

Nimotuzumab in Pancreatic Cancer

Updates on the current evidences

Jnokeys

CIMaHer Product Profile

Brand Name	CIMaHer
Composition	Vial contain: Nimotuzumab 50 mg
Dosage Form	Injection
Manufacturer	Centro De Inmunología Molecular (CIM), La Habana, Cuba
Mechanism of Action	Anti EGFR

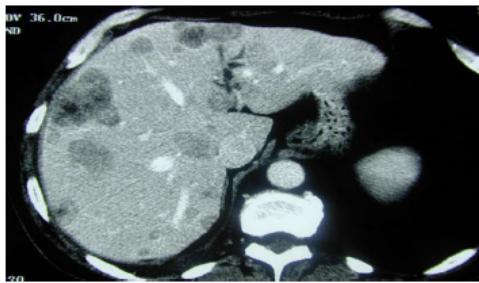


Nimotuzumab
(Indonesia)

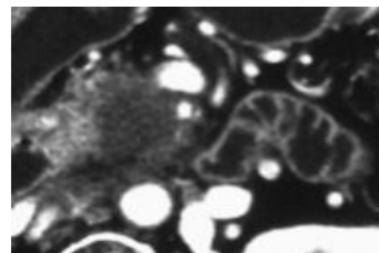


DISEASE AT PRESENTATION

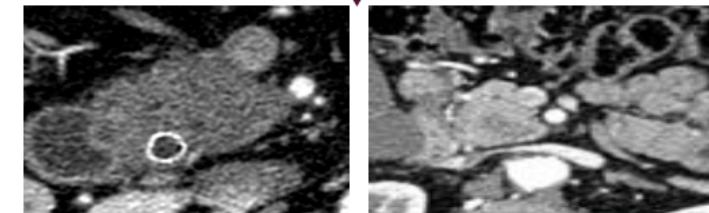
**Metastatic
disease
60%**



**Locally advanced
disease
25%**



Resectable disease 15%



Borderline

R0 surgery

Overall survival 5-11 mo

9-16 mo

15-30 mo

> 2 years

Courtesy of Pr Pascal Hammel Beaujon Hospital. Clichy France

ESMO

ADVANCED STAGE MANAGEMENT

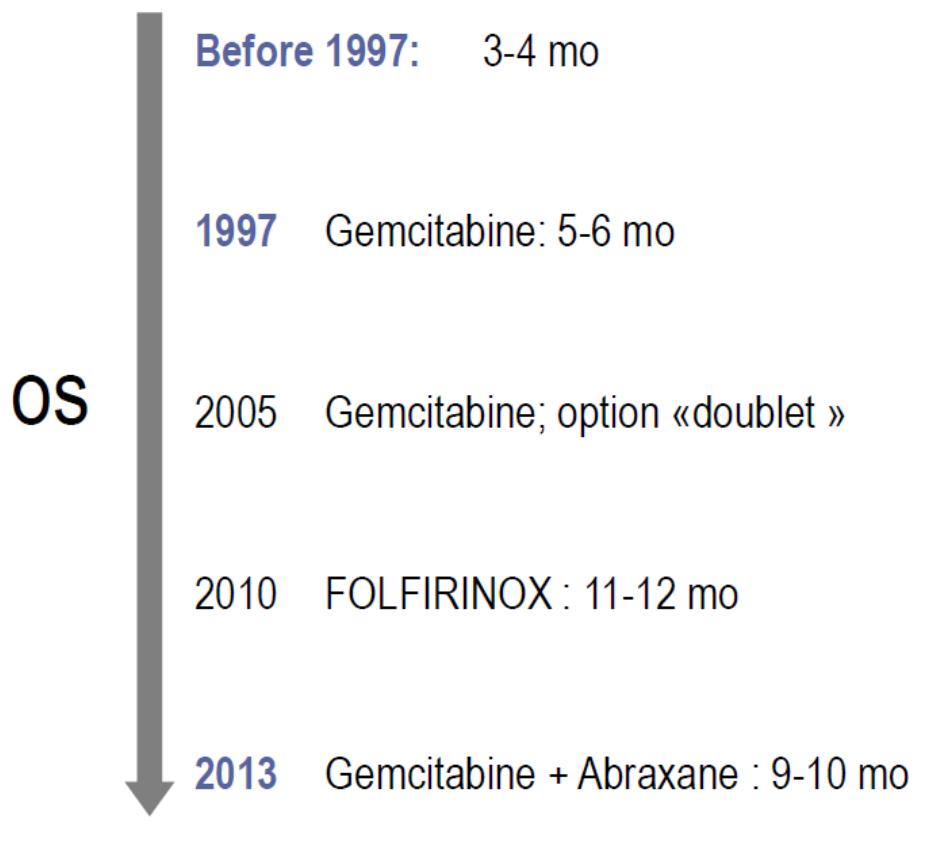
Metastatic disease





IMPROVEMENT IN OS SINCE 20 YEARS

However OS remains poor for metastatic pancreatic cancer



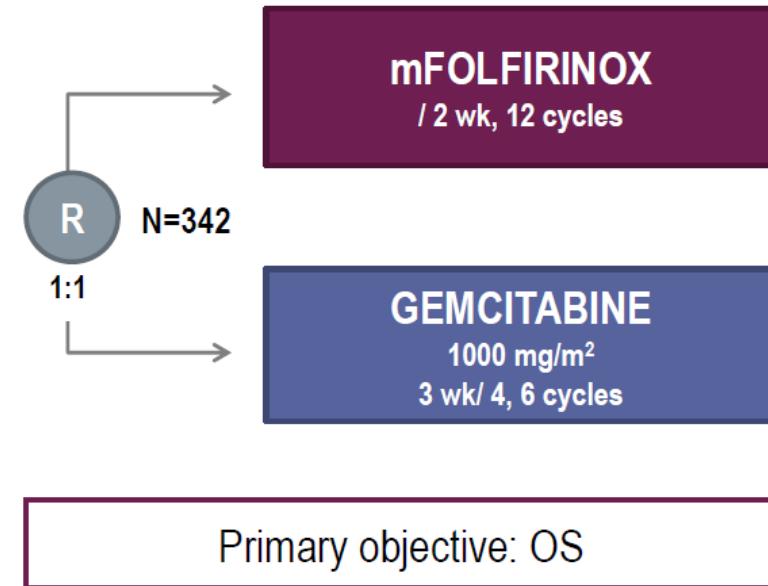


FIRST-LINE TREATMENT FOR METASTATIC DISEASE

FOLFIRINOX the PRODIGE 4 study

- Oxaliplatin 85 mg/m²
- LV 400 mg/m²
- Irinotecan 180 mg/m²,*
- 5 FU continue 2.4 g/m² 46 h

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



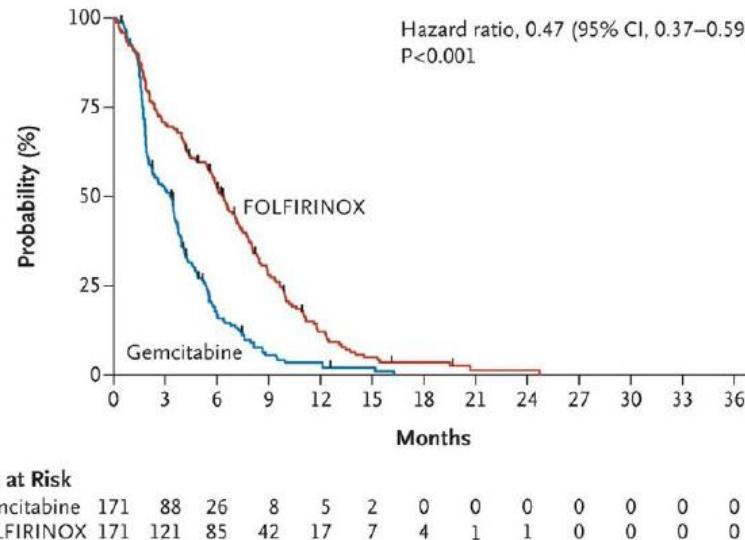


FIRST-LINE TREATMENT FOR METASTATIC DISEASE

FOLFIRINOX the PRODIGE 4 study

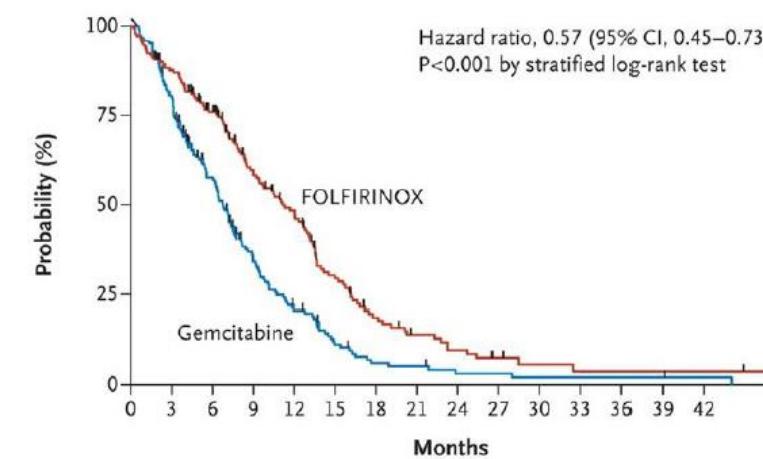
PFS

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



6.4 mo vs. 3.3 mo

OS



11.1 mo vs. 6.8 mo

From N Engl J Med, Conroy T, et al. FOLFIRINOX versus Gemcitabine for Metastatic Pancreatic Cancer, 364(19), 1817–25. Copyright © 2011 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

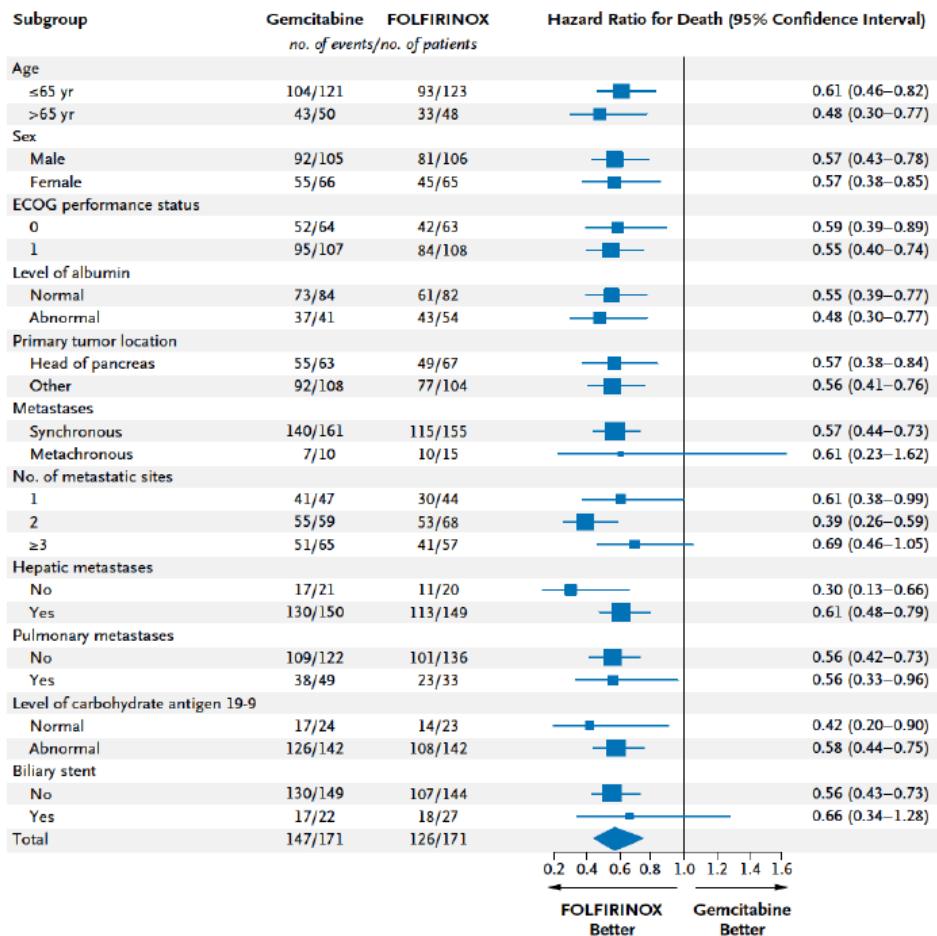
ESMO



FIRST-LINE TREATMENT FOR METASTATIC DISEASE

FOLFIRINOX the PRODIGE 4 study

**The FOLFIRINOX regimen
was favoured in all subgroups**



From N Engl J Med, Conroy T, et al. FOLFIRINOX versus Gemcitabine for Metastatic Pancreatic Cancer, 364(19), 1817–25. Copyright © 2011 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.



