ESMO GUIDELINES:
REAL WORLD CASES

PANCREATIC CANCER

Michel Ducreux

Chair

Gustave Roussy

ESMO WEBINAR SERIES

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Programme

27 November 2024

10 min	**Welcome and introduction** Michel Ducreux
10 min	**Case Presentation** Ana Landa
20 min	**Presentation of the ESMO Clinical Practice Guideline for Critical Analysis of the Case** Berta Laquete
10 min	**Considerations Related to Guideline Implementation in Everyday Clinical Practice and Discussion** Gabor Liposits
10 min	**Live Q&A and Discussion** All speakers and Dr Eva Versteijne

Michel Ducreux
Chair
Gustave Roussy

Ana Landa-Magdalena
Speaker
Cancer Center Clinica Universidad de Navarra

Berta Laquente Sáez
Speaker
L'Hospitalet de Llobregat Barcelona

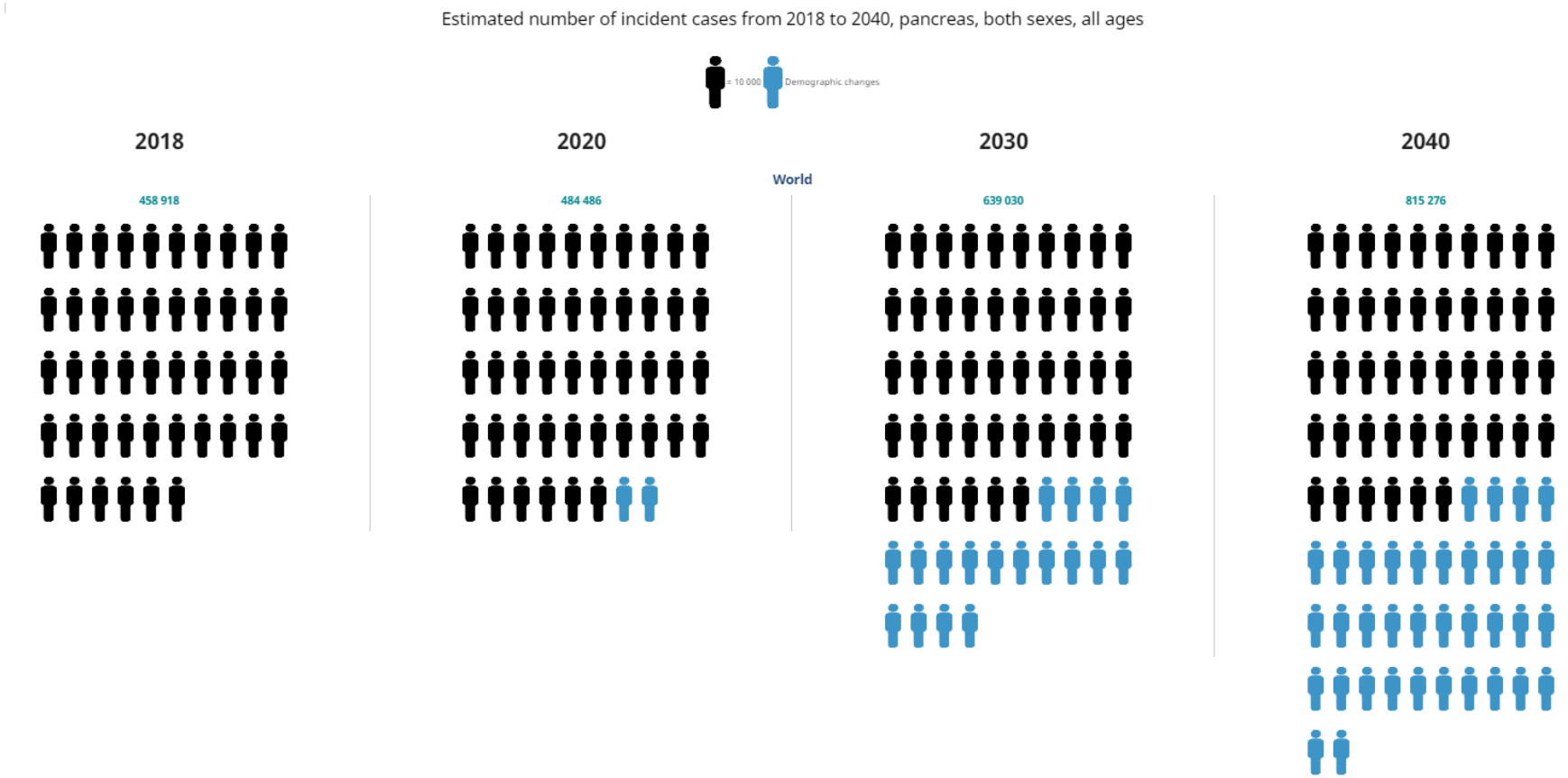
Gabor Liposits
Speaker
Western Hospital Trust

LEARNING OBJECTIVES

- Promote evidence-based quality cancer care by disseminating the ESMO Clinical Practice Guidelines (CPG) in the oncology community.
- Present a clinical case for each of the selected topics for discussion in the context of the ESMO CPG recommendations.
- Present and critically review the ESMO CPG recommendations for each selected cancer type.
- Discuss the case, the ESMO CPG recommendations, their impact on care and implementability in the daily practice setting under the guidance of a moderator senior expert, with participation of the guideline authors, practicing oncologists and young oncologists.
- Audit the fulfillment of the learning objectives and acceptability of the ESMO CPG recommendations by means of an online questionnaire.

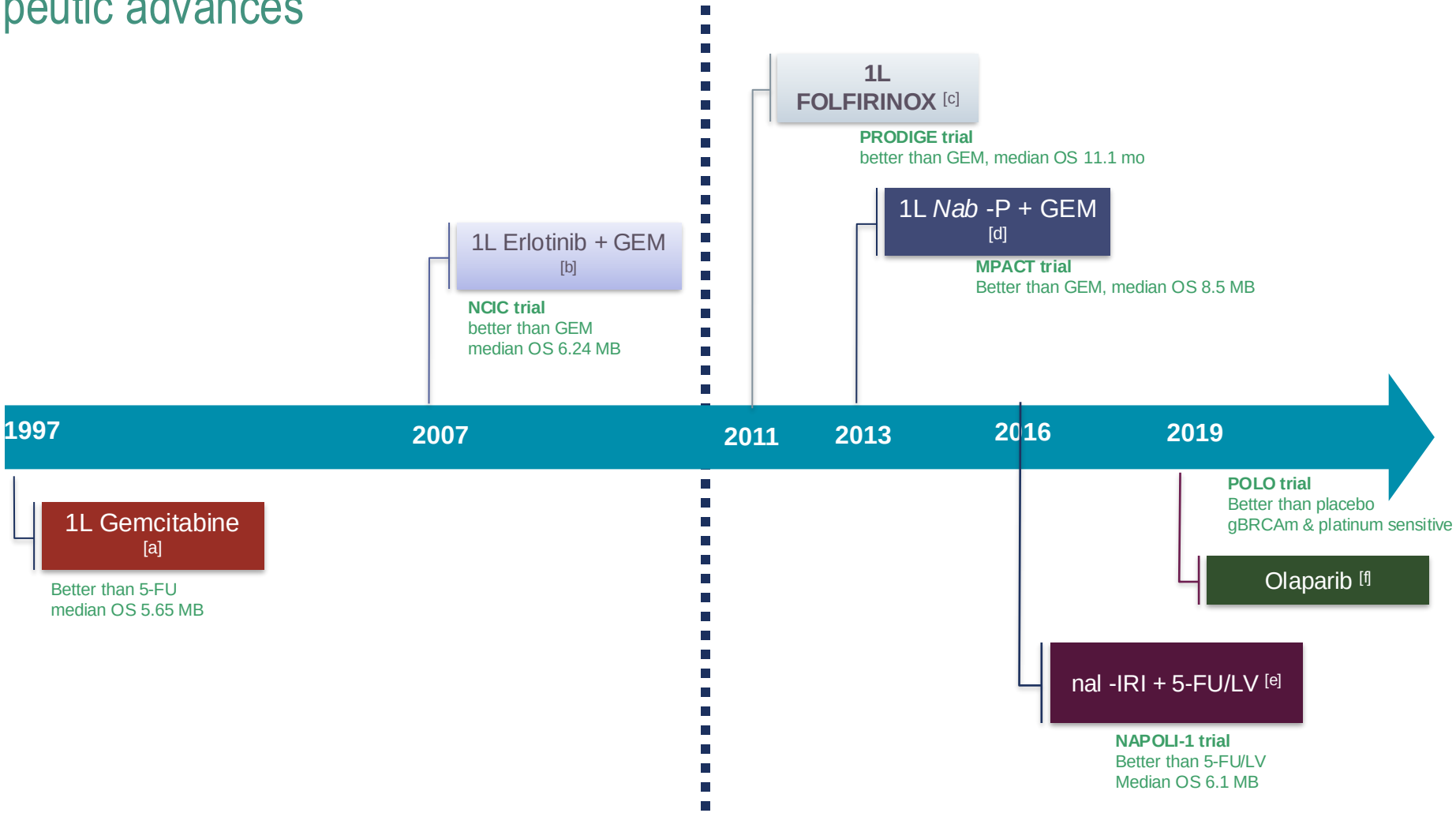
PANCREATIC CANCER

A problem in terms of incidence (and mortality)



PANCREATIC CANCER

Few therapeutic advances



a. Burris HA 3rd · et al. *J Clin Oncol* . 1997;15:2403-2413; b. Moore MJ, et al. *J Clin Oncol* . 2007;25:1960-1966; c. Conroy T, et al. *N Engl J Med.* 2011;364:1817-1825; d. Von Hoff DD, et al. *N Engl J Med.* 2013;369:1691-1703; e. Wang-Gillam A, et al. *Lancet.* 2016;387:545-557 ; f. Golan T, et al. *N Engl J Med.* 2019;381:317-327.

ESMO GUIDELINES: REAL WORLD CASES

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PANCREATIC CANCER

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DISCLOSURE STATEMENT

Travel and educational support from: Pfizer, Roche, Sanofi, Rovi, Pharma-Mar, BMS, Merck, Incyte, Astra Zeneca.

DIAGNOSIS

At diagnosis 74 years old male (YOB 1947)

Previous medical history: arterial hypertension and apendicectomy (2005)

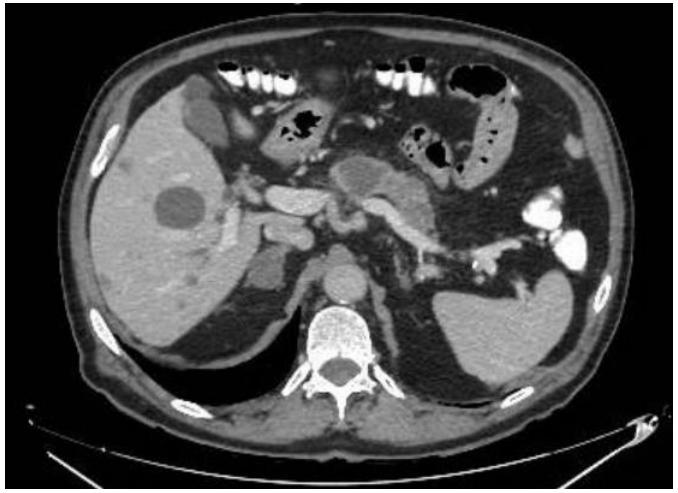
Smoking history: sporadically; Alcohol: 1 glass wine/day.

