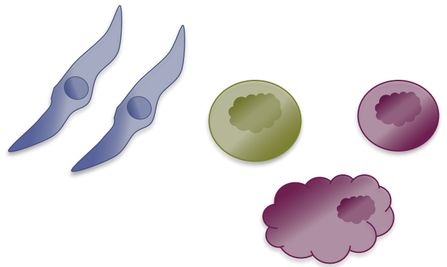
Cellule tumorale

- **Profil moléculaire de routine :** gBRCA, KRAS, MMR ± NGS ADN/ARN de grande taille
- **Avenir :** chimiogramme ARN ?
- **Cibler les mécanismes de résistance et de dissémination métastatique précoce**



Microenvironnement

- Cellules immunitaires
- Fibroblastes (CAF)
- Microbiote intratumoral



Hôte

- Nutrition
- Activité physique adaptée
- Douleur
- Anxiété/dépression
- Préadaptation
- Prévention des maladies thromboemboliques
- Obstruction des voies biliaires/gastro-intestinales