FIRST LINE TREATMENT FOR METASTATIC DISEASE

FOLFIRINOX the PRODIGE 4 study

Table 3. Most Common Grade 3 or 4 Adverse Events Occurring in More Than 5% of Patients in the Safety Population.*

Event	FOLFIRINOX (N=171)	Gemcitabine (N=171)	P Value
	<i>no. of patients/total no. (%)</i>		
Hematologic			
Neutropenia	75/164 (45.7)	35/167 (21.0)	<0.001
Febrile neutropenia	9/166 (5.4)	2/169 (1.2)	0.03
Thrombocytopenia	15/165 (9.1)	6/168 (3.6)	0.04
Anemia	13/166 (7.8)	10/168 (6.0)	NS
Nonhematologic			
Fatigue	39/165 (23.6)	30/169 (17.8)	NS
Vomiting	24/166 (14.5)	14/169 (8.3)	NS
Diarrhea	21/165 (12.7)	3/169 (1.8)	<0.001
Sensory neuropathy	15/166 (9.0)	0/169	<0.001
Elevated level of alanine aminotransferase	12/165 (7.3)	35/168 (20.8)	<0.001
Thromboembolism	11/166 (6.6)	7/169 (4.1)	NS

* Events listed are those that occurred in more than 5% of patients in either group. NS denotes not significant.

From N Engl J Med, Conroy T, et al. FOLFIRINOX versus Gemcitabine for Metastatic Pancreatic Cancer, 364(19), 1817–25. Copyright © 2011 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.



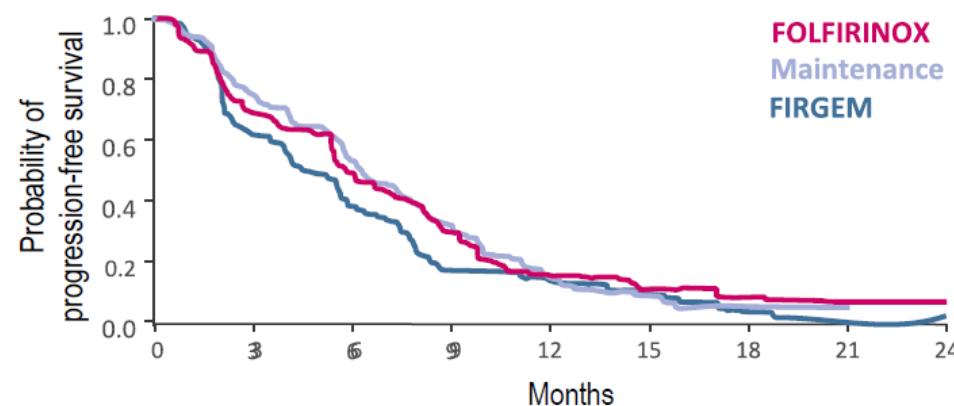
IS MAINTENANCE POSSIBLE WITH FOLFIRINOX?

The PRODIGE 35 study

De-escalation from FOLFIRINOX to LV5FU2 after 3 to 6 mo of induction is possible without impairing PFS nor OS

PFS

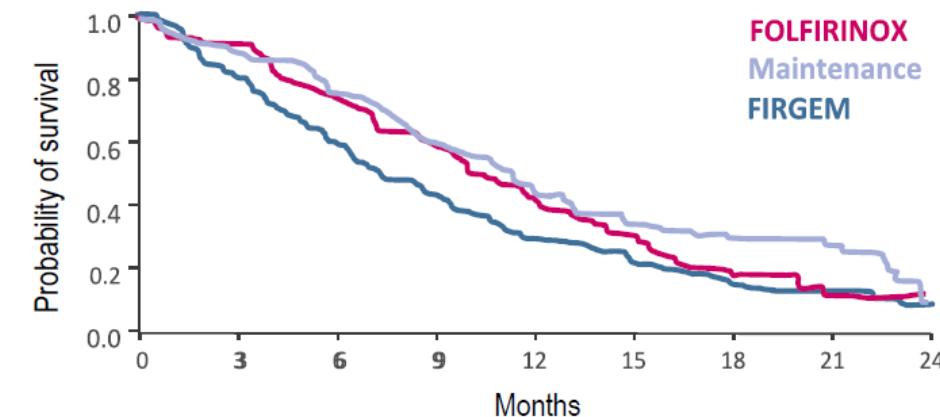
ITT population	FOLFIRINOX	Maintenance	FIRGEM
PFS (mo)	6.3	5.7	4.5
9 mo PFS (%)	32	29	16
12 mo PFS (%)	15	15	13



FIRGEM: FOLFIRI.3 followed by gemcitabine.
Dahan L, et al. ASCO 2018; Abstract #4000.

OS

ITT population	FOLFIRINOX	Maintenance	FIRGEM
OS (mo)	10.1	11.0	7.3
9 mo OS(%)	74	75	60
12 mo OS(%)	43	44	28





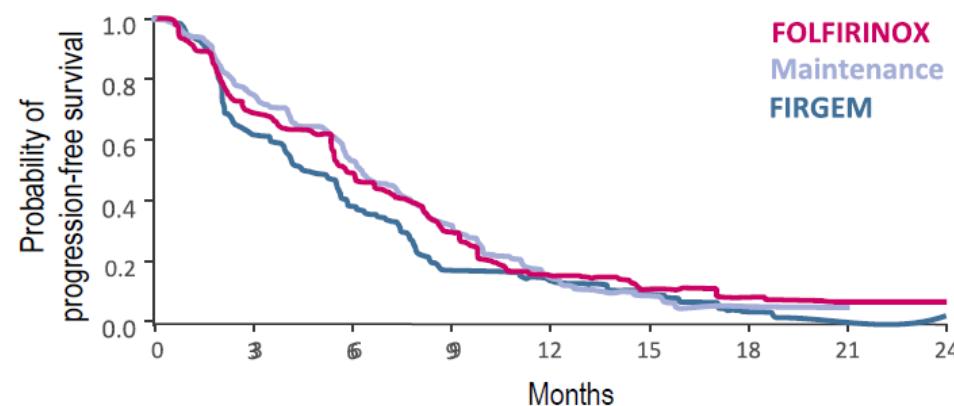
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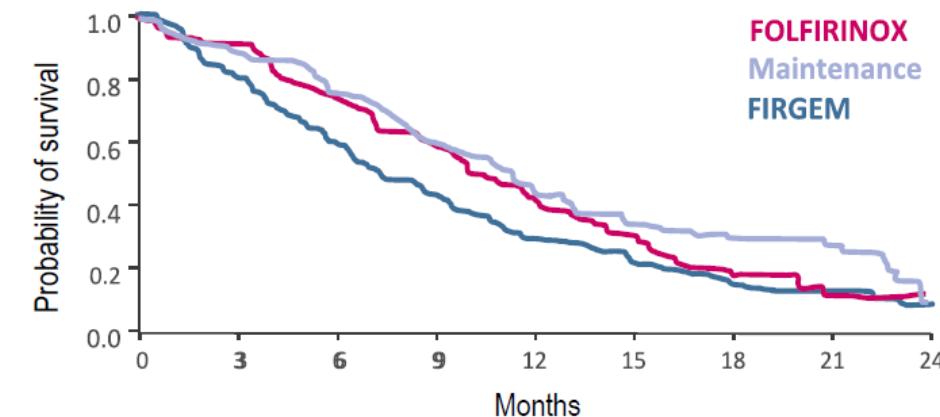
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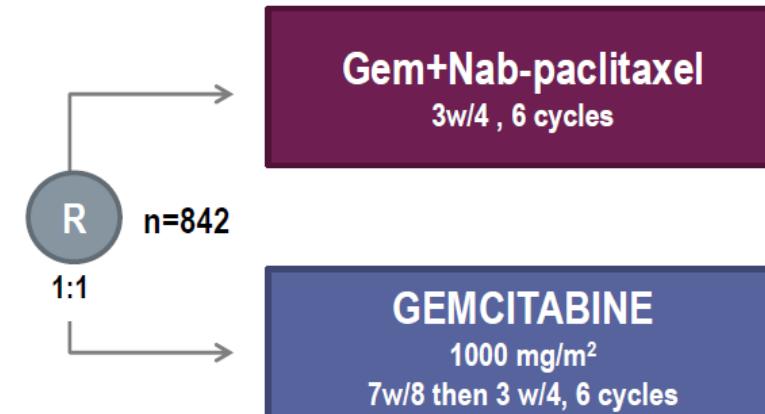
FIRST LINE TREATMENT FOR METASTATIC DISEASE

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

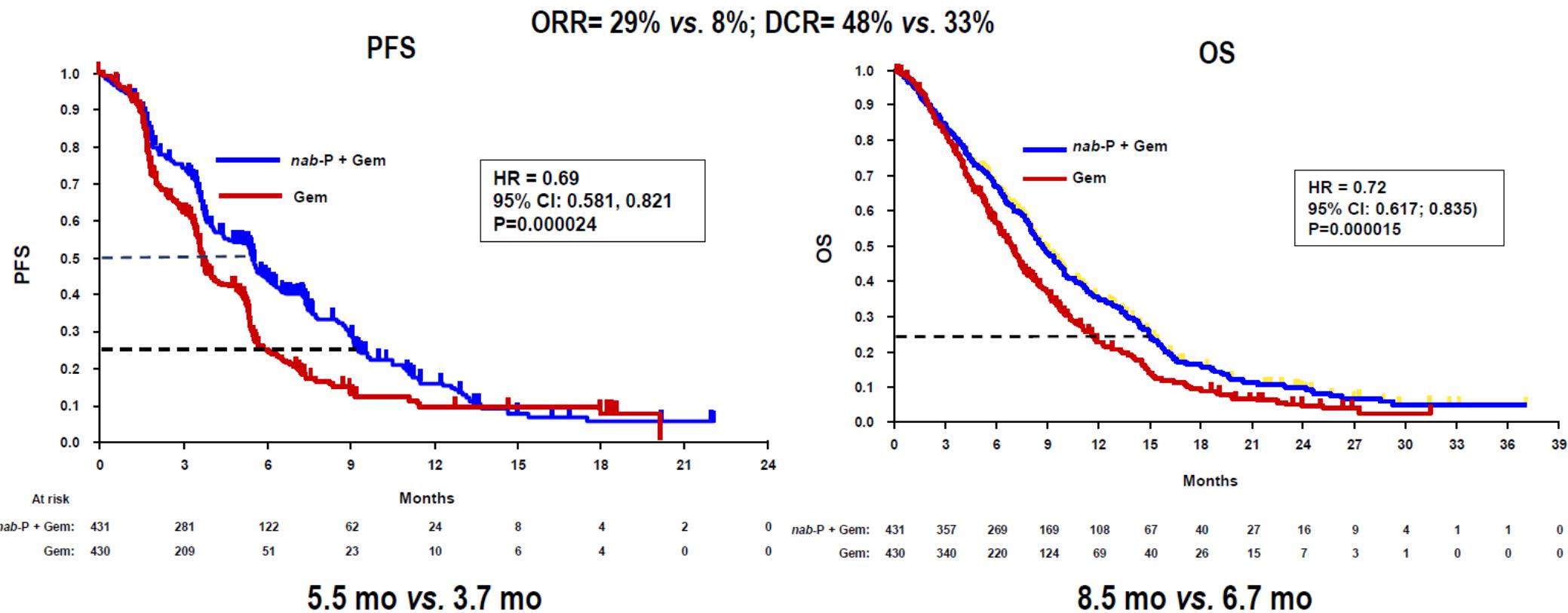


Primary objective: OS



FIRST LINE TREATMENT FOR METASTATIC DISEASE

Gem+ Nab-paclitaxel (the MPACT study)