ONCOLOGICAL HISTORY

Incidental finding CT scan March 2021 (hypertension follow-up): pancreatic body lesión (35x33mm) without arterial invasión but with suspicious liver lesions.

Patient came to our institution where diagnosis was completed:

- Liver MRI: confirming liver metástasis (also multiple benign liver cysts)



STAGING

Staging ultrasound endoscopy:

A neoplastic formation approximately **45 mm in maximum diameter** is visualized in the body of the pancreas, with infiltrative borders. Anteriorly, it **breaches the pancreatic capsule, reaching the parietal peritoneum of the epiploic retrocavity, where fat striation compatible with local peritoneal carcinomatosis is visualized**. The lesion obstructs the main pancreatic duct, which shows retrograde dilation with subtotal atrophy of the gland parenchyma. It also **contacts the hepatic artery and more clearly the splenic artery**. The lesion **touches the mesenteric-portal confluence** on its anterior side without definitive signs of infiltration.

Pathologic samples obtained from pancreas and liver

Pathological diagnosis: Confirmed pancreatic adenocarcinoma in both pancreatic and liver samples.

No germline NGS performed

TNM (8th Edition): T3 (>4cm by USE) N0 (no pathological nodes described) M1 = STAGE IV

RISK FACTORS

Personal history:

- 74 years old.
- Smoking history: sporadically
- Alcohol: 1 glass wine/day.

Familiar history:

- No relevant known cáncer history

MANAGEMENT

First line treatment FOLFIRINOX

Metabolic assessment:

- Basal elevated endogen uracil concentración → 5Fu dose reduction recommended (15-20%)
- UGT1A1 genotype *1/*1 → no problem for irinotecan metabolization.

C1D1 of FOLFIRINOX 20th Apr 2021 with correct tolerance.

After 5 cycles: admitted due to septic shock with dyarrea as unique infection symptom with no bacterial isolation in blood/stools but singificantly elevated CMV viral charge in blood. Improvement with Ganciclovir.

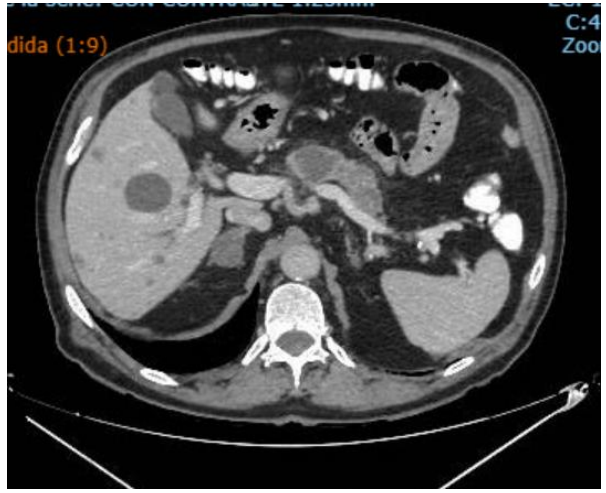
First response assessment CT scan 1st July: PR pancreas and liver.

Patient completed up to 9 cycles (last 7th Sep 2021) with confirmed PR páncreas and liver. After 9th cycle he required admission due to G2 dyarrea with acute kidney failure. **ECOG impairment.** Chemo discontinuation.

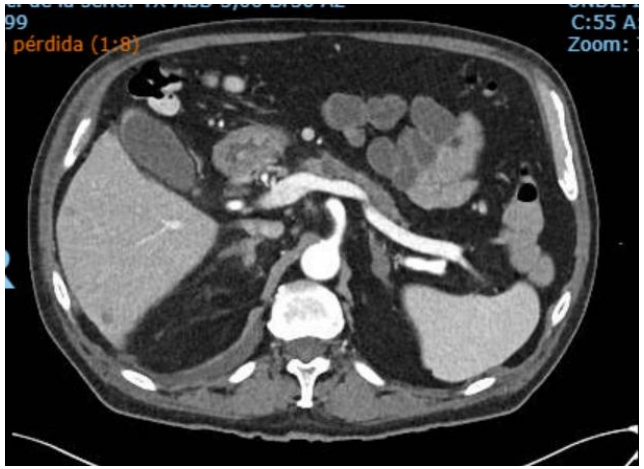
Continues on follow-up programm every 3 months. **May 2023**: no evidence of disease in páncreas and liver but non significant bilateral lung nodes.

Primary tumor response

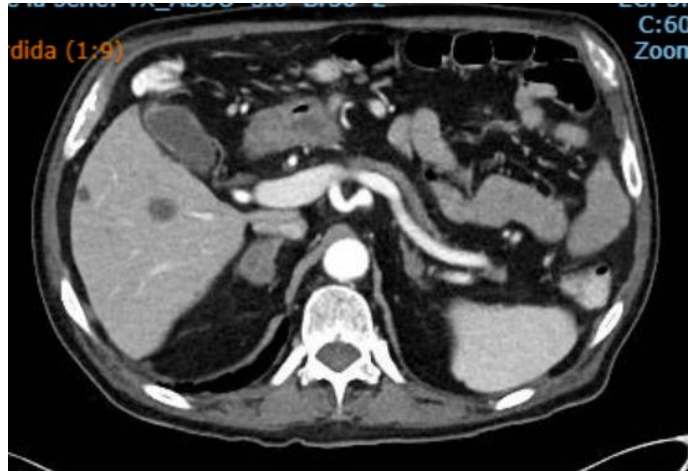
Basal (March 2021)



1st reevaluation (1st Jul 21)



2nd reevaluation (23rd Sep 21)



MANAGEMENT

Second line treatment: FOLFIRINOX re-challenge

October 2023 → progressively growing lung nodes.

- Atipic resection of one node (middle lung lobe) performed by surgery (16th Oct23) for pathological confirmation: **Pancreatic adenocarcinoma.**
- NGS test on that sample: **KRAS G12D; TP53; CDKN2A**

Gen (NM)	Alteración	Frecuencia alélica (profundidad de lectura)
KRAS (NM_033360.4)	c.35G>A; p.(Gly12Asp)	15% (1990x)
TP53 (NM_000546.6)	c.524G>A; p.(Arg175His)	17% (2000x)
CDKN2A (NM_001195132.2)	c.110_119del; p.(Leu37HisfsTer13)	9% (800x)

MANAGEMENT

Second line treatment: FOLFIRINOX re-challenge

76 years old male. Correct recovering to ECOG 0. Good functional status. G1 neurotoxicity.

Stage IV PDAC with CR after 1st line FOLFIRINOX.

Lung progression after 24months of progression free interval, without actionable molecular alterations.

C1D1 of FOLFIRINOX rechallenge 13th November 2023 → 5 cycles (last 29th Jan 24)

Response assessment CT scan after 5 cycles 16th Feb 2024: PR lung nodes; no evidence of disease in abdominal cavity. Patient asked for “therapeutic holidays”. ECOG 1. G2 Neurotoxicity.

Continues on follow-up programm.

MANAGEMENT

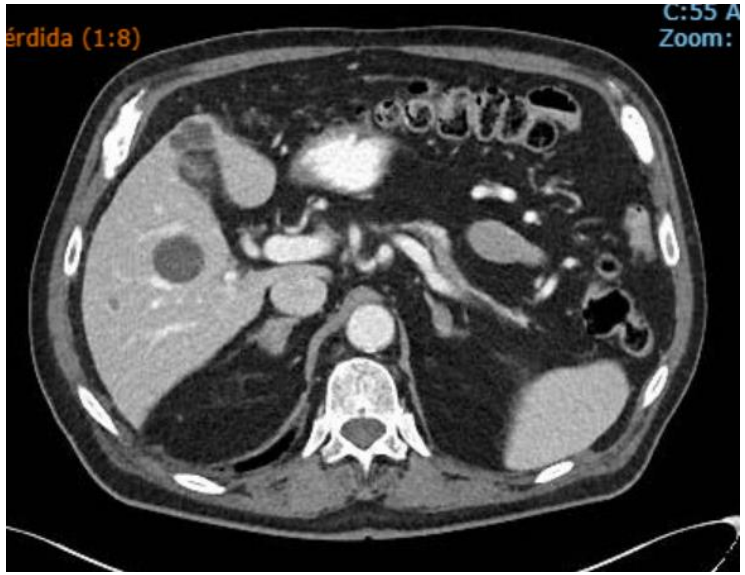
Third line treatment: FOLFIRINOX re-challenge

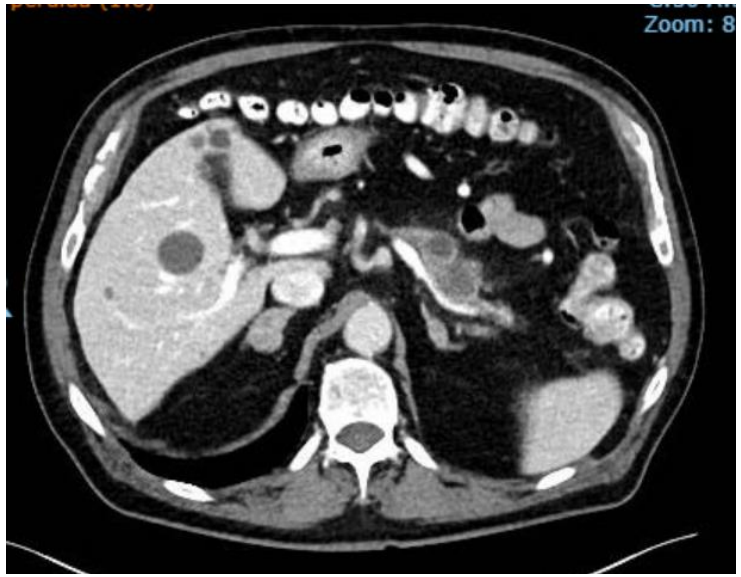
No evidence of progression until **25th October 2024: lung PD and pancreatic tumor PD.**

77 years old male. Again recovered to ECOG 0. G1 neurotixicity, mantained good funcional status.

Stage IV PDAC with CR after 1st line FOLFIRINOX (24months PFS); lung PD FOLFIRINOX re-challenge with PR (8months PFS); current lung and pancreatic PD.

Feb 2024 → **Oct 2024**





OUTCOMES

C1D1 of FOLFIRINOX re-challenge (2.0) started on 6th November 2024

THANKS FOR YOUR ATTENTION

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DISCLOSURE STATEMENT

Advisory Boards: Astra-Zeneca, Jazz Pharmaceuticals

Travel support: Astra-Zeneca

Speaker support: Jazz Pharmaceuticals, Astra-Zeneca

Educational support: Incyte

CASE SUMMARY

Stage IV (liver, peritoneal) PDAC, 74y, ECOG 0, good functional status, mKRASG12D, no germline test

1st LINE FOLFIRINOX: April-Sep 2021 9 cycles, BOR CR.