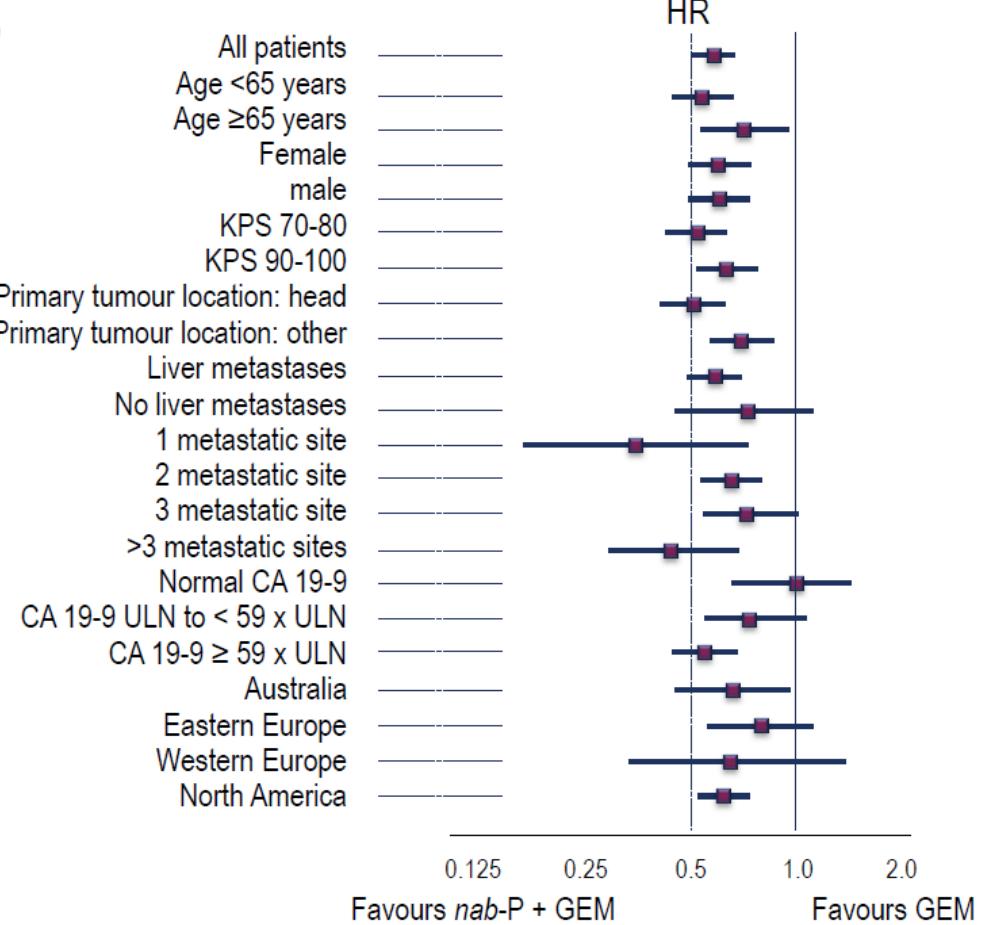
From N Engl J Med, Von Hoff DD, et al. Increased Survival in Pancreatic Cancer with nab-Paclitaxel plus Gemcitabine, 369:1691-1703. Copyright © 2013. Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.



FIRST LINE TREATMENT FOR METASTATIC DISEASE

Gem+ Nab-paclitaxel (the MPACT study)

The combination Gem+ Nab-paclitaxel
was favoured in all subgroups
except normal CA 19.9



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

Gem+ Nab-paclitaxel (the MPACT study)

Table 3. Common Adverse Events of Grade 3 or Higher and Growth-Factor Use.*

Event	nab-Paclitaxel plus Gemcitabine (N = 421)	Gemcitabine Alone (N = 402)
Adverse event leading to death — no. (%)	18 (4)	18 (4)
Grade ≥3 hematologic adverse event — no./total no. (%)†		
Neutropenia	153/405 (38)	103/388 (27)
Leukopenia	124/405 (31)	63/388 (16)
Thrombocytopenia	52/405 (13)	36/388 (9)
Anemia	53/405 (13)	48/388 (12)
Receipt of growth factors — no./total no. (%)	110/431 (26)	63/431 (15)
Febrile neutropenia — no. (%)‡	14 (3)	6 (1)
Grade ≥3 nonhematologic adverse event occurring in >5% of patients — no. (%)‡		
Fatigue	70 (17)	27 (7)
Peripheral neuropathy§	70 (17)	3 (1)
Diarrhea	24 (6)	3 (1)
Grade ≥3 peripheral neuropathy		
Median time to onset — days	140	113
Median time to improvement by one grade — days	21	29
Median time to improvement to grade ≤1 — days	29	NR
Use of nab-paclitaxel resumed — no./total no. (%)	31/70 (44)	NA

* NA denotes not applicable, and NR not reached.

† Assessment of the event was made on the basis of laboratory values.

‡ Assessment of the event was made on the basis of investigator assessment of treatment-related adverse events.

§ Peripheral neuropathy was reported on the basis of groupings of preferred terms defined by standardized queries in the *Medical Dictionary for Regulatory Activities*.

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.



FOLFIRINOX VS. GEM+ NAB-PACLITAXEL

Efficacy¹

	FOLFIRINOX	Gem+ Nab-pacli
Performance status	PS2 <1%	KPS 70-80: 40%
ORR	31.6%	29%
PFS	6.4 mo	5.5 mo
with gem	3.3 mo	3.7 mo
2nd Line	47%	38%
OS	11.1 mo	8.5 mo
with gem	6.8 mo	6.7 mo

Safety²

	FOLFIRINOX	Gem+ Nab-pacli
Neutropenia	45.7%	38%
+ febrile	5.4%	3%
Thrombopenia	9.1%	13%
Anaemia	7.8%	13%
Neuropathy*	9%	17%
Diarrhea	12.7%	6%
Alopecia	11.4%	50%

1. Conroy T, et al. N Engl J Med 2011; 2. Von Hoff DD, et al., N Engl J Med 2013.

Benefit from Palliative Chemotherapy: First-line

Overall survival (median)	Control arm	Experimental arm	Improvement between arms	What did we learn?
Gemcitabine	5FU: 4.4 months	5.6 months	1.2 months	Gemcitabine standard first line
Gem + Erlotinib	Gem: 5.91 months	6.2 months	15 days	No clinically significant benefit
Gem + Cap	Gem: 6.2 months	7.1 months	0.9 month	Moderate clinical benefit
FOLFIRINOX	Gem: 6.8 months	11.1 months	4.3 months	Best survival results
Gem + NabPaclitaxel	Gem: 6.7 months	8.5 months	1.8 months	No QoL data



METASTATIC PANCREATIC CANCER

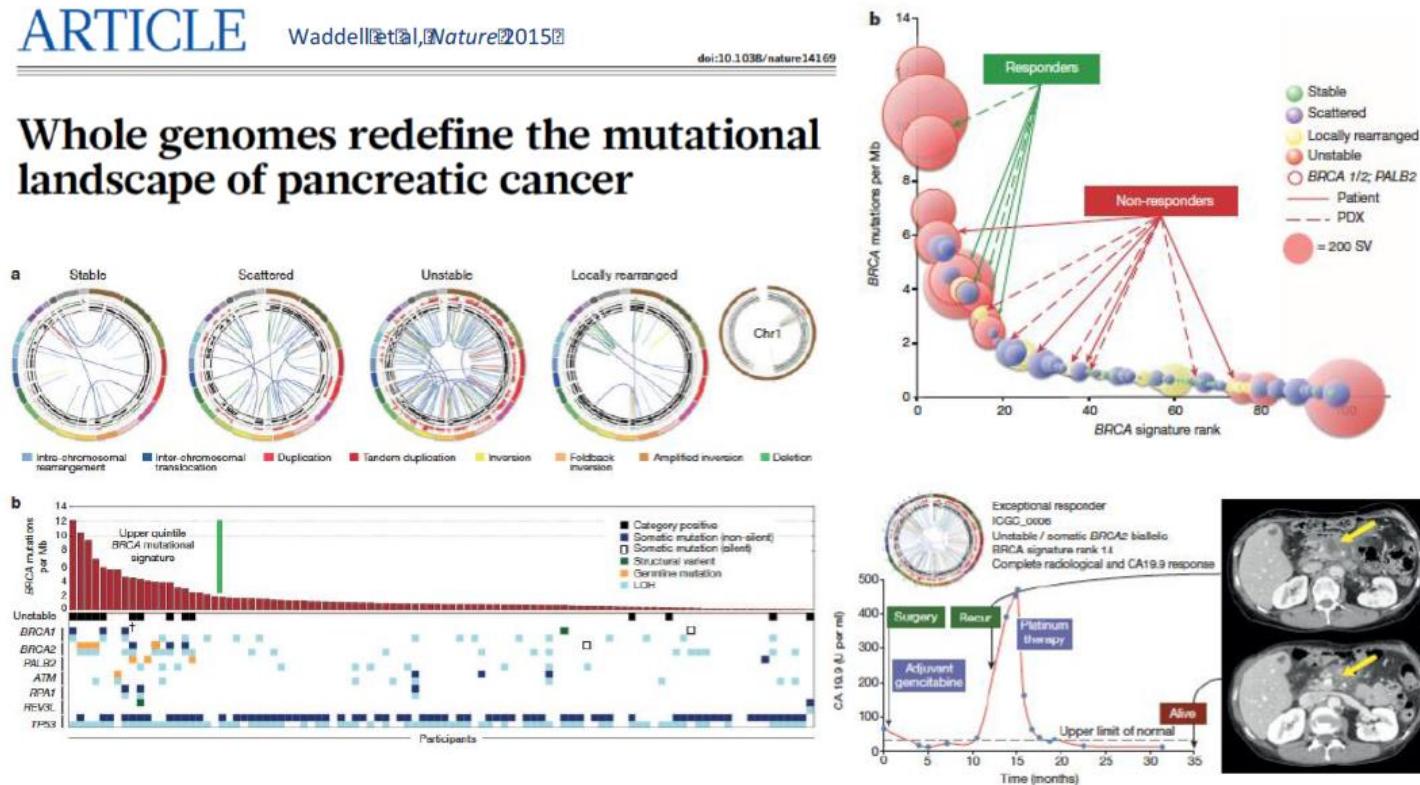
Rare subtypes: BRCAness. Some pancreatic cancers are BRCA mutated and as shown in ovarian cancer may be more sensitive to platin salts and PARP inhibitors

ARTICLE

Waddell N et al., *Nature* 2015

doi:10.1038/nature14169

Whole genomes redefine the mutational landscape of pancreatic cancer



POLO study
NCT02184195
Phase III
Maintenance
Olaparib

ESMO

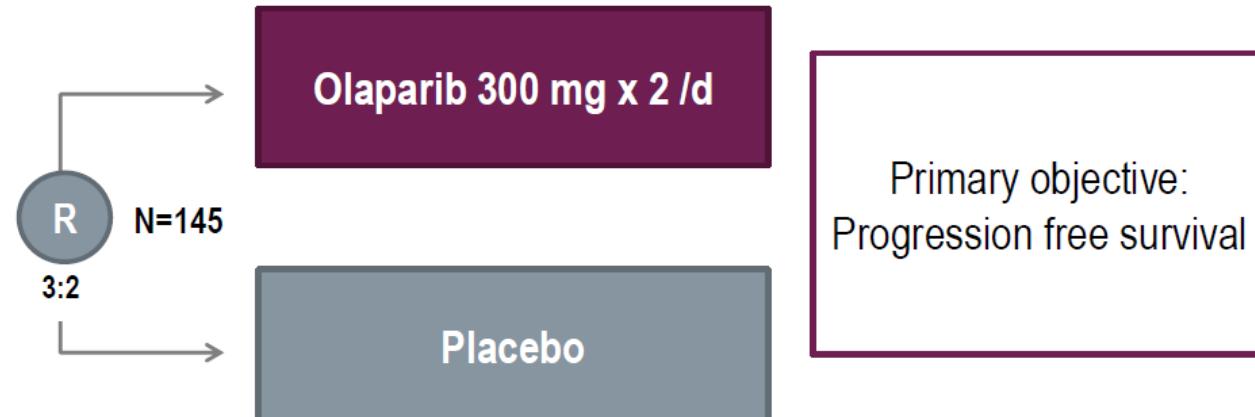
Reprinted by permission from Springer Nature, *Nature*, Whole genomes redefine the mutational landscape of pancreatic cancer, Waddell N, et al., Copyright 2015



GERMLINE BRCA2 MUTATED PANCREATIC CANCER

The POLO study

- Pancreatic adenocarcinoma
- Germline Mutated *BRCA 1/2*
- Treated with a first line platinum
- Without disease progression within 16 weeks

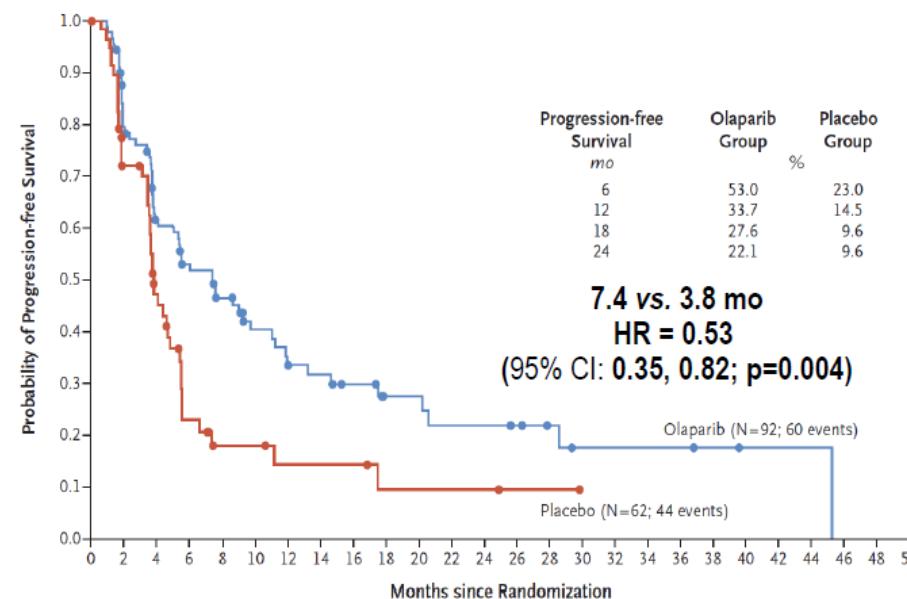




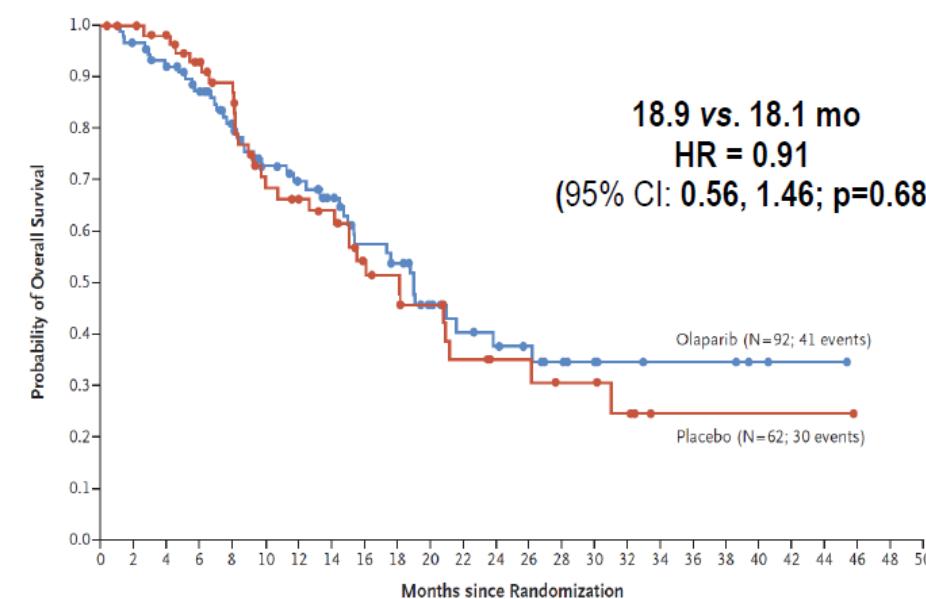
GERMLINE BRCA MUTATED PANCREATIC CANCER

The POLO study

PFS



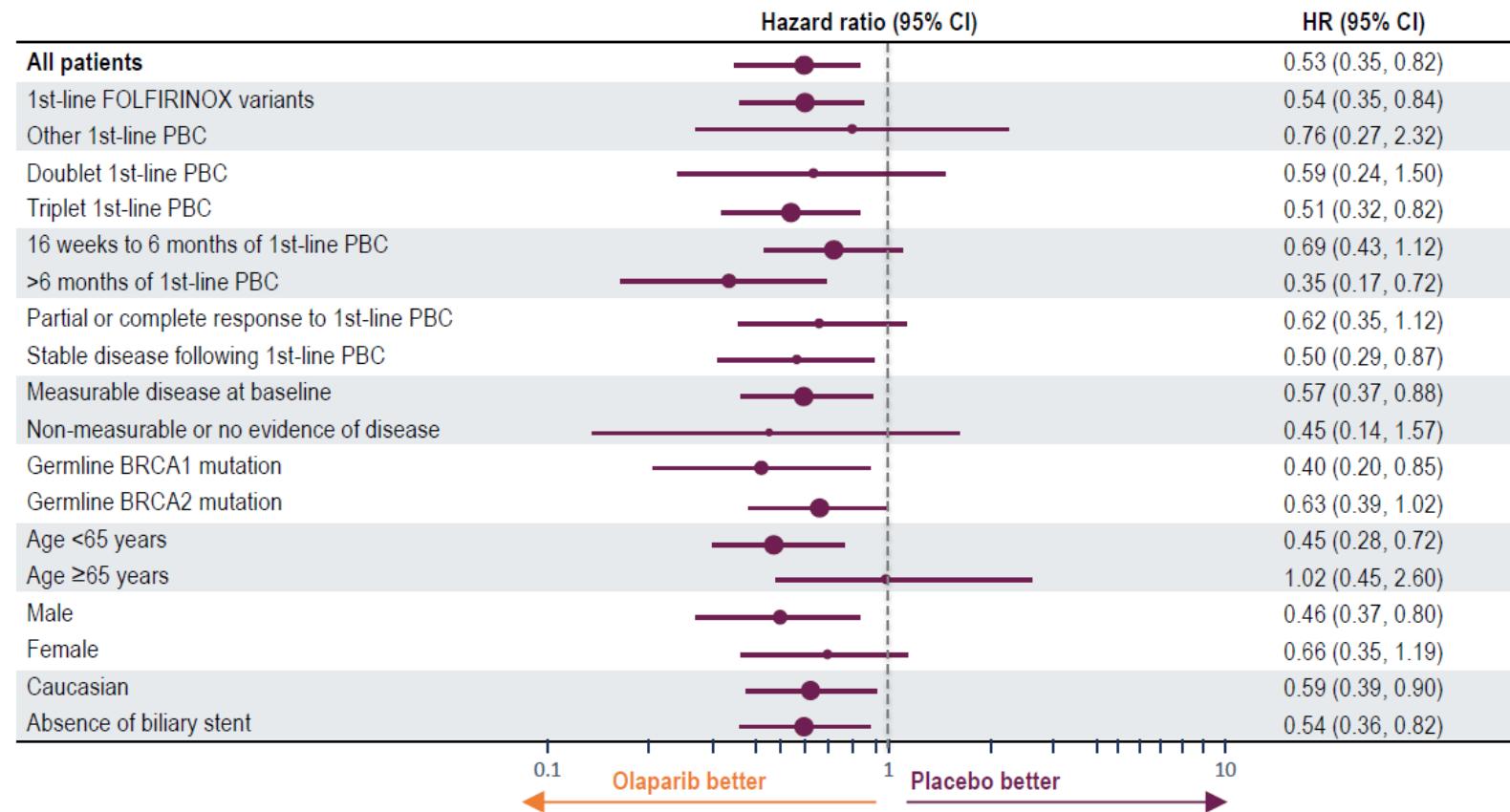
OS



From N Engl J Med, Golan T, et al. Maintenance Olaparib for Germline BRCA-Mutated Metastatic Pancreatic Cancer, 381(4):317–27. Copyright © 2019 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.



GERMLINE BRCA MUTATED PANCREATIC CANCER



Kindler HL, et al. Presented at ASCO 2019, Abstract #LBA4. By permission of Prof Kindler.