SEP 2021 → OCT 23

PROGRESION AND TREATMENT FREE INTERVAL: 2 years

2nd LINE FOLFIRINOX RE-CHALLENGE (LUNG PD): Nov 2023-Jan 2024 5 cycles, BOR PR lung, CR abdominal lesions

FEB 2024 → OCT 2024

PROGRESSION AND TREATMENT FREE INTERVAL:8 m

3rd LINE FOLFIRINOX RE-CHALLENGE (x2): LUNG, PANCREAS PD . NOV 24, on going.

DIAGNOSIS

At diagnosis 74 years old male (YOB 1947)

Previous medical history: arterial hypertension and apendicectomy (2005)

Smoking history: sporadically; Alcohol: 1 glass wine/day.

ONCOLOGICAL HISTORY

Incidental finding CT scan March 2021 (hypertension follow-up): pancreatic body lesion (35x33mm) without arterial invasion but with suspicious liver lesions.

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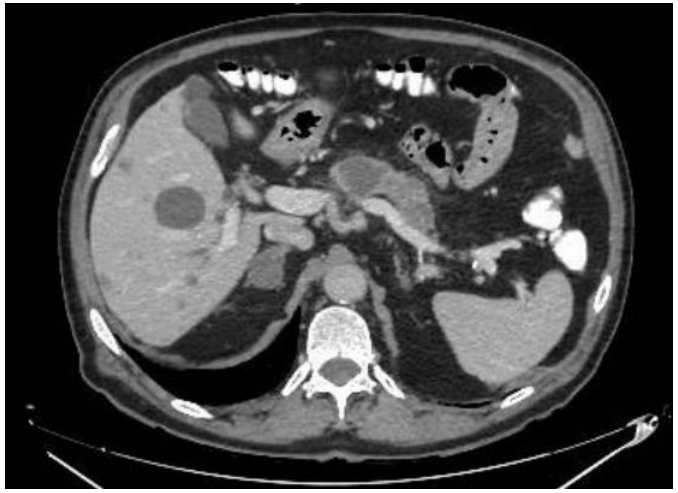


STAGING

1. Multiphasic contrast-enhanced thoracic-abdominal and pelvic CT, including late arterial phase and portal venous phase, should be used as the first-line imaging modality for suspected PC

2. LIVER MRI. Abdominal MRI is usually used **when CT is inconclusive**, such as for isoattenuating tumours or when a contrast enhanced CT is contraindicated**; in this case confirmed the liver M1.**

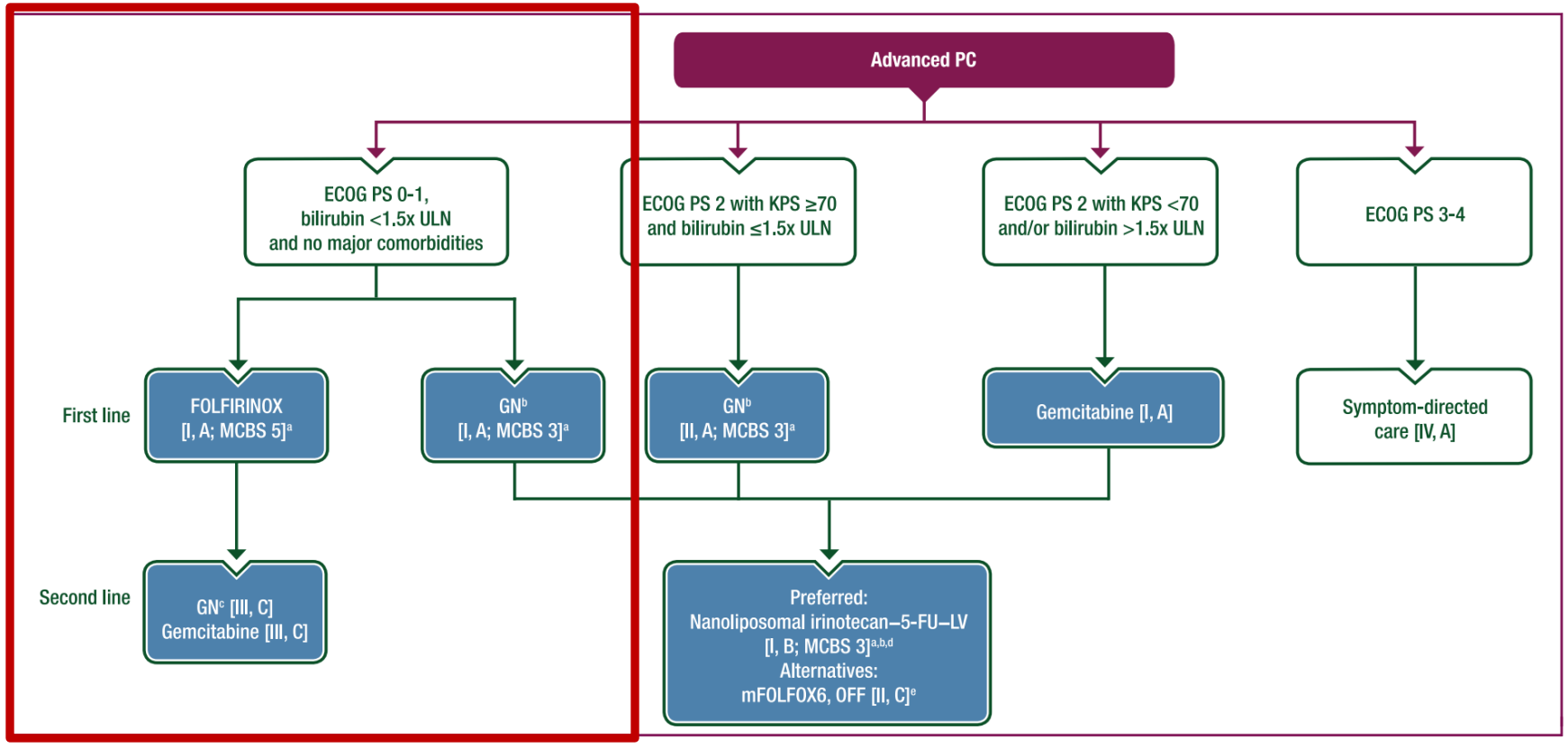
3. **EUS** is indicated for tumour staging in selected cases, e.g. isodense tumour at CT or when assessing venous involvement. EUS is used to biopsy pancreas, lymph nodes and lesions in the left liver or to sample ascites**. In our case completed the staging describing local peritoneal carcinomatosis and allowed the primary biopsy.**

4.CA 19.9? CA 19-9 can be used as a serum marker to measure disease burden and potentially guide treatment decisions [III, B]

Standard TNM by imaging testing **STAGE IV**

MANAGEMENT

First line treatment FOLFIRINOX. 74y, ECOG 0, Good functional status



FIRST LINE TREATMENT FOR METASTATIC DISEASE

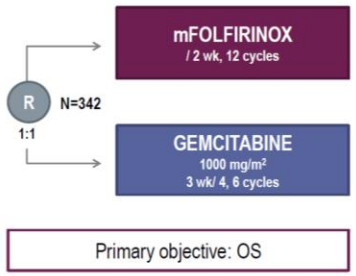
FOLFIRINOX

FIRST-LINE TREATMENT FOR METASTATIC DISEASE

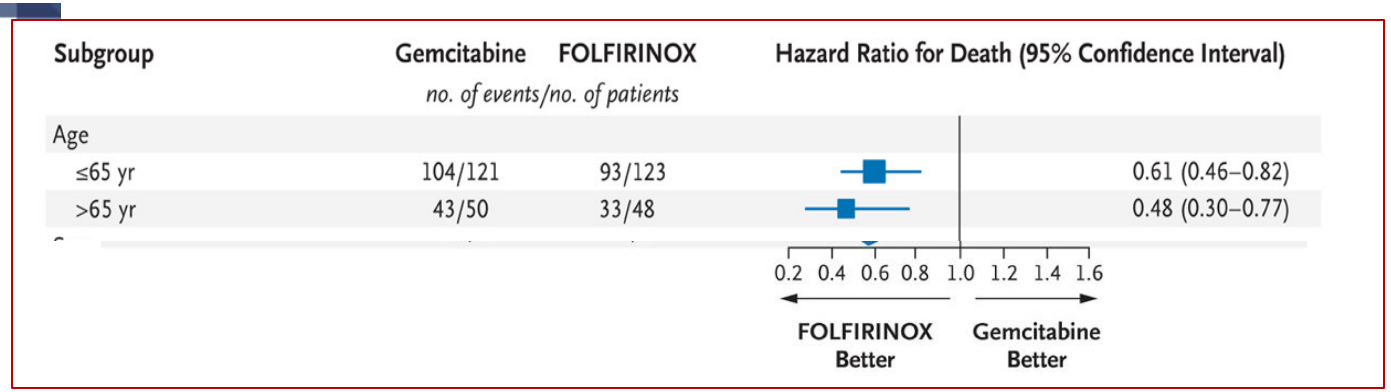
FOLFIRINOX the PRODIGE 4 study

- Oxaliplatin 85 mg/m^2
- LV 400 mg/m^2
- Irinotecan 180 mg/m^2,*
- 5 FU continue 2.4 g/m^2 46 h

- Metastatic
- Chemotherapy naïve
- PS 0 or 1
- 18-75-year-old
- Bilirubinemia <1.5 xN



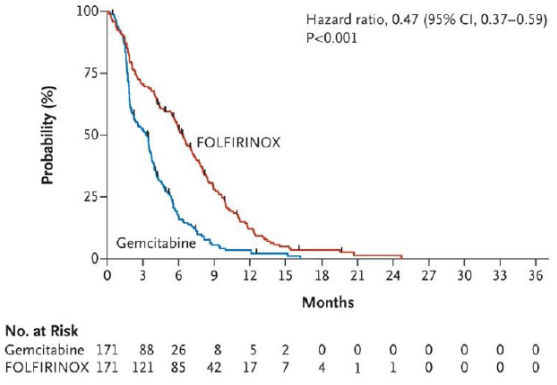
Conroy T, *et al.* N Engl J Med 2019.