IMMUNOTHERAPY FOR METASTATIC PANCREATIC CANCER



Poor results of PC patients in basket studies due to poor local immune cells except for MSI+ tumours

Potential explanations to poor results of Checkpoint inhibitors in PC patients:

Type of response, n (%) ¹	Pancreas N=8
Complete Response	2 (25)
Partial Response	3 (37)
Stable Disease	1 (12)
Progressive Disease	0 (0)
Non Evaluable ^a	2 (25)
Objective Response Rate (%)	62
Disease Control Rate (%) ^b	75

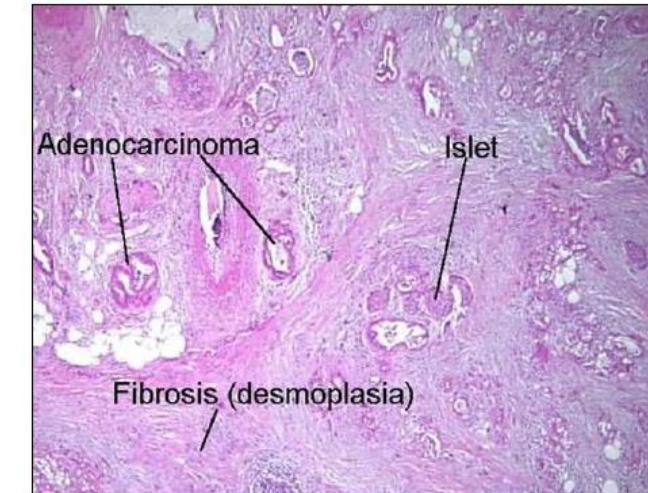
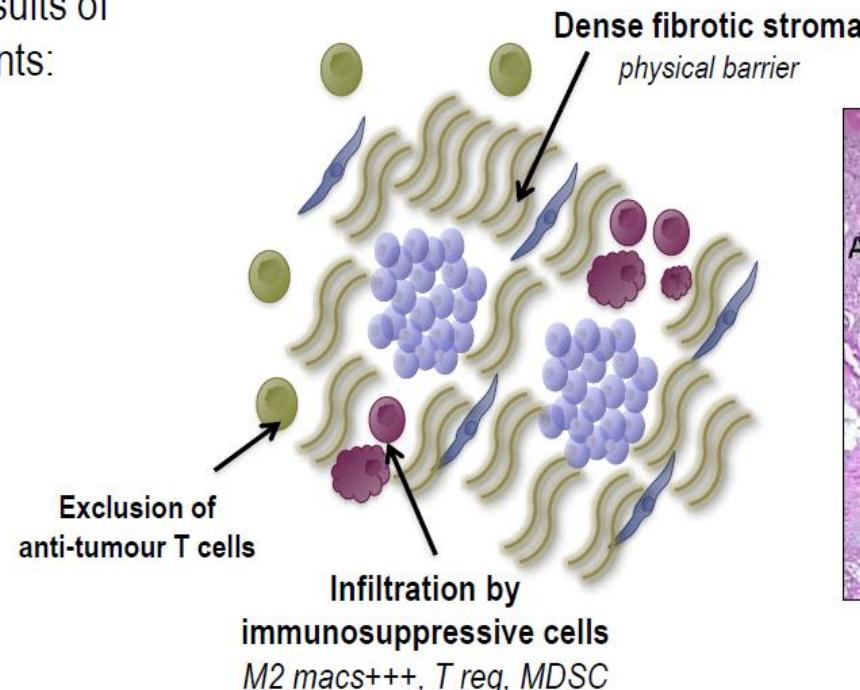


Image courtesy of Dr Cindy Neuzillet, Curie Institute Saint-Cloud

^aPatients were considered not evaluable if they did not undergo a 12 week scan due to clinical progression;

^bThe rate of disease control was defined as the percentage of patients who had a complete response, partial response or stable disease for 12 weeks or more.

1. Le DT, et al. Science 2017;357(6349):409–13.



IMMUNOTHERAPY FOR METASTATIC PANCREATIC CANCER

Ongoing combination trials

Drugs	Study Phase	Estimated numbers	NCT number
GVAX + CRS-207 +/- nivolumab	2	108	02243371
ACP-196 +/- pembrolizumab	2	76	02362048
Gem/Nabpacli +/- durvalumab/tremelimumab	2	180	02879318
Durvalumab + pexidartinib	1	58	02777710
Tremelimumab, durvalumab, SBRT (in 3 combos/arms)	1	60	02311361
Epacadostat, Pembro, CRS-207	2	70	03006302

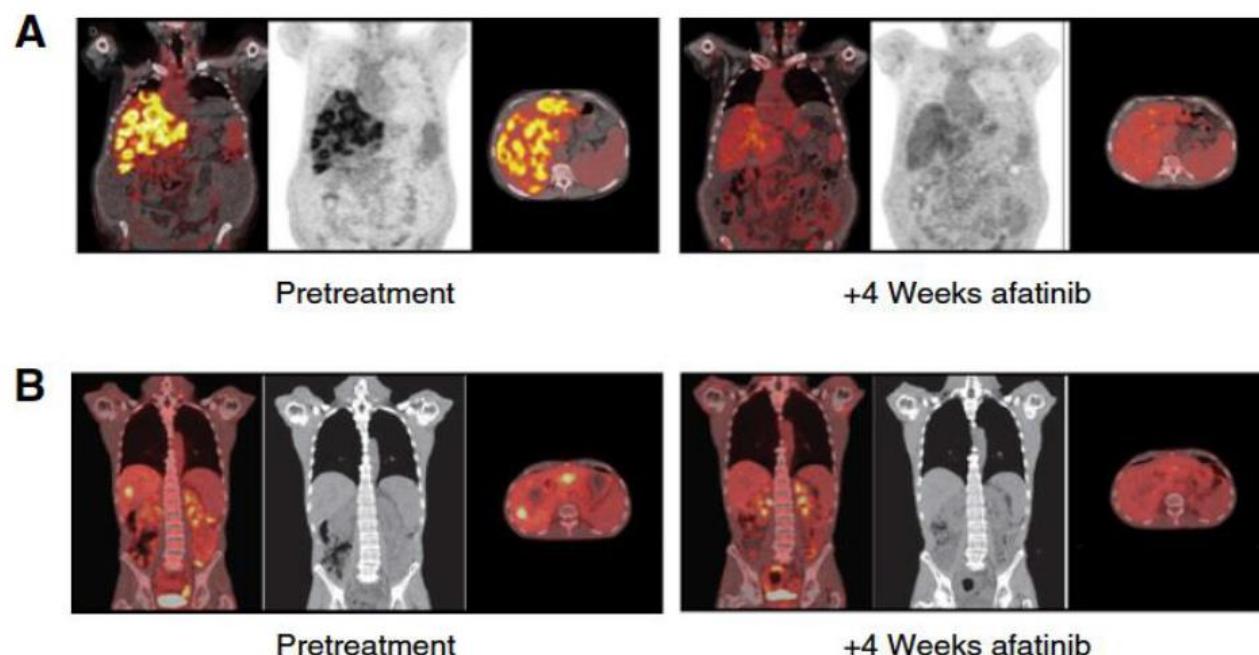


NRG1 GENE FUSIONS

NRG1 Gene fusions are recurrent, clinically actionable gene rearrangements in KRAS wild-type pancreatic ductal adenocarcinoma

Occurrence not well documented but <5%

Efficacy of afatinib in *NRG1* gene fusion KRAS metastatic pancreatic cancer patients

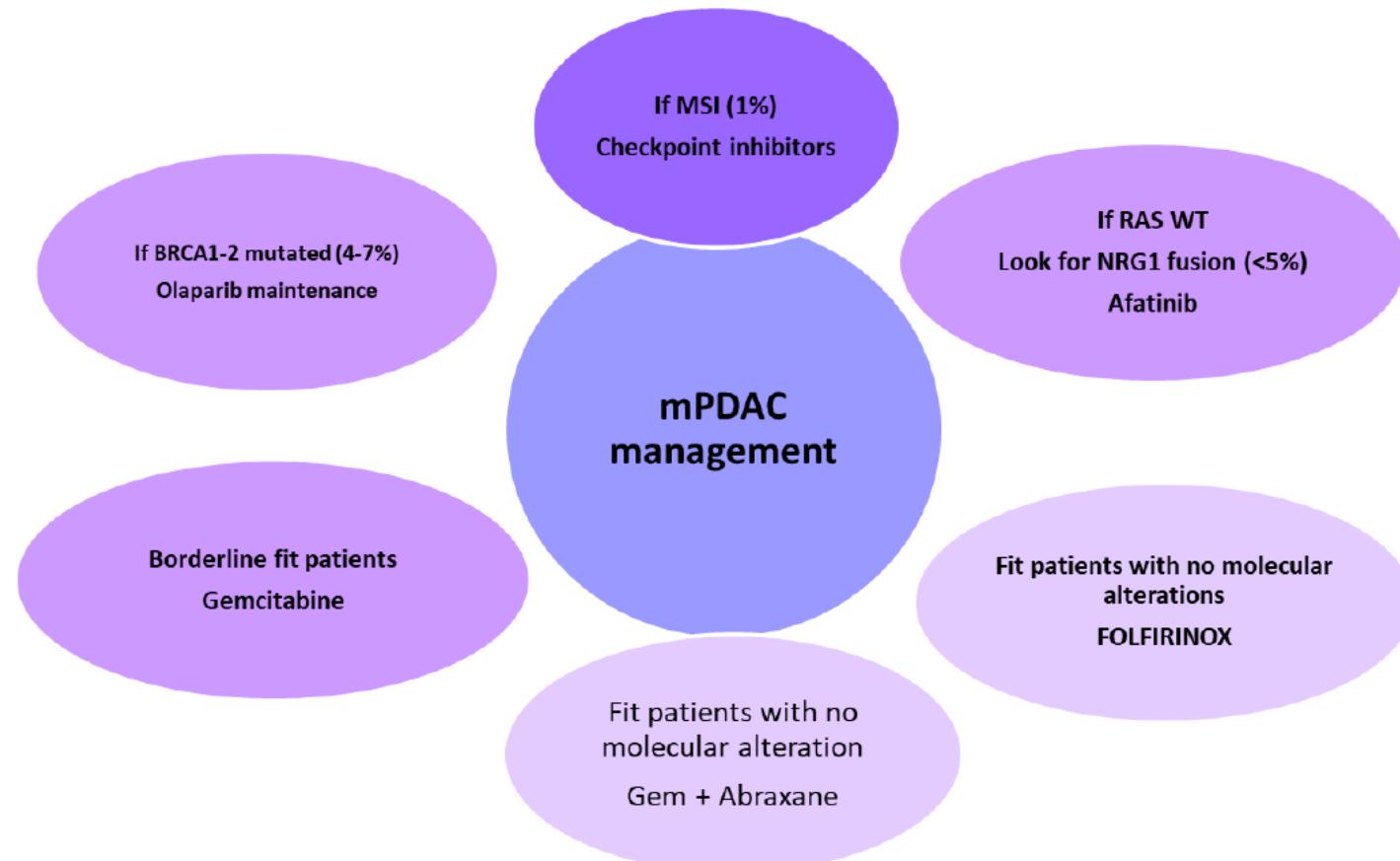


Reprinted from Clin Can Res, Copyright 2019, Jones MR, et al. doi: 10.1158/1078-0432.CCR-19-0191 NRG1 gene fusions are recurrent, clinically actionable gene rearrangements in KRAS wild-type pancreatic ductal adenocarcinoma, with permission from AACR.



In an expert centre

Molecular profiling and therapeutic options for first line metastatic pancreatic cancer





BEYOND GEMCITABINE FIRST LINE

Few randomised trials

40 to 50% of patients will receive a second line therapy after progression with a 1st line regimen

Author, year	Treatment	n	PFS (mo)	OS (mo)	
Oettle H, et al. J Clin Oncol 2014	5FU	84	2.0	HR=0.68 p=0.019	3.3 5.9
	5FU+Oxali	76	2.9		
Von Hoff DD, et al. WCGIC 2014	5FU	398	1.5	HR=0.56 p<0.001	4.2 6.1
	5FU+MM-398		3.1		
	MM-398		2.7		4.9
Gill S, et al. 2014	5FU		2.9	NS	9.1 6.1
	FOLFOX		3.1		
Yoo C, et al. 2009	FOLFOX		2	NS	4.2 3.7
	FOLFIRI.3		1.5		

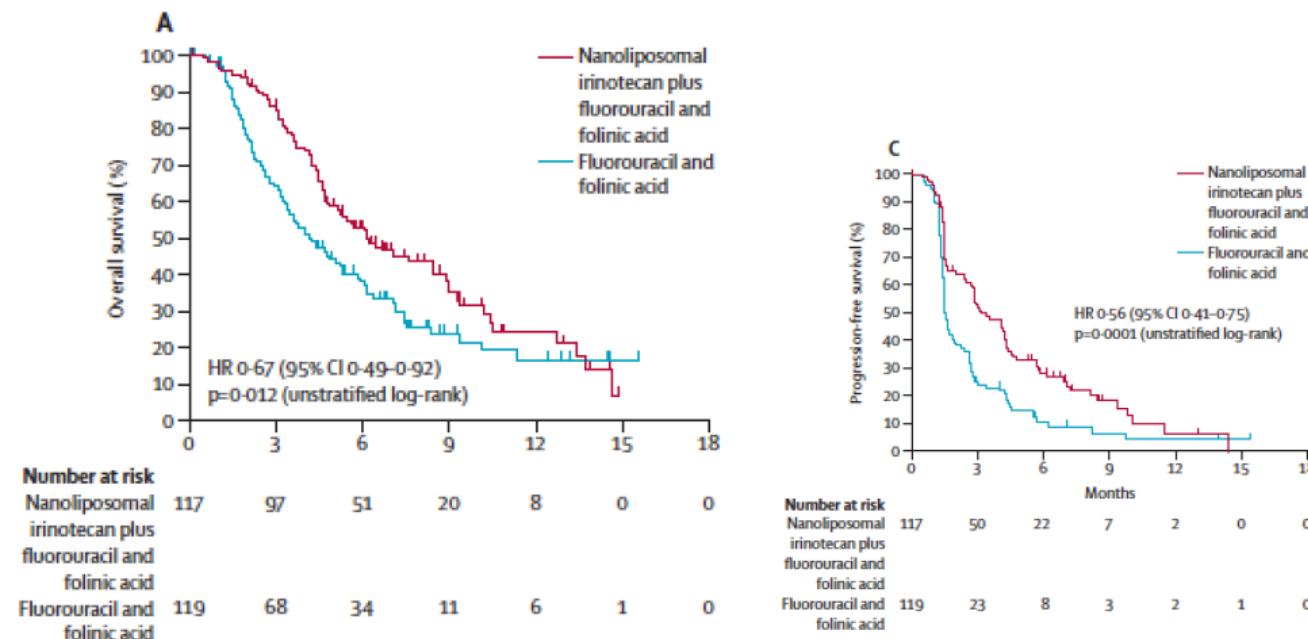
Mainly in the era of gem-based first line treatments



BEYOND FIRST LINE

The NAPOLI 01 study

OS: 6.1 vs. 4.2 mo, p=0.012



Reprinted from The Lancet, 387(10018), Wang-Gillam A, et al. Nanoliposomal irinotecan with fluorouracil and folinic acid in metastatic pancreatic cancer after previous gemcitabine-based therapy (NAPOLI-1): a global, randomised, open-label, phase 3 trial, 545-557, Copyright 2016, with permission from Elsevier.

Phase III
N=417, post-Gemcitabine

5FU/AF vs. Nal-IRI
vs. 5FU/AF + Nal-IRI

Primary endpoint:
OS

Benefit from Palliative Chemotherapy: Second-line

Overall survival (median)	Control arm	Experimental arm	Improvement between arms	What did we learn?
FOLFOX	BSC: 2.3 months	4.8 months	2.5 months	FOLFOX standard second line
FOLFOX	5-FU: 3.3 months	5.9 months	2.6 months	FOLFOX standard second line
5-FU + liposomal irinotecal	5-FU: 4.2 months Liposomal irinotecan: 4.9 months	6.2 months	1.3-2 month	5-FU + liposomal irinotecan standard second line

If no prior exposure to Gem (i.e. 1st line FOLFIRINOX):
gemcitabine-based chemotherapy in the 2nd-line setting



CONCLUSIONS: FOR THE PRACTICE

Resectable: adjuvant FOLFIRINOX in fit patients, Gem+capecitabine or Gem in the others

Metastatic:

- First line FOLFIRINOX for fit patients or Gem+Nab-paclitaxel or Gem in the others
- Second line: 5FU+ Nal-IRI or FOLFOX or gem-based if FOLFIRINOX 1st line

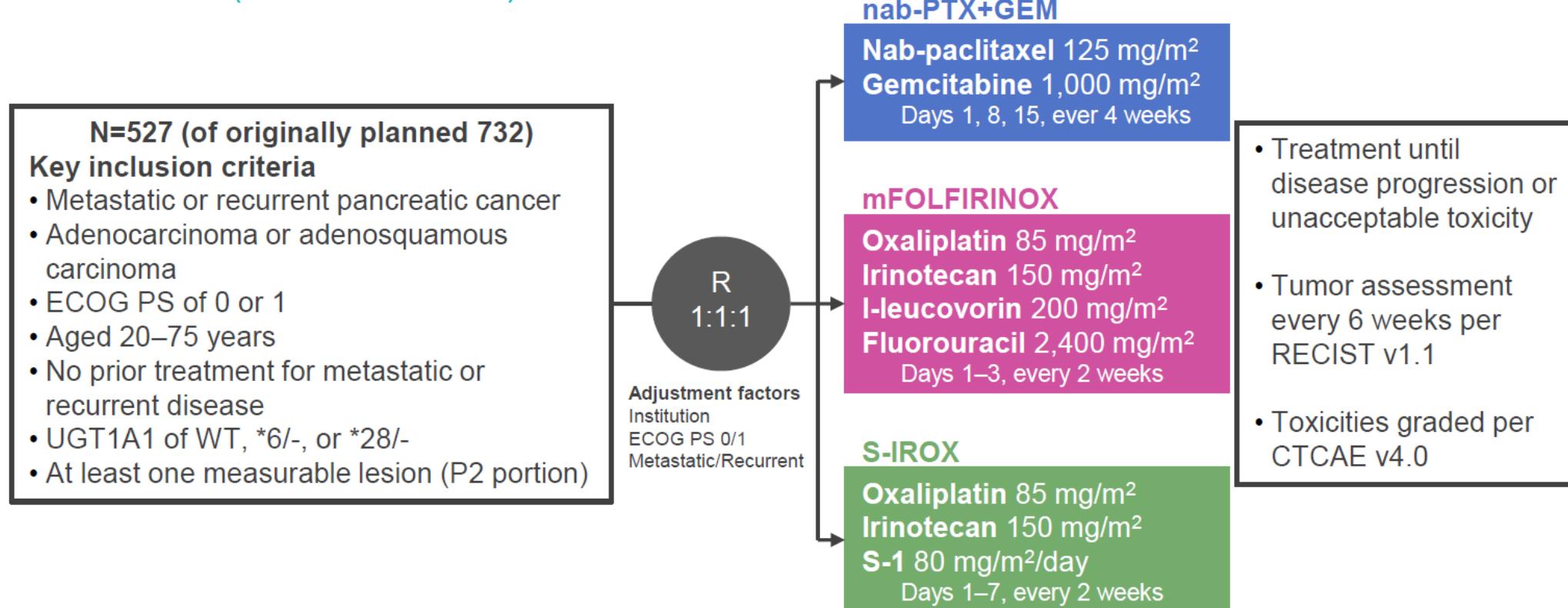
New approaches:

- BRCAness: olaparib in the near future for germline mutated mPC after platinum containing induction chemotherapy (FOLFIRINOX)
- IO agents in MSI high pancreatic cancer patients (<1%)

Clinical trials: always try to enrol your mPC patients in clinical trials +++

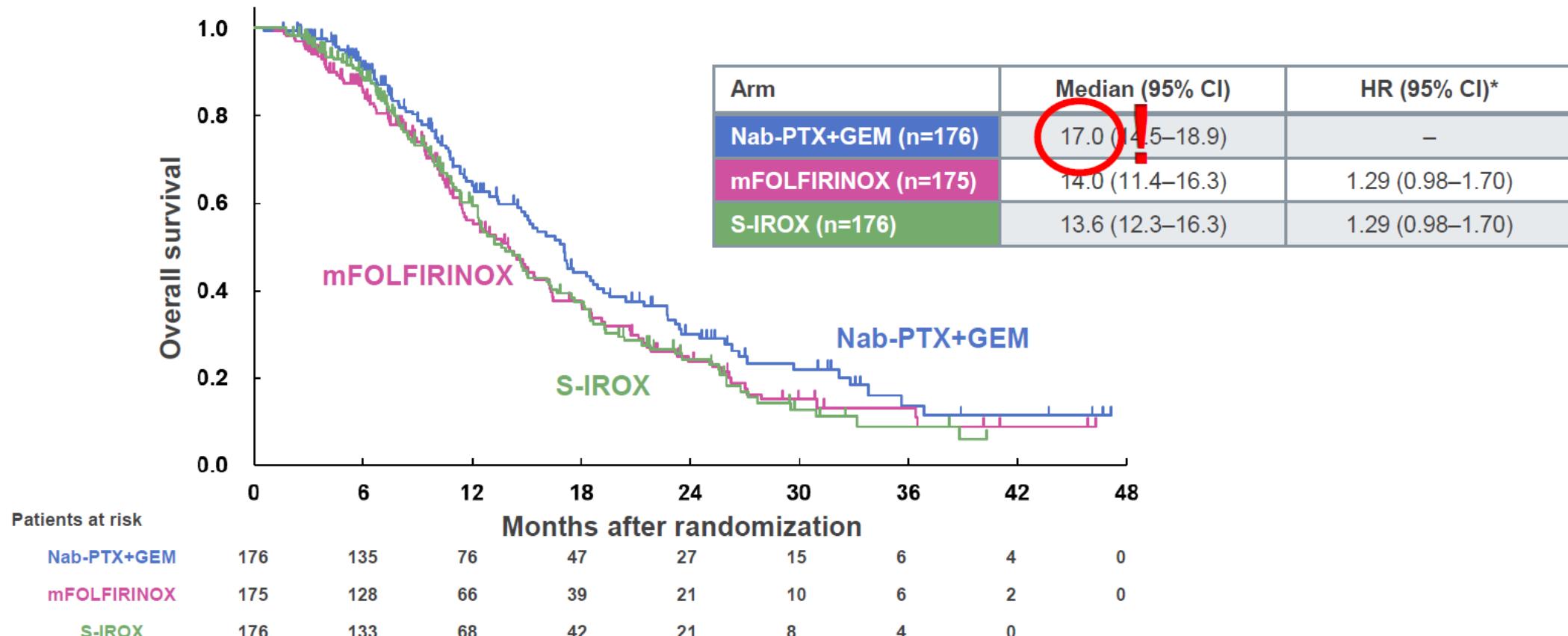
JCOG1611 (GENERATE): Trial Design

Ohba et al. (abstract 16160)