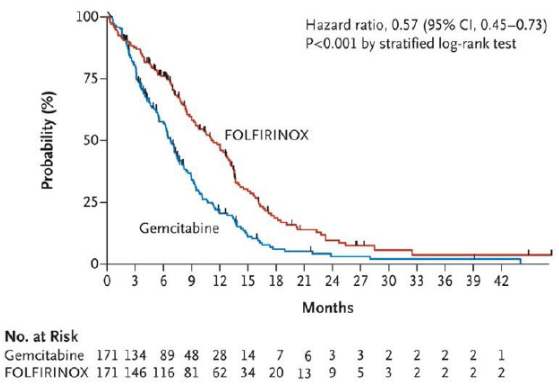
PFS

ORR = 31% *vs.* 9%; DCR = 70% *vs.* 51%

OS



6.4 mo *vs.* 3.3 mo



11.1 mo *vs.* 6.8 mo

ESMO GUIDELINES: REAL WORLD CASES

FIRST LINE TREATMENT FOR METASTATIC DISEASE

GEMCITABINE+ Nab-PACLITAXEL

FIRST LINE TREATMENT FOR METASTATIC DISEASE

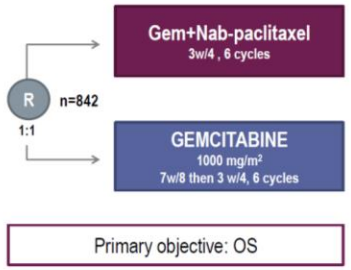
Gem+ Nab-paclitaxel (the MPACT study)

- Gemcitabine 1000 mg/m²
- Nab-paclitaxel 125 mg/m²

- Metastatic
- Chemotherapy naive
- KPS ≥70
- Measurable tumour
- Bilirubinemia normal

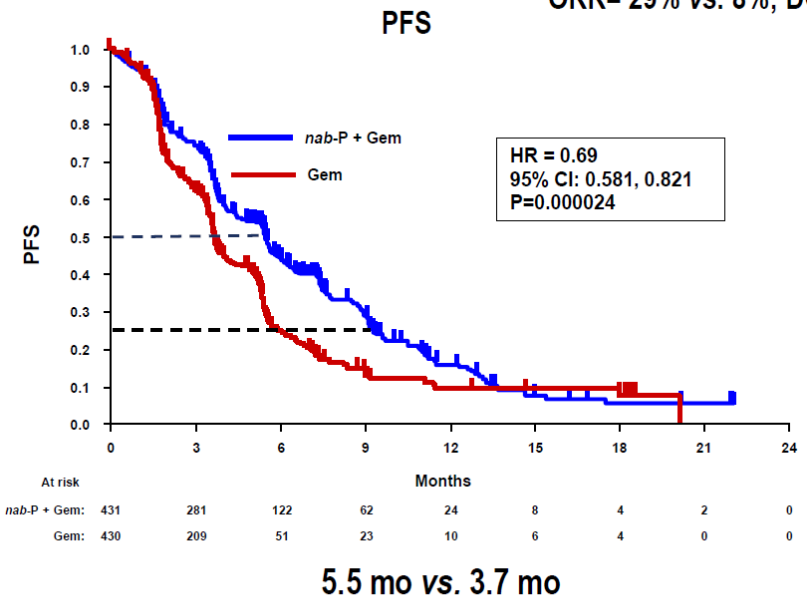
Stratification:

- PS
- Liver metastases
- Country

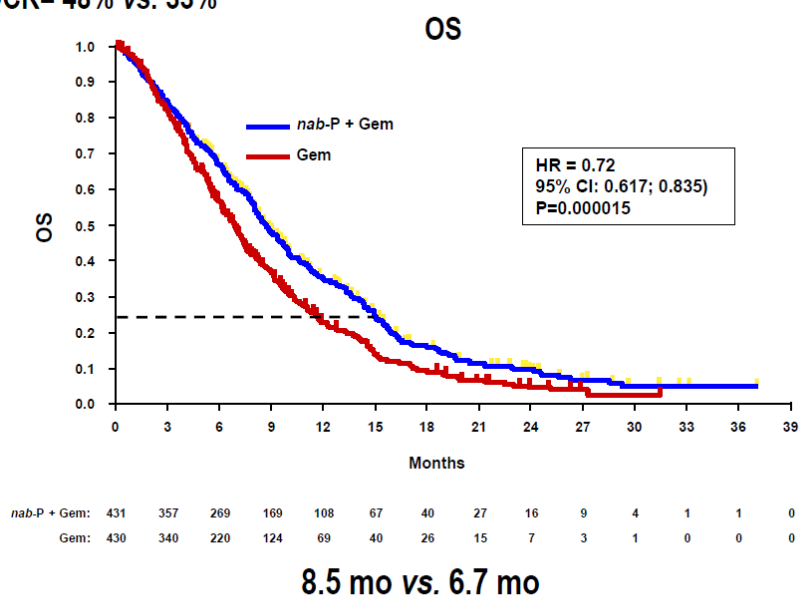


Von Hoff DD, *et al.*, N Engl J Med 2013.

ORR= 29% *vs.* 8%; DCR= 48% *vs.* 33%



5.5 mo *vs.* 3.7 mo

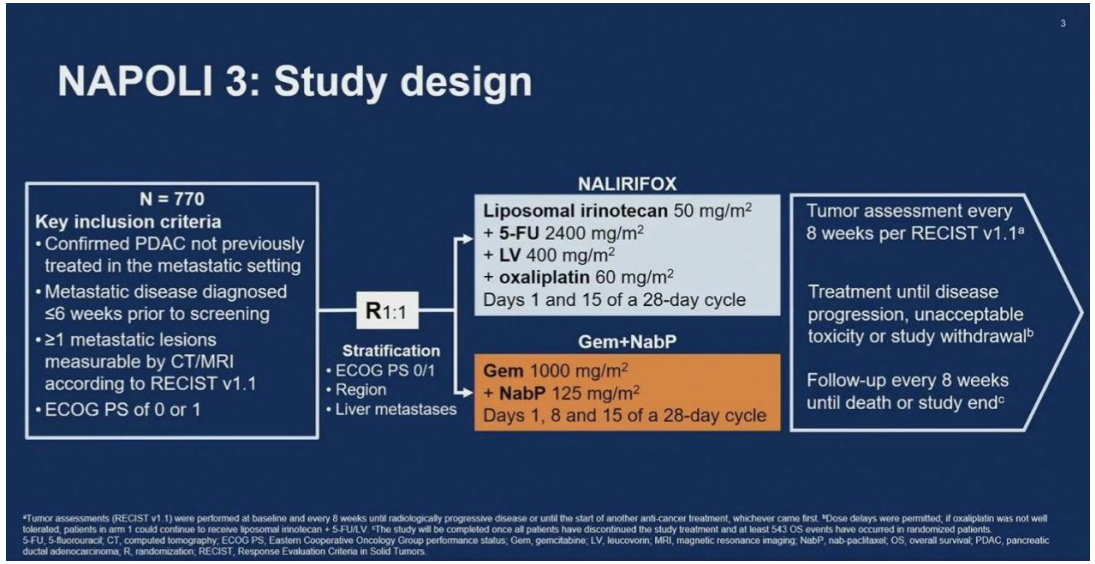


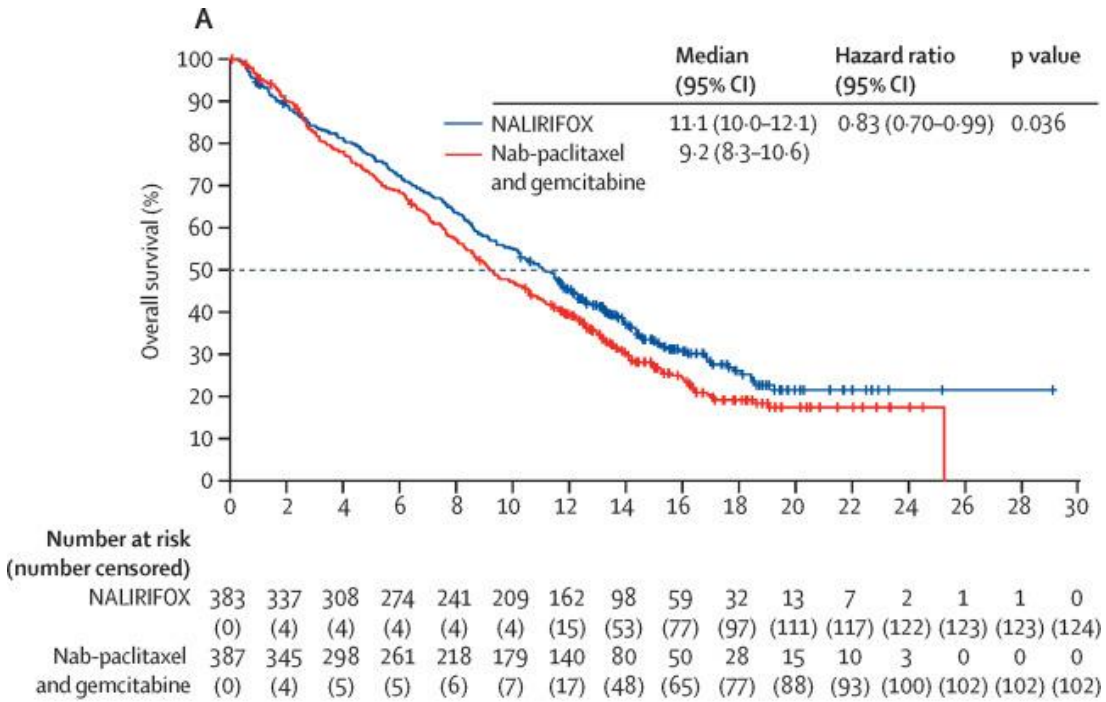
8.5 mo *vs.* 6.7 mo

From N Engl J Med, Von Hoff DD, *et al.* Increased Survival in Pancreatic Cancer with nab-Paclitaxel plus Gemcitabine, 369:1691-1703. Copyright © 2013. Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

FIRST LINE TREATMENT FOR METASTATIC DISEASE

NALIRIFOX

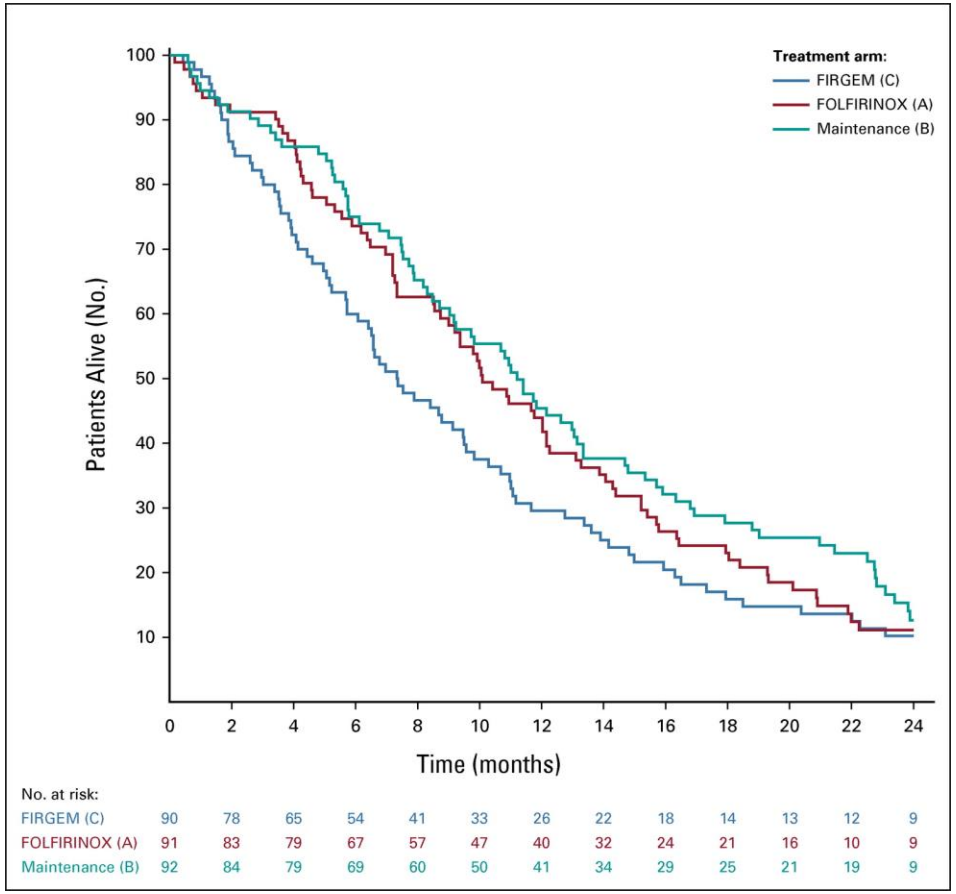




Wainberg et al. Lancet 2023

TREATMENT DURATION?

PANOPTIMOX TRIAL vs 6 months



Dahan et al, JCO 2021

Sep 2021 → Oct 2023

PROGRESION AND TREATMENT FREE INTERVAL: 2 years

PRODIGE 4/FOLFIRINOX: Six months of chemotherapy was recommended for patients who had a response. Patients were followed every 3 months until death.

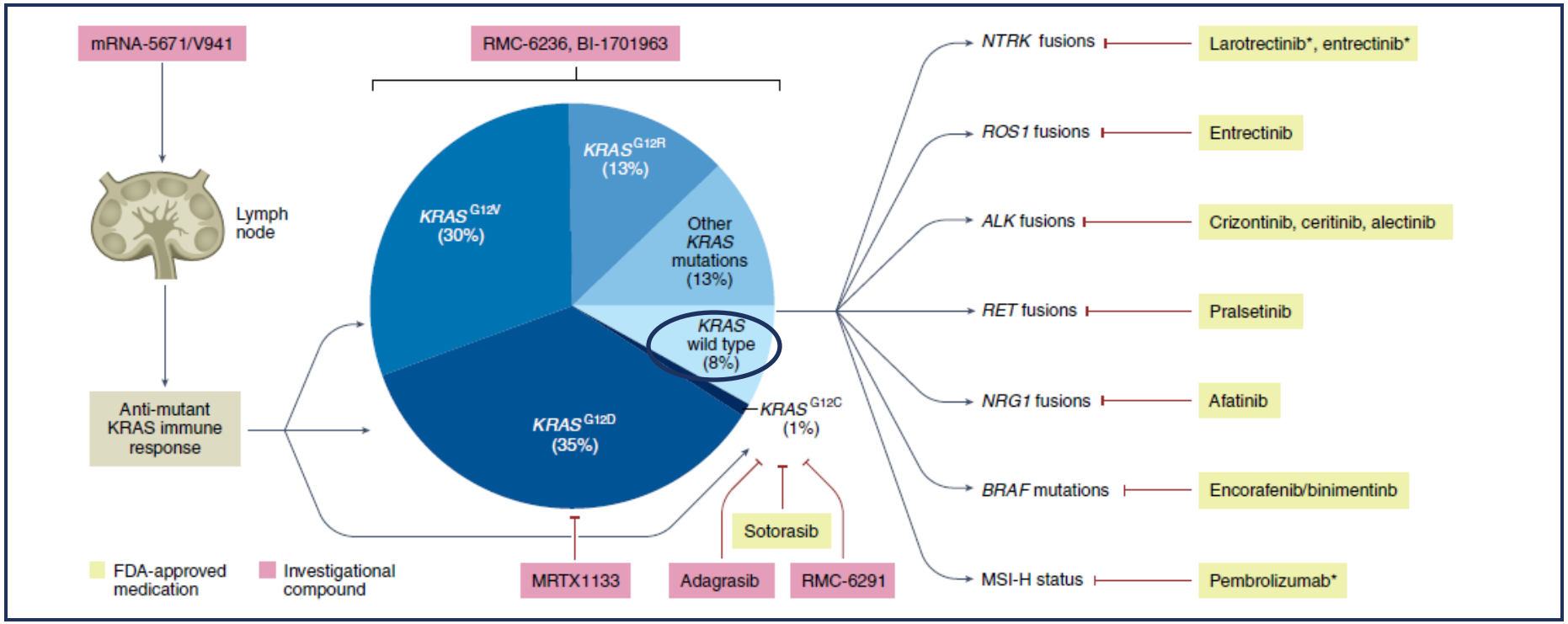
TABLE 2. Treatment Efficacy (intent-to-treat population)

Efficacy	Arm A (n = 91; 12 cycles of FOLFIRINOX)	Arm B (n = 92; maintenance treatment)	Arm C (n = 90; sequential treatment)
6-month PFS rate			
No. (%)	41 (47.1)	39 (42.86)	30 (34.1)
95% CI		34.3 to 51.4	25.7 to 43.3
Overall PFS, months			
Median	6.3	5.7	4.5
95% CI	5.3 to 7.6	5.3 to 7.3	3.5 to 5.7
9-month PFS, %	31.9	27.2	16.7
12-month PFS, %	15.4	15.9	12.2

GENE PROFILE. ESMO RECOMMENDATIONS

KRAS and BRCA testing are generally recommended [IV, B].

If a KRAS-WT tumour is identified, additional profiling with NGS can be carried out to evaluate for rare, potentially actionable findings

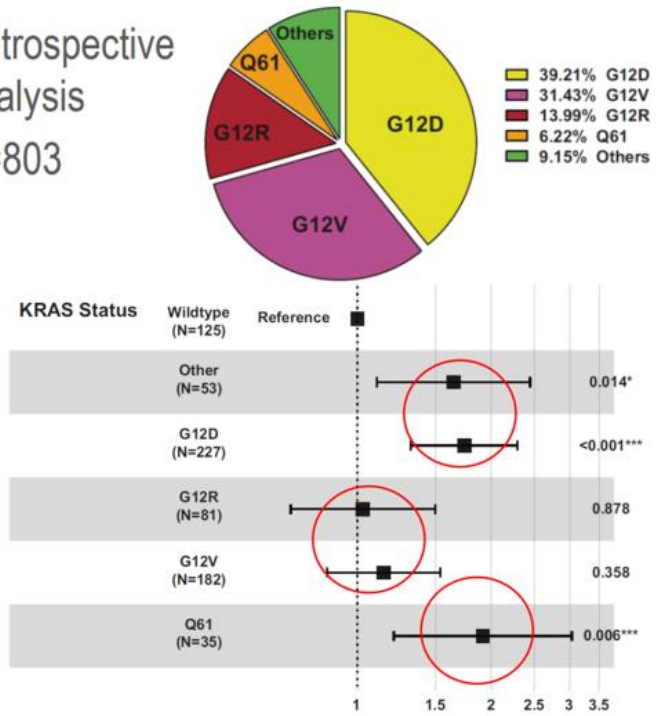


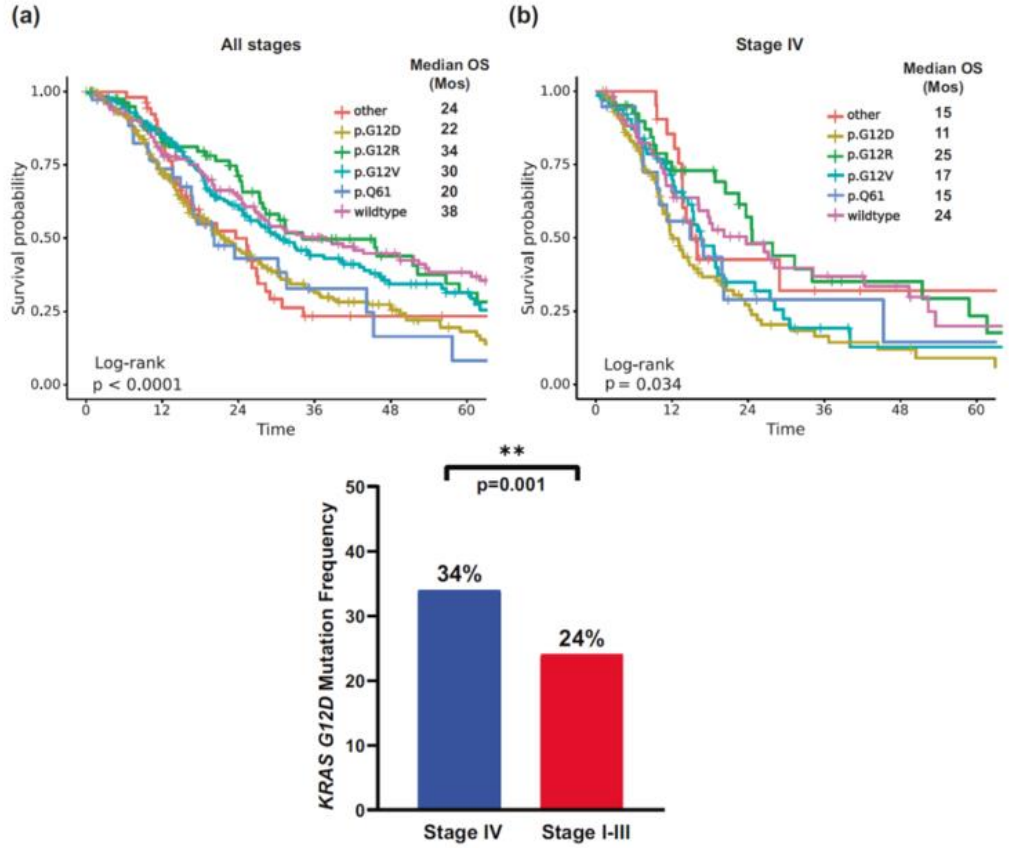
Nasser Hossein et al, Nature 2022

GENE PROFILE

NGS test lung sample: **KRAS G12D; TP53; CDKN2A. Germline test lacking**

- Retrospective analysis
- N=803





2024 ESMO GASTROINTESTINAL CANCERS

Youssef A et al, NPJ Precis Oncol, 2024

TARGETING KRAS: PRESENT AND FUTURE

Isoform-specific:

- KRAS G12C: Sotorasib, Adagrasib, Divarasib,…
- G12D: MRTX1133,…

panRas

Mutant-specific KRAS inhibitors

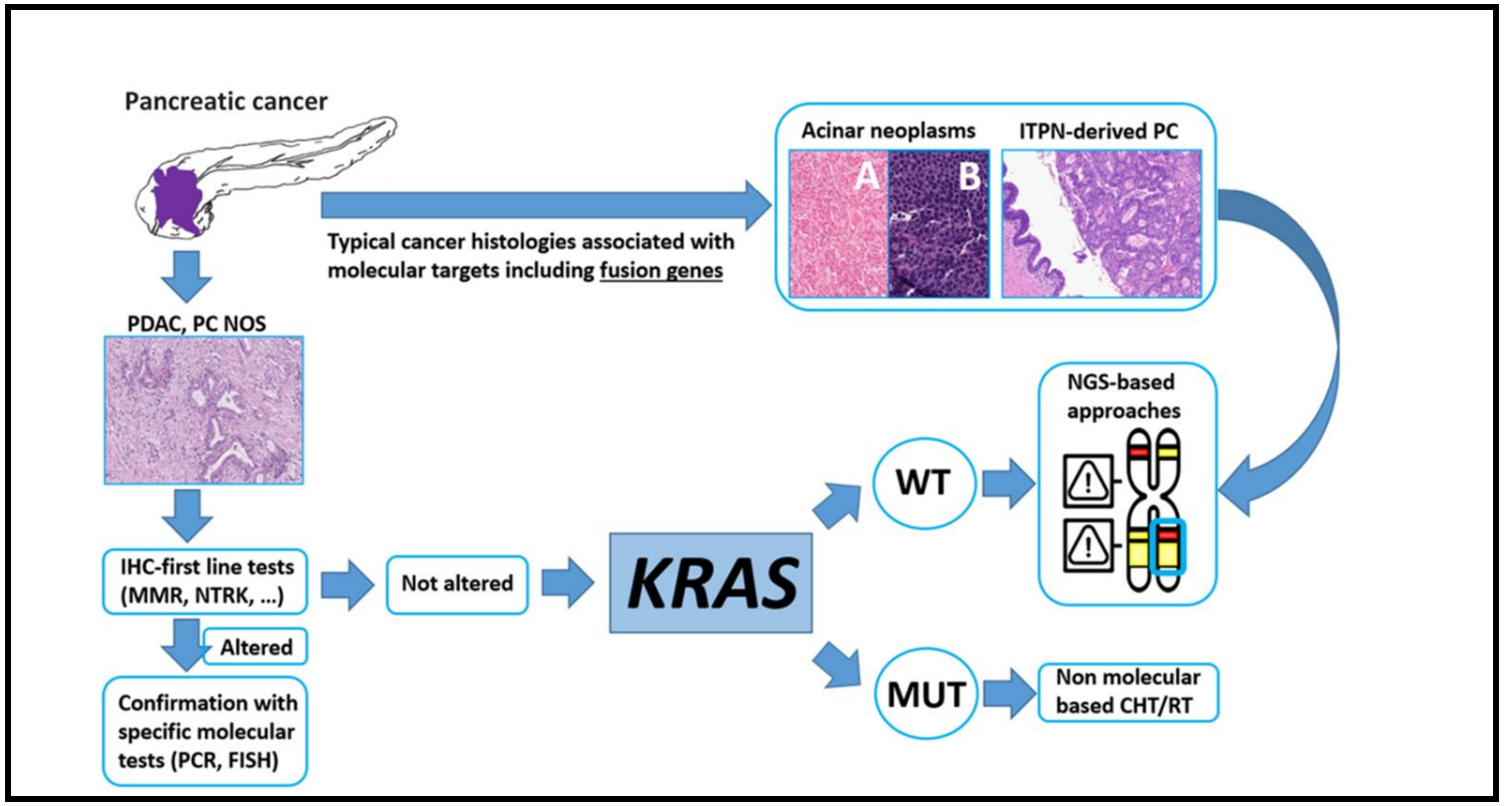
Programs (company)	IND	Target	Phase
Sotorasib/AMG 510 (Amgen)			Approved
Adagrasib/MRTX849 (Mirati)			
D-1553 (InventisBio)			
JDQ443 (Novartis)			
RG6330/GDC-6036 (Roche)		$KRAS^{G12C}$	
LY3537982 (Eli Lilly)			Clinical
BI 1823911 (Boehringer Ingelheim)			
JAB-21822 (Jacobio)			
GFH925 (GenFleet)			
GH35 (Genhouse Bio)			
MRTX1133 (Mirati)			
KRASG12D1-3 (Boehringer Ingelheim)		$KRAS^{G12D}$	
RAS(ON) G12D (Revolution Medicines)			Preclinical
RAS(ON) G13C (Revolution Medicines)		$KRAS^{G13C}$	

Pan-(K)RAS inhibitors

Programs (company)	IND	Target	Phase
RSC-1255 (RasCal Therapeutics)		Pan-RAS	Clinical
BI-pan-KRAS1-4 inhibitors (Boehringer Ingelheim)		Pan-KRAS: $KRAS^{G12D/V}$, KRAS wild-type	
BI-pan-KRASdegrader1 (Boehringer Ingelheim)		Pan-KRAS: $KRAS^{G12C/D/V/A}$, $KRAS^{G13C}$, $KRAS^{A146T/P}$, $KRAS^{Q61E/P}$, KRAS wild-type	Preclinical
RMC-6236 (Revolution Medicines)		Pan-RAS: $KRAS^{G12D/V}$, $KRAS^{G13D}$, $KRAS^{Q61K}$, RAS wild-type	

Hofmann et al, Cancer Discov, 2022

POSSIBLE APPROACH TO MOLECULAR PROFILING



Gkountakos A et al, Trends in Cancer 2024

HRD AND RESPONSE TO PLATINUM TREATMENTS

"Precision medicine in metastatic PC: BRCA/germline genetic testing should be offered to all patients with metastatic PC to determine eligibility for selection of platinum-based ChT followed by maintenance with olaparib [I, B; olaparib ESMO-MCBS v1.1 score: 2] "

A Novel HRD Signature Is Predictive of FOLFIRINOX Benefit in Metastatic Pancreatic Cancer

Kuei-Ting Chen[1], Russell Madison[1], Jay Moore[1], Dexter Jin[1], Zoe Fleischmann[1], Justin Newberg[1], Alexa Schrock[1], Neeru Bhardwaj[1], Katherine T. Lofgren[1], Jie He[1], Garrett Frampton[1], Priti Hegde[1], David Fabrizio[1], Michael J. Pishvaian[2], Ericka Ebot[1], Aatur Singhi[*,3,‡], Ethan Sokol[*,1,‡]

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[2]Department of Oncology, Johns Hopkins University School of Medicine, SKCC, Washington, DC, USA
[3]Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, PA, USA

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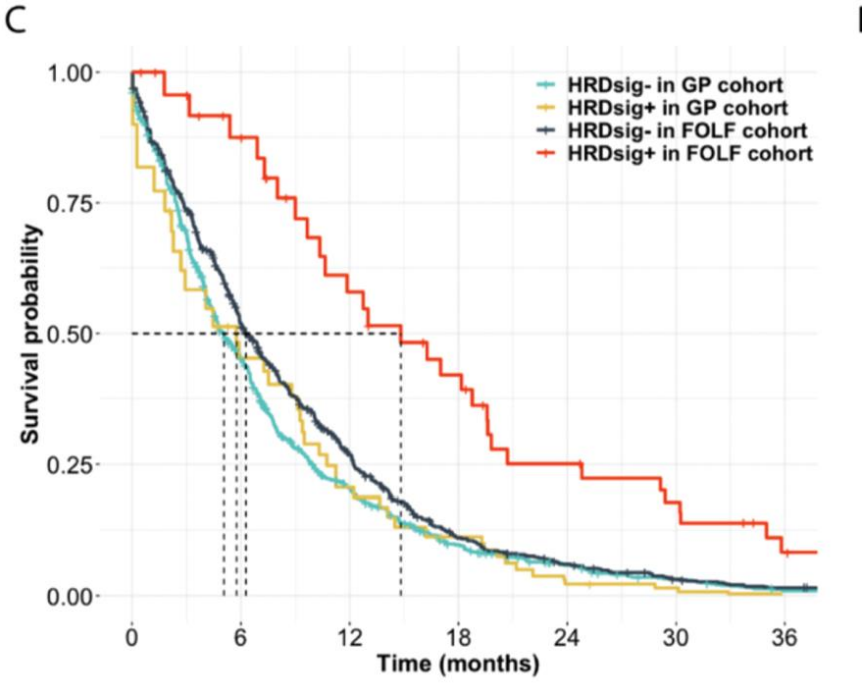
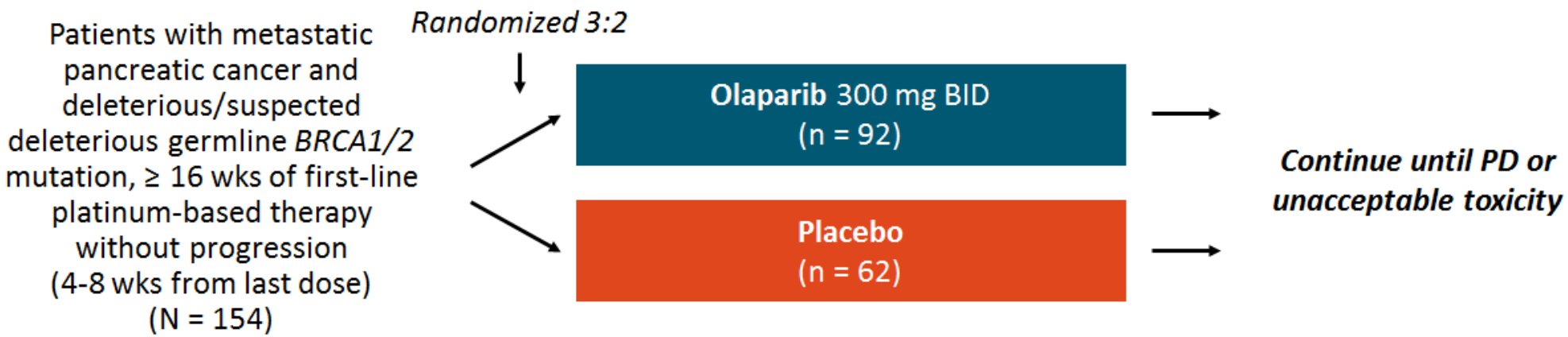
[‡]Contributed equally.



Chen et al. The Oncologist, 2023

POLO: Olaparib as Maintenance Therapy in Germline *BRCA* Mutated Pancreatic Cancer

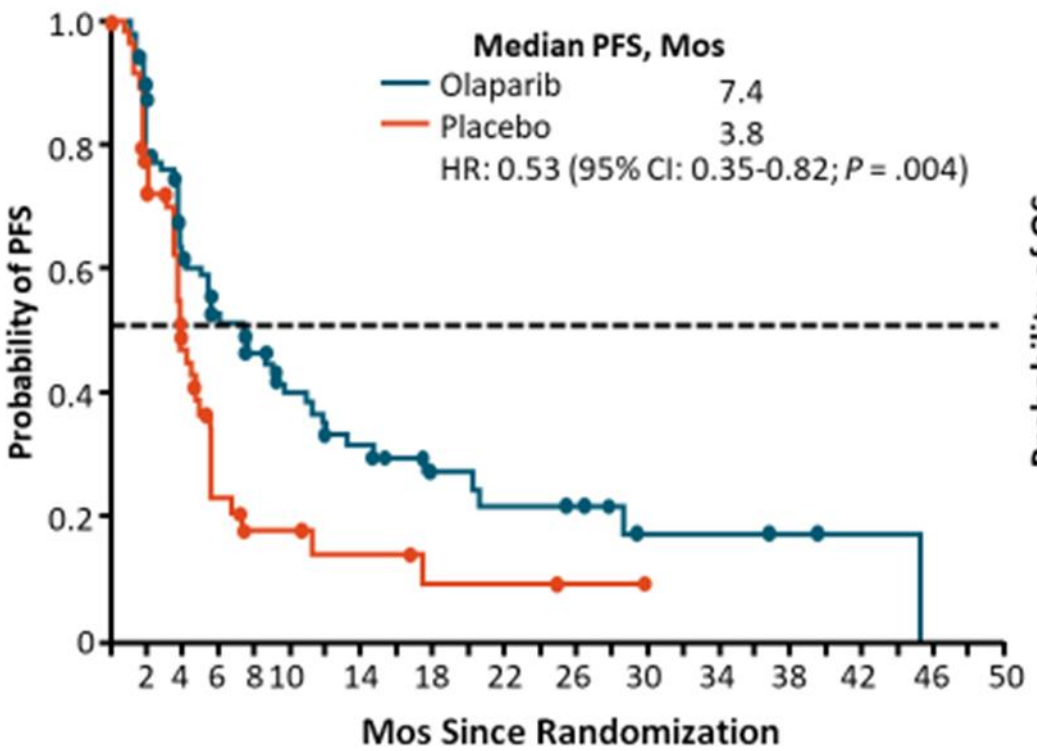
- International, randomized, double-blind phase III trial