- Primary endpoint of phase 3 = OVERALL SURVIVAL

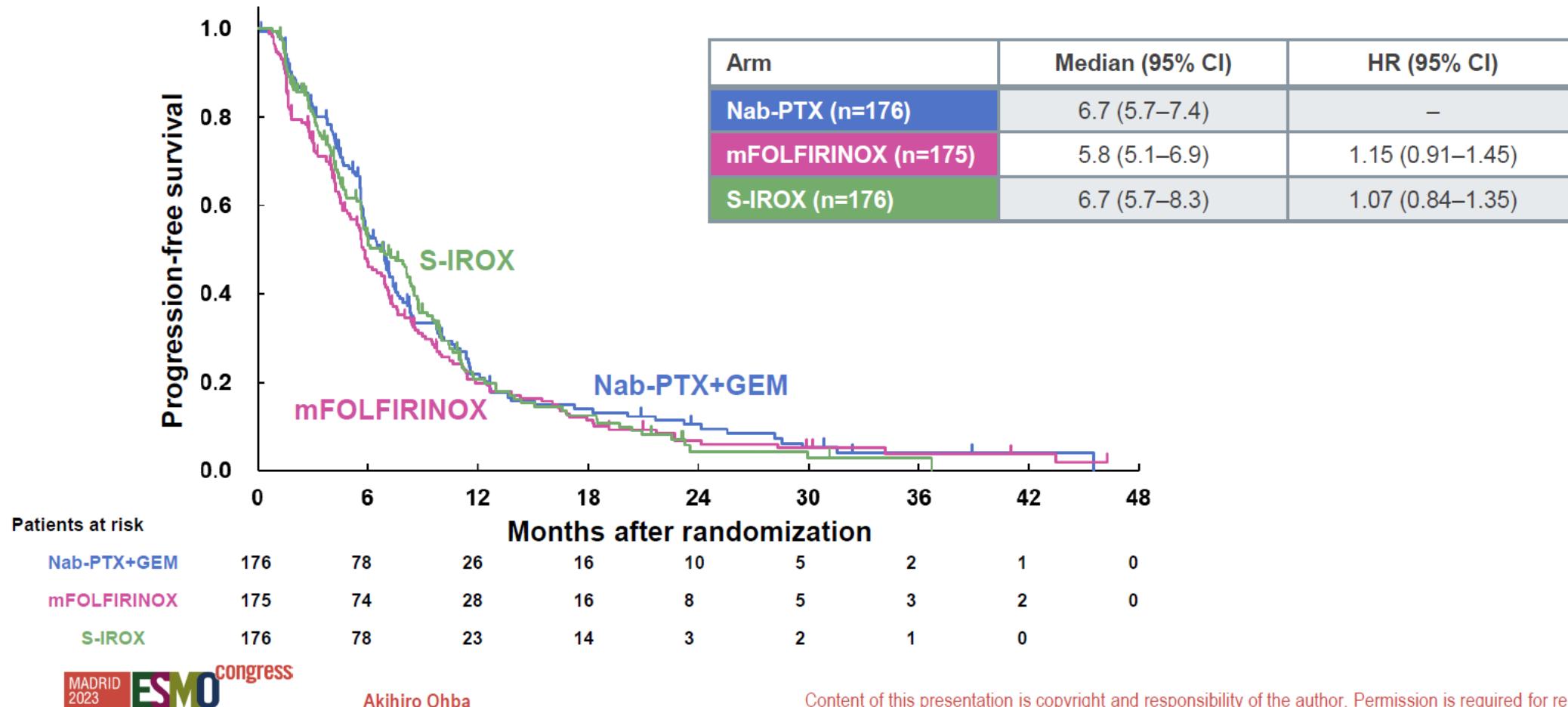
Overall Survival (Updated: May 2023)



* By stratified Cox regression model

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Progression-free Survival



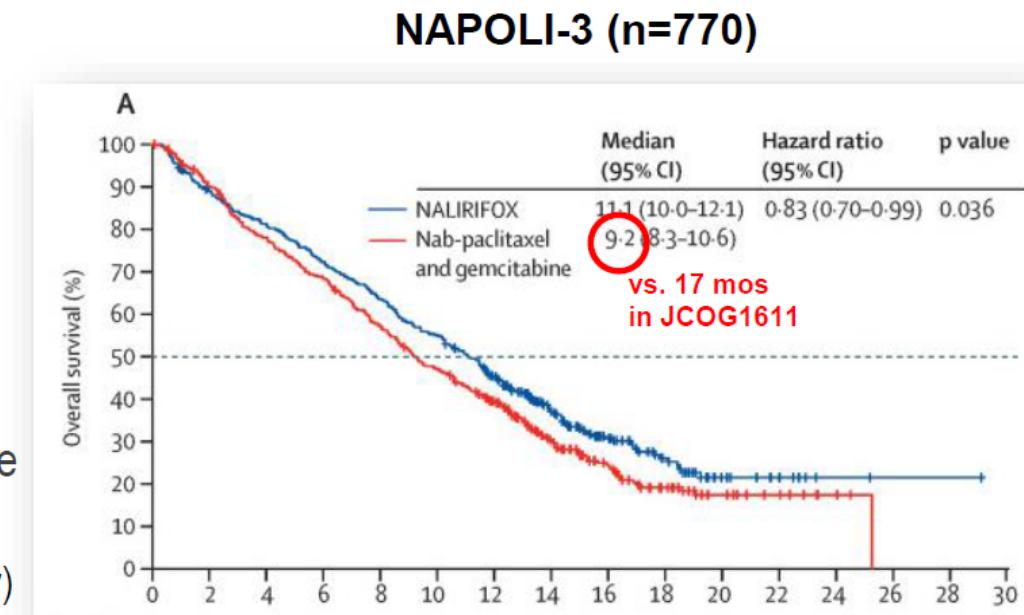
Other outcome measures

	Nab-PTX+GEM	mFOLFIRINOX	S-IROX
ORR (%)	35.4	32.4	42.4
Grade 3+ adverse events (%)			
Neutropenia	60.3	51.5	38.7
Febrile neutropenia	3.4	8.8	7.5
Anorexia	5.2	22.8	27.6
Diarrhea	1.1	8.8	23.0
Subseq rx (%)	59.7	63.4	62.5

JCOG1611 (GENERATE): Take-home messages

Ohba et al. (abstract 1616O)

- Trial terminated for futility after pre-planned interim analysis -- unlikely that mFOLFIRINOX or S-IROX would prove to be superior to gemcitabine/nab-paclitaxel
- Authors conclude that **gemcitabine/nab-paclitaxel** should represent the 1L standard of care for metastatic PDAC, given its numerical superiority in OS and overall better safety profile
- Results: surprising, esp in light of recently reported phase III NAPOLI-3 data! (Wainberg et al, *Lancet* 2023)
 - Is mFOLFIRINOX somehow inferior to NALIRIFOX? (unlikely)
 - Is the Japanese PDAC population unique in terms of chemosensitivity?



Mounting evidence in support of gemcitabine/nab-paclitaxel in pancreatic cancer?

Studies comparing gemcitabine/nab-paclitaxel to (m)FOLFIRINOX

Trial	Setting	n	Gem/nab-P vs (m)FOLFIRINOX		
			Med OS (mos)	Med PFS (mos)	ORR
JCOG 1611 (GENERATE)	Metastatic	527	17.0 vs 14.0	6.7 vs 5.8	35.4% vs 32.4%
SWOG1505 ¹	Perioperative rx for resectable disease	147	23.6 vs 23.2	(Med DFS): 14.2 vs 10.9	21% vs 9%
JCOG 1407 ²	Locally advanced	126	21.3 vs 23.0	9.4 vs 11.2	42.1% vs 30.9%

1. Ozaka et al, *Eur J Cancer* 2023. 2. Sohal et al, *JAMA Oncol* 2021.

JCOG1611 (GENERATE): Take-home messages

Ohba et al. (abstract 1616O)

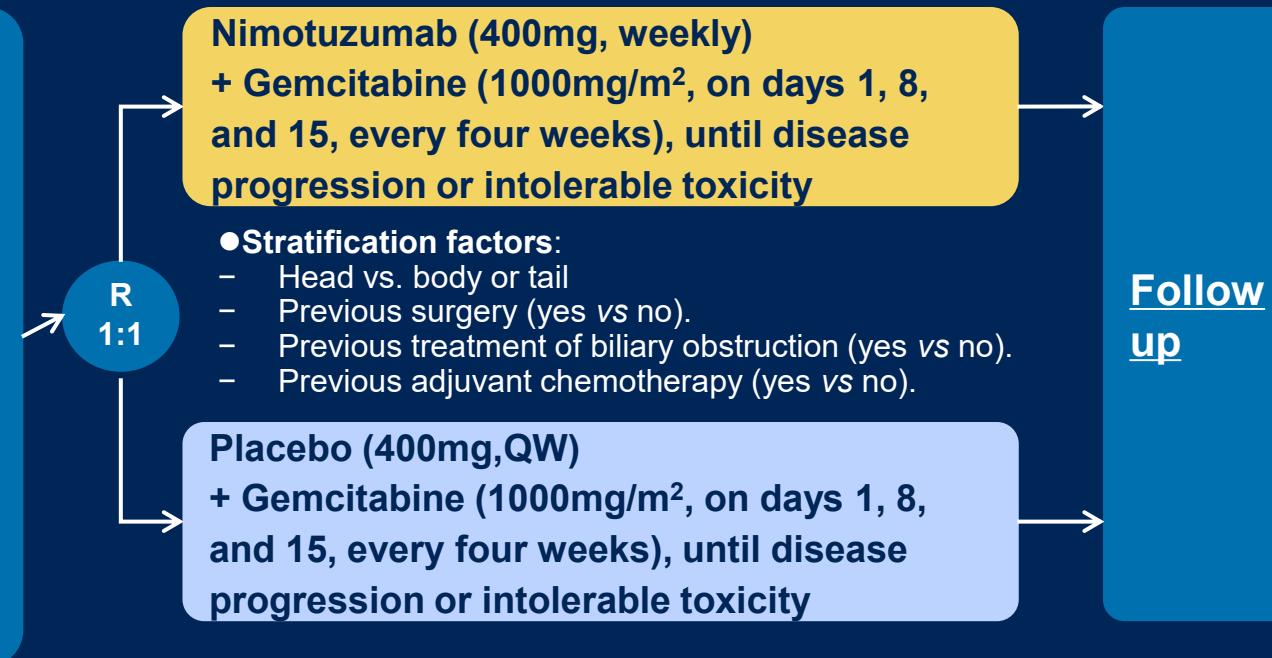
- The study investigators are to be commended for finally doing the head-to-head comparison we have long wanted to see: FOLFIRINOX vs gemcitabine/nab-paclitaxel for metastatic PDAC!
- These data lead to greater uncertainty re: the selection of front-line chemotherapy, both in clinical practice and as the backbone/reference standard in clinical trial design
 - For my U.S. practice, I will continue to use mFOLFIRINOX as the 1L treatment for fit patients with metastatic PDAC
 - At the same time, I have no qualms enrolling patients on clinical trials that use gemcitabine/nab-paclitaxel as a chemotherapy backbone and/or as a comparator SoC arm
- Predictive biomarkers/genetic signatures (e.g. HRD status) – and perhaps other clinical and demographic characteristics – may allow for more rational decision-making

NOTABLE Study design (NCT01074021)

- A Prospective, Randomized-controlled, Double-blinded, Multicenter Phase III Clinical trial, the Registered & Pivotal Study

Key eligibility criteria:

- Aged 18-75 years;
- Histologically confirmed locally advanced or metastatic pancreatic cancer;
- At least one measurable lesion evaluated by RECIST version 1.1;
- K-Ras wild-type;
- Karnofsky Performance Status ≥60.



- Primary endpoint: OS
- Secondary endpoints: PFS, TTP, ORR, DCR, CBR & Safety

A sample size of 79 patients, the study would have 80% power to detect a 5.95 months difference of mOS with Nimo (11.62 months) vs. Placebo (5.65 months) at a two-sided alpha level of 0.05. Finally it will be a sample size of 92 patients at 20% drop out.