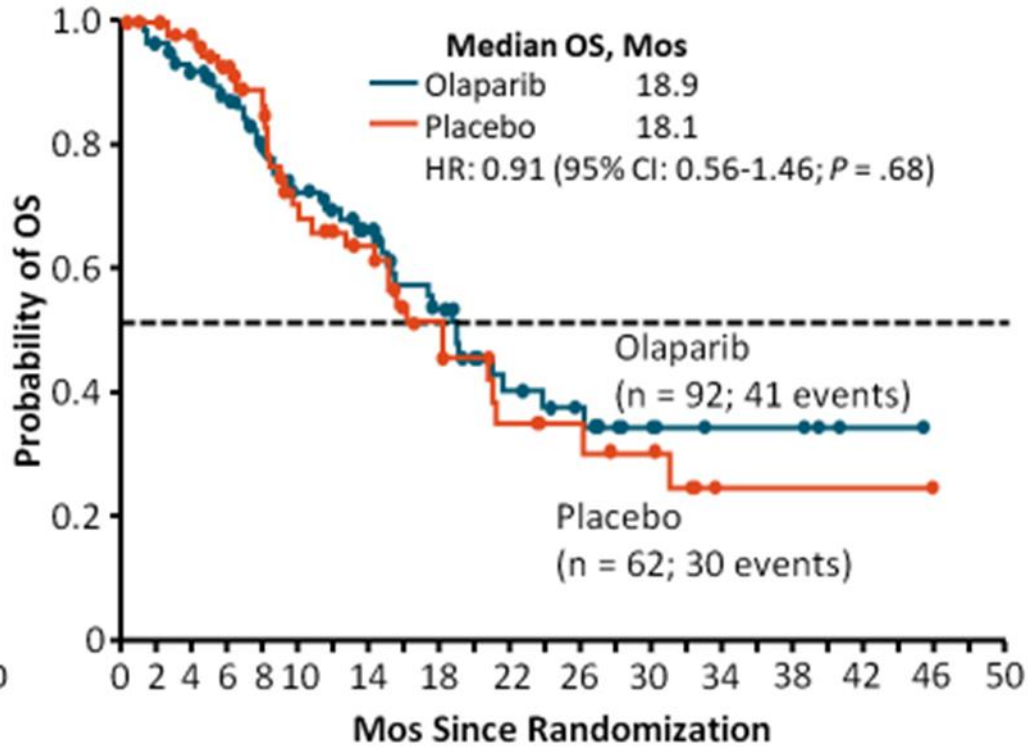


- 3315 patients screened; 247 had germline *BRCA* mutation (7.5%)
- Primary endpoint: PFS by blinded independent central review (modified RECIST v1.1)
  - 87 PFS events required for 80% power with 1-sided alpha of .025; assumed PFS HR: 0.54
- Key secondary endpoints: safety/tolerability, PFS2, ORR, OS, HRQoL

Kindler. ASCO 2019. Abstr LBA4. Golan. NEJM. 2019;381:317.

POLO: PFS and OS





Golan, NEJM 2019

OPEN DISCUSSION

- Standard therapy selection, based on clinical features. HRD predictive response to platinum.
- Treatment duration in clinical practicing
- Gene profiling: *KRAS* status, NGS in *KRAS* WT
- Germline testing: only *BRCA 1-2* + *PALB 2* ? BRCAness. Reason of amazing response and survival?

ESMO GUIDELINES: REAL WORLD CASES

THANK YOU FOR YOU ATTENTION

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PANCREATIC CANCER

A practice perspective on guideline implementation and the current case

Gabor Liposits, MD, PhD

On behalf of the Practising Oncologist Working Group

DECLARATION OF INTERESTS

Gabor Liposits, MD, PhD

Financial interests:

Honoraria: Danone, Servier
Congress support (travel and accommodation): Servier
Institutional funding: Servier, MSD, Amgen, Astra Zeneca
Advisory board: MSD

Non-financial interests:

ESMO POWG member
ESMO DCWG member
SIOG Board member

The ESMO POWG serves to identify the practice needs of oncologists who are hospital and office-based by developing educational services, practice tools and quality indicators that will facilitate the implementation of best practice at the point of care.

The POWG members are relevant stakeholders to the ESMO Guidelines Webinars as experts who are consulting and implementing the guidelines in their daily practices

For more information about the ESMO POWG visit **esmo.org**

ESMO > About ESMO > Organisational Structure > Educational Committee

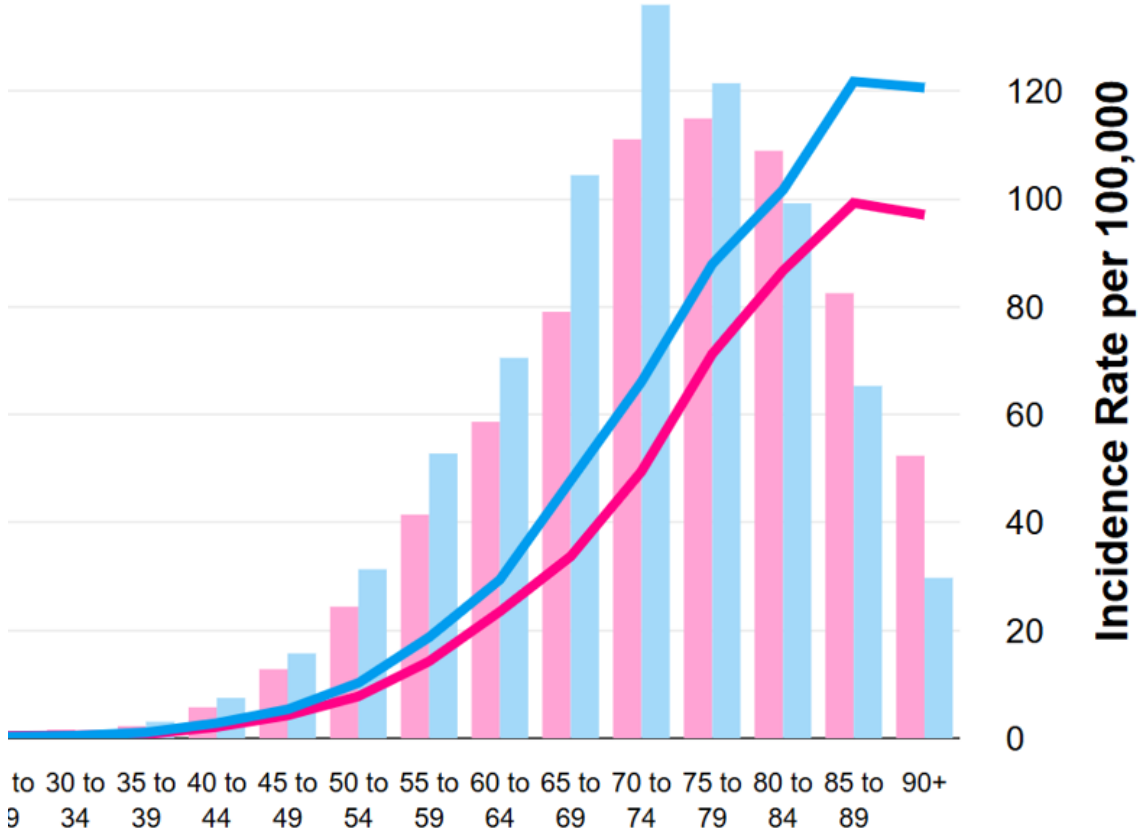
ESMO PRACTISING ONCOLOGISTS WORKING GROUP

Don't miss:

- The «ESMO Checklists» on OncologyPRO

Aging is a non-modifiable risk factor for (pancreatic) cancer

Along with the aging populations worldwide, the incidence of PDAC rises.



Age-specific incidence rates steeply increase ≥65 years.

Half of the patients are ≥70 years.

PDAC disproportionately affects older adults.

Cancer Research UK, https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/pancreatic-cancer/incidence#heading-One, Accessed November 2024.

Precision medicine – in-depth characterization

TUMOR

Diagnostic work-up

mPDAC – CT-scan often provides a reliable diagnosis.

Liver MRI, endoscopic US are not essential in mPDAC.

Biopsy from a liver metastasis is sufficient.

CA19-9 can be considered at baseline and for response evaluation.

PDAC is one of the most lethal primary malignancies

Time factor is important during diagnostic work-up

Resource utilization

Precision medicine – in-depth characterization

PATIENT

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

REVIEW

Adequate assessment yields appropriate care—the role of geriatric assessment and management in older adults with cancer: a position paper from the ESMO/SIOG Cancer in the Elderly Working Group

Functional decline might rapidly occur.

Comprehensive evaluation beyond ECOG PS is needed.

Patient-related factors are crucial in most mPDAC cases.

(Low) BMI, weight loss, cachexia/anorexia, systemic inflammation.

Often high symptom burden.

Early integrated supportive and palliative care are crucial.

Loh et al, ESMO OPEN 2024

Treatment options – for a fit patient

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

FOLFIRINOX versus Gemcitabine for Metastatic Pancreatic Cancer

Characteristic	FOLFIRINOX (N=171)	Gemcitabine (N=171)
Age — yr		
Median	61	61
Range	25–76	34–75
Sex — no. (%)		
Male	106 (62.0)	105 (61.4)
Female	65 (38.0)	66 (38.6)
ECOG performance status score — no. (%)		
0	64 (37.4)	66 (38.6)
1	106 (61.9)	105 (61.4)
2	1 (0.6)	0
Pancreatic tumor location — no. (%)		
Head	67 (39.2)	63 (36.8)
Body	53 (31.0)	58 (33.9)
Tail	45 (26.3)	45 (26.3)
Multicentric	6 (3.5)	5 (2.9)
Biliary stent — no. (%)		
Yes	27 (15.8)	22 (12.9)
No	144 (84.2)	149 (87.1)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Increased Survival in Pancreatic Cancer with nab-Paclitaxel plus Gemcitabine

Table 1. Characteristics of the Patients at Baseline.*

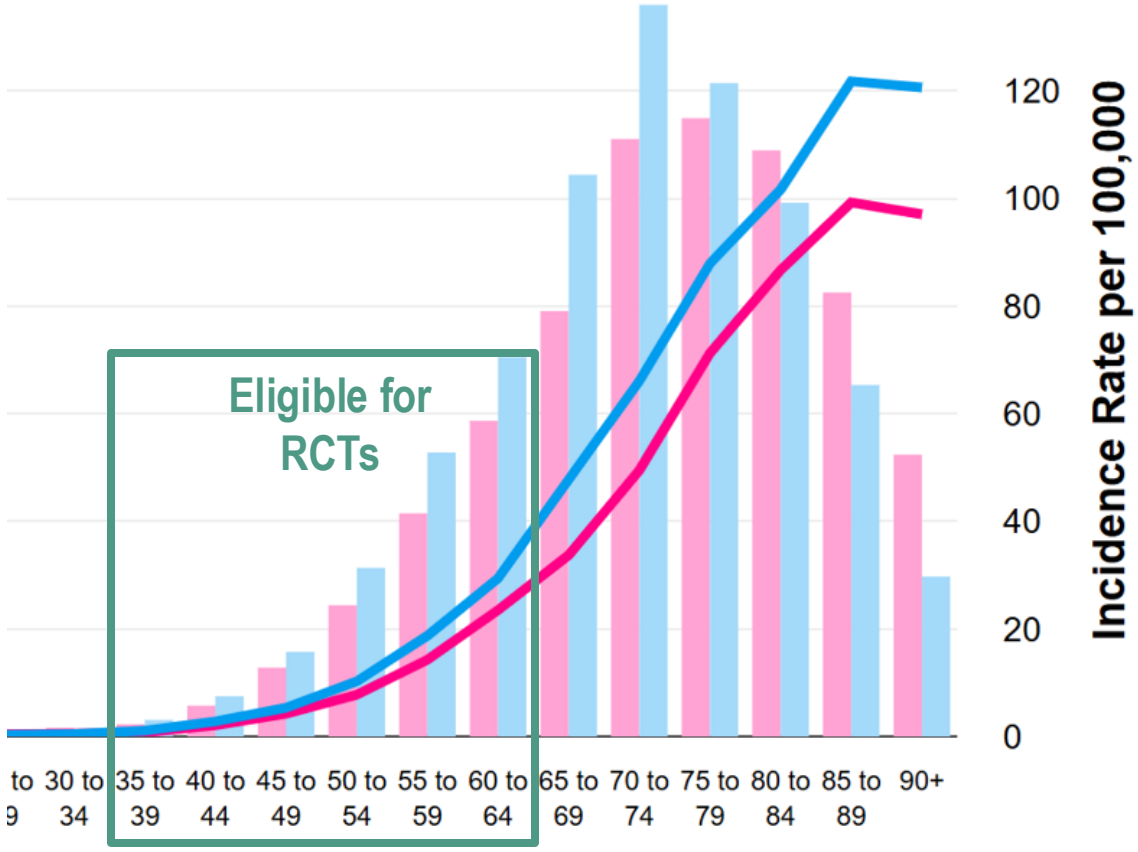
Characteristic	nab-Paclitaxel plus Gemcitabine (N=431)	Gemcitabine Alone (N=430)	Total (N=861)
Age			
No. of yr			
Median	62	63	63
Range	27–86	32–88	27–88
Distribution — no. (%)			
<65 yr	254 (59)	242 (56)	496 (58)
≥65 yr	177 (41)	188 (44)	365 (42)
Sex — no. (%)			
Female	186 (43)	173 (40)	359 (42)
Male	245 (57)	257 (60)	502 (58)
Karnofsky performance-status score — no./total no. (%)‡			
100	69/429 (16)	69/429 (16)	138/858 (16)
90	179/429 (42)	199/429 (46)	378/858 (44)
80	149/429 (35)	128/429 (30)	277/858 (32)
70	30/429 (7)	33/429 (8)	63/858 (7)
60	2/429 (<1)	0/429	2/858 (<1)

NALIRIFOX versus nab-paclitaxel and gemcitabine in treatment-naive patients with metastatic pancreatic ductal adenocarcinoma (NAPOLI 3): a randomised, open-label, phase 3 trial

	NALIRIFOX (n=383)	Nab-paclitaxel and gemcitabine (n=387)
Age, years		
Mean (SD)	62·8 (9·7)	64·0 (8·3)
Median (range; IQR)	64·0 (20–85; 57–70)	65·0 (36–82; 59–70)
Sex		
Female	179 (47%)	157 (41%)
Male	204 (53%)	230 (59%)
Race		
White	315 (82%)	324 (84%)
Asian	20 (5%)	18 (5%)
Black or African American	12 (3%)	7 (2%)
Other	7 (2%)	6 (2%)
Multiple	3 (1%)	0
American Indian or Alaska Native	0	2 (1%)
Native Hawaiian or other Pacific Islander	0	1 (<1%)
Not reported	26 (7%)	29 (7%)
ECOG performance status score		
0	160 (42%)	168 (43%)
1	222 (58%)	219 (57%)
2	1 (<1%)*	0
Metastatic sites		
1	114 (30%)	138 (36%)
2	120 (31%)	108 (28%)
≥3	149 (39%)	141 (36%)
Liver metastases	307 (80%)	311 (80%)

Conroy et al, NEJM, 2011, Van Hoff et al, NEJM, 2013, Wainberg et al. Lancet, 2023

Older/vulnerable patients are under-represented in RCTs



Most patients seen in daily practice are not represented in RCTs

Those included in RCTs are younger and fit

Less benefit and more toxicities observed in real-world setting

Cancer Research UK, https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/pancreatic-cancer/incidence#heading-One, Accessed November 2024.

Best regimen?

Original Investigation | Oncology

NALIRIFOX, FOLFIRINOX, and Gemcitabine With Nab-Paclitaxel as First-Line Chemotherapy for Metastatic Pancreatic Cancer

A Systematic Review and Meta-Analysis

Regimen	FOLFIRINOX	NAB-PAC./GEMCITABINE	NALIRIFOX
Median OS (months)	11.7	10.4	11.1

HR: 1.18 [95%CI, 1.00-1.39]; *p*= 0.05

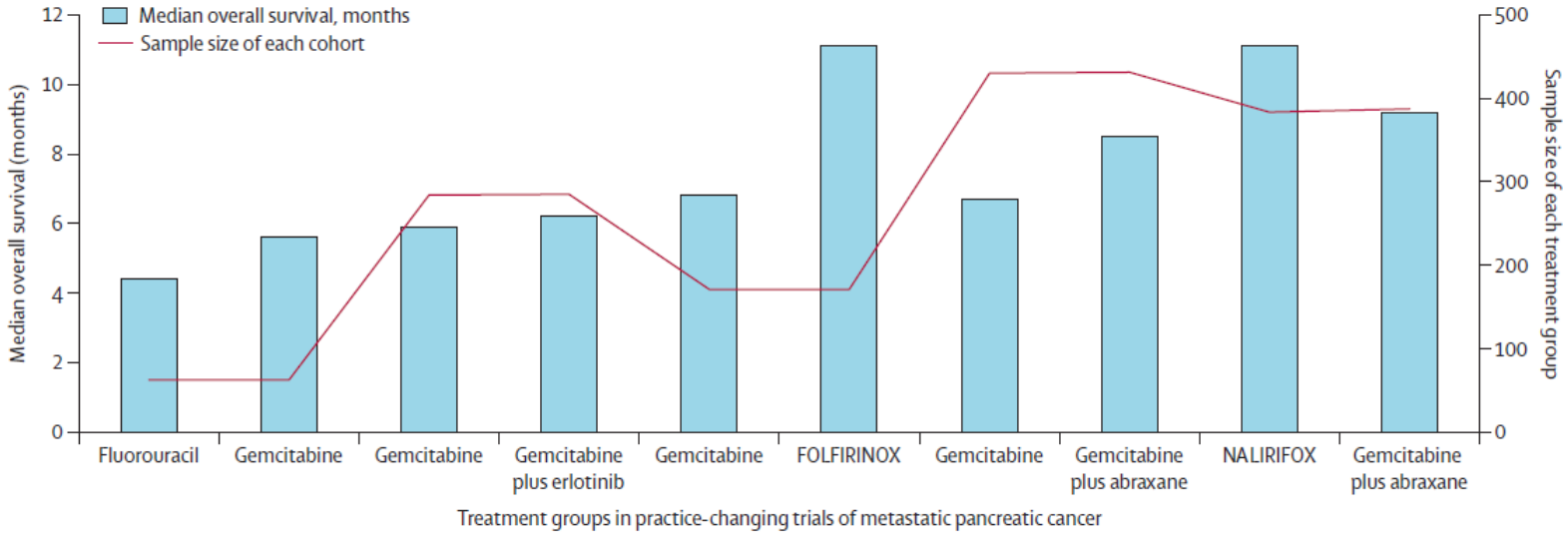
Neither statistically, nor clinically meaningful OS differences between regimens

Nichetti et al. JAMA Network Open 2024

Treatment options

Essay

Treatment of metastatic pancreatic cancer: 25 years of innovation with little progress for patients



	Burris et al (1997)[3]	Burris et al (1997)[3]	Moore et al (2007)[4]	Moore et al (2007)[4]	Conroy et al (2011)[5]	Conroy et al (2011)[5]	Von Hoff et al (2013)[6]	Von Hoff et al (2013)[6]	Wainberg et al (2023)[12]	Wainberg et al (2023)[12]
Median overall survival, months	4·4	5·6	5·9	6·2	6·8	11·1	6·7	8·5	11·1	9·2
Sample size of each cohort	63	63	284	285	171	171	430	431	383	387

Figure: **Changes in median overall survival versus sample size of treatment groups in pivotal trials of drugs for first-line treatment of advanced pancreatic cancer, 1997–2023**
Data are shown by individual treatment groups in each trial. The line plots the sample size for each individual treatment group in each study, and the bars show the median overall survival.

Gyawali B, Booth CM. Lancet Oncol. 2024

Further considerations and discussion

Deficits in geriatric domains are frequent despite ECOG PS:0, geriatric screening is recommended (Geriatric 8).

Patient's preferences and shared decision-making should be considered regarding the treatment of choice.

DPD testing/se-uracil measurement guided the dose of 5FU according to ESMO guidelines.

Remarkable platinum-sensitivity with a durable response. BRCA mutation or Homologous Recombination Deficiency (HRD)?

Upon oligometastatic disease/progression, local treatment (percutaneous interv./SBRT) might be considered (EXTEND-trial*)?

Short re-introduction (5 cycles) upon PD – toxicities/tolerability issues?

PFS1: 24 months, PFS2: 8 months.

Second re-introduction with FOLFIRINOX? Cumulative toxicities? Change the regimen? Local treatment in addition?

*Roberts et al, JCO 2024

Food for thoughts

Excellent, yet an exceptional case, not representative for most patients with mPDAC managed in clinical practice.

Given the limited survival benefit, quality of life (QoL) and symptom control are important endpoints.

Older adults often prefer patient-centered endpoints – QoL, preservation of functioning, independence.

Cumulative toxicity, especially oxaliplatin induced peripheral neuropathy is a concern regarding QoL and ADL/IADL.

Local therapeutic modalities in addition to systemic treatment can provide benefit in selected cases. MDT discussion!

Comprehensive molecular characterization is important even in older adults who are fit for treatment.

Geriatric co-management and early supportive and palliative care are essential in most patients with mPDAC.

THANK YOU !