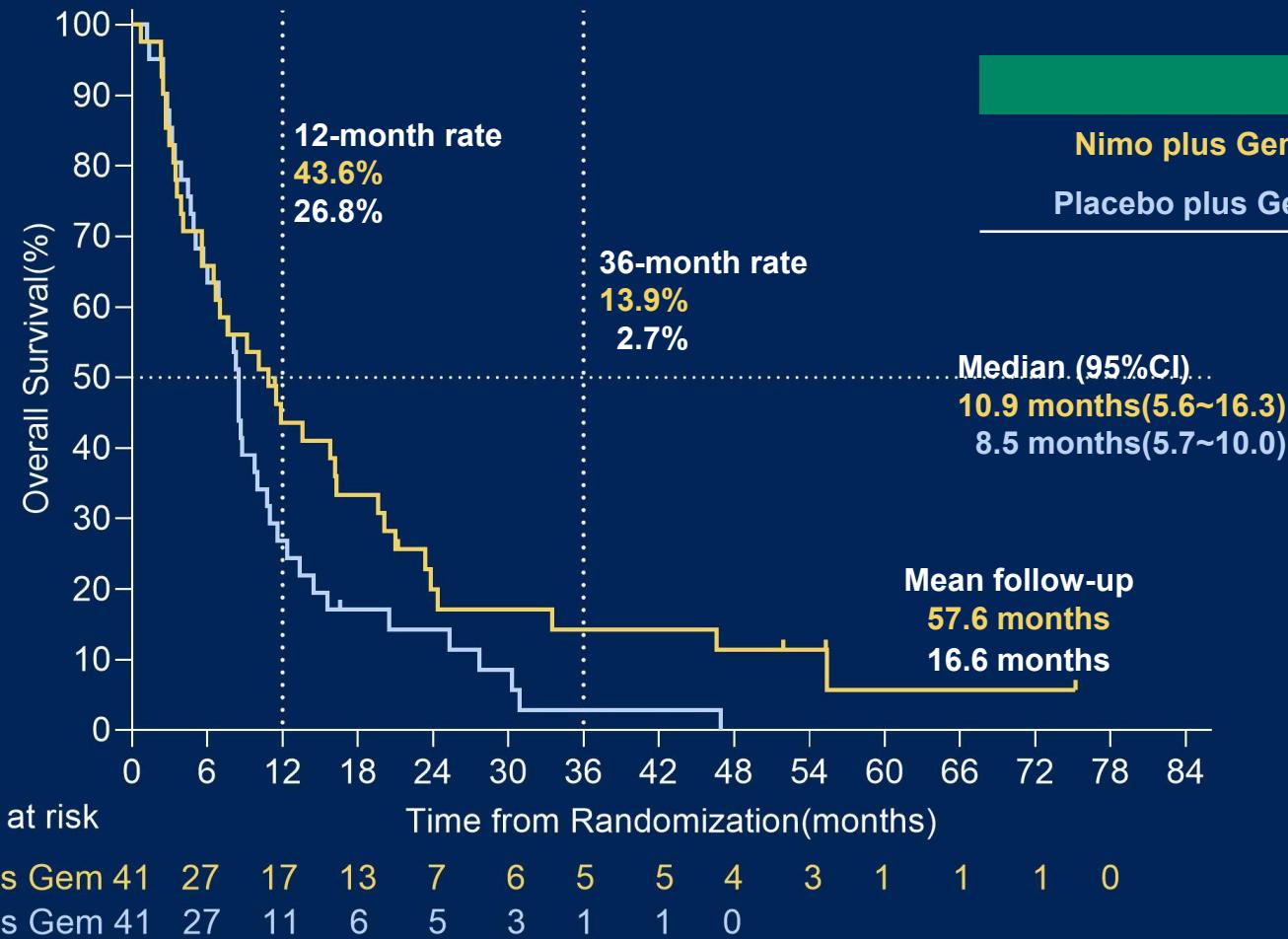
* OS, overall survival; PFS, progression-free survival; TTP, time to disease progression; ORR, objective response rate; DCR, disease control rate, CBR, clinical benefit response

NOTABLE study: Baseline characteristics

- Both groups were well balanced regarding to baseline demographic and clinical characteristics.

	Nimotuzumab plus Gem (n=41)	Placebo plus Gem (n=41)	P-value
Age (yr, Mean±SD)	55.0±11.22	57.5±8.89	0.265
Gender-male, n(%)	27(65.9)	24(58.5)	0.494
Previous surgery, n(%)	23(56.1)	23(56.1)	>0.999
Course of disease (<1 year), n(%)	34(82.9)	37(90.2)	0.331
Disease type, n(%)			0.787
locally advanced	9(22.0)	8(19.5)	
metastatic	32(78.0)	33(80.5)	
Tumors site, n(%)			0.949
Head	17(41.5)	17(41.5)	
Body	6(14.6)	7(17.1)	
Tail	18(43.9)	17(41.5)	
Previous adjuvant chemotherapy, n(%)	3(7.3)	3(7.3)	>0.999
Previous adjuvant radiotherapy, n(%)	1(2.4)	1(2.4)	>0.999
Previous treatment of biliary obstruction, n(%)	4(9.8)	4(9.8)	>0.999

Overall Survival (Full Analysis Set)



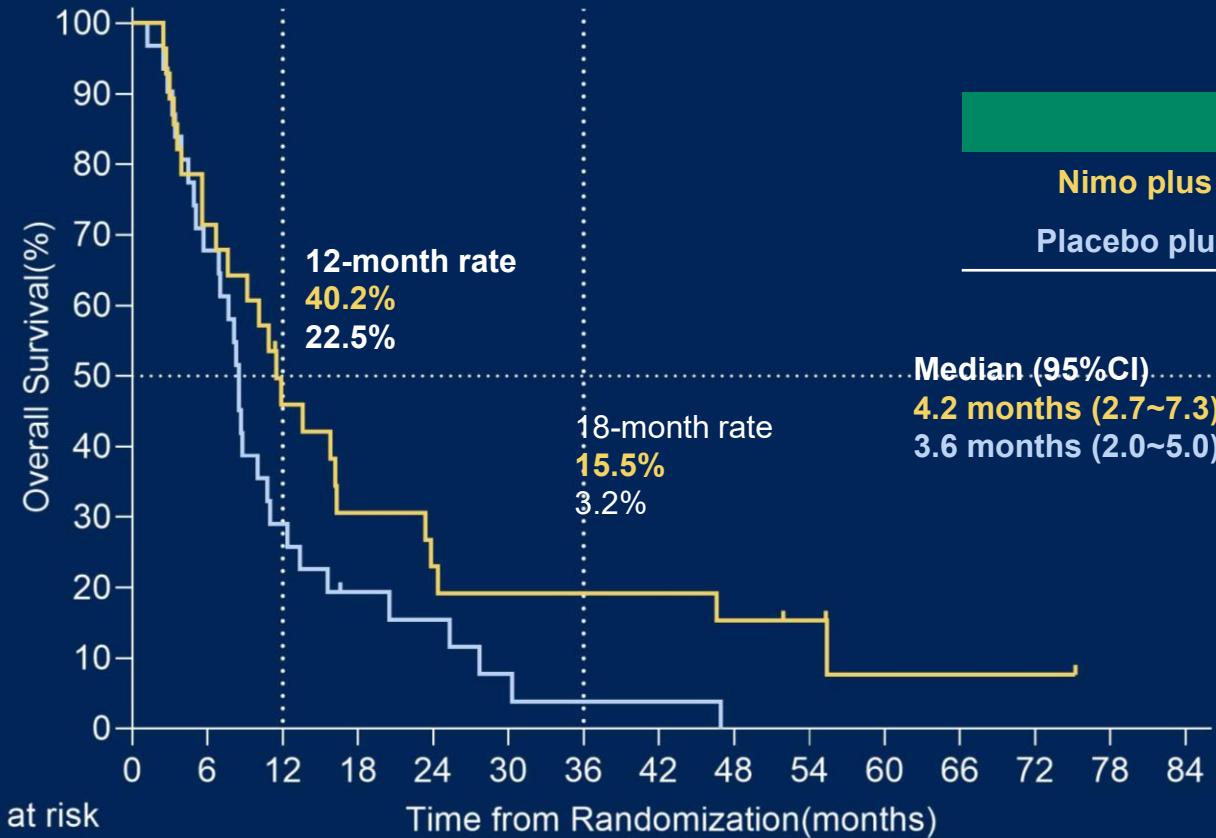
	mOS	HR(95%CI)	P
Nimo plus Gem	10.9 months	0.50 (0.06-0.94)	RMST-Log
Placebo plus Gem	8.5 months		<i>P=0.024</i>

- **Nimo plus Gem regime improved mOS compared with Placebo plus Gem, with a decrease of 50% mortality risk.**

Nimotuzumab plus Gem 41 27 17 13 7 6 5 5 4 3 1 1 0
Placebo plus Gem 41 27 11 6 5 3 1 1 0

* There was a violation of the proportional hazards (PH) because the two survival curves cross. Restricted Mean Survival Time (RMST) method (RMSTREG procedure, log-linear models) was used to estimate hazard risk. The adjusted HR with 95% CI was used as primary estimate of the difference between the arms, stratified by tumor location, previous surgery history, previous treatment of bile obstruction, previous adjuvant chemotherapy history at baseline. Data cut-off, Nov.23,2021.

Progression-Free Survival (Full Analysis Set)



	mPFS	HR(95%CI)	P
Nimo plus Gem	4.2 months	0.56	RMST-log
Placebo plus Gem	3.6 months	(0.12-0.99)	P=0.013

- Nimo plus Gem improved mPFS compared with placebo plus Gem, with a decrease of 44% disease progression risk.

Nimotuzumab plus Gem 28 20 12 8 6 5 5 4 3 1 1 0
Placebo plus Gem 31 21 9 5 4 2 1 0

*Restricted Mean Survival Time (RMST) method (RMSTREG procedure, log-linear models) was used to estimate hazard risk. The adjusted HR with 95% CI was used as primary estimate of the difference between the arms, stratified by tumor location, previous surgery history, previous treatment of bile obstruction, previous adjuvant chemotherapy history at baseline. Data cut-off, Nov.23,2021

Safety profile (1)

- The incidence of adverse drug reactions of Nimo plus Gem group was comparable to that of Placebo plus Gem group.

Adverse drug reactions	Nimo plus Gem	Placebo plus Gem	P value
N	45	45	
ADR n(%)	31(68.9)	29(64.4)	0.655
SADR n(%)	1(2.2)	2(4.4)	>0.999
Drug reduction or discontinued for ADR n(%)	4(8.9)	6(13.3)	0.502
Drug discontinued for ADR n(%)	2(4.4)	2(4.4)	>0.999
Death for ADR n(%)	0(0)	1(2.2)	>0.999
Withdrawal for ADR n(%)	2(4.4)	1(2.2)	>0.999

* Fisher's exact tests were used to compare the toxicities between treatment groups, when appropriate.

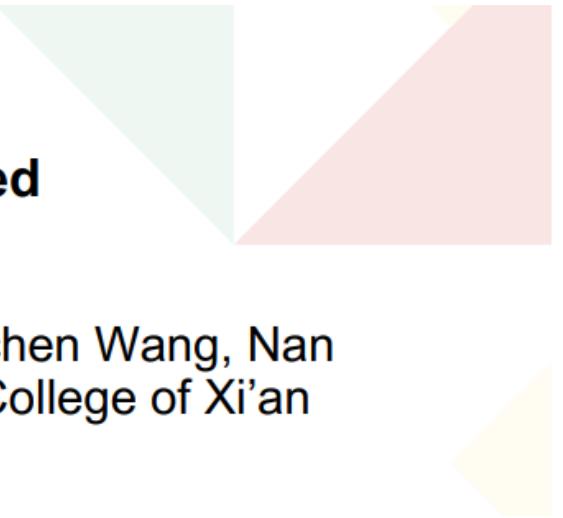
Safety profile (2)

- The common grade 3 adverse drug reactions (ADRs) were neutrophil counts reduction, platelet count reduction and etc.
- No grade 4-5 adverse drug reactions occurred.

ADRs(>10%) Preferred term	Nimo plus Gem (n=45)				Placebo plus Gem (n=45)			
	Grade 1	Grade 2	Grade 3	Total	Grade 1	Grade 2	Grade 3	Total
Neutrophil count reduction n(%)	9(20.0)	9(20.0)	4(8.9)	12(26.7)	9(20.0)	8(17.8)	3(6.7)	11(24.4)
Platelet count reduction n(%)	9(20.0)	4(8.9)	3(6.7)	10(22.2)	8(17.8)	5(11.1)	4(8.9)	9(20.0)
AST increased n(%)	9(20.0)	0	0	9(20.0)	8(17.8)	1(2.2)	0	9(20.0)
ALT increased n(%)	6(13.3)	0	0	6(13.3)	9(20.0)	2(4.4)	0	10(22.2)
Leukocyte count reduction n(%)	5(11.1)	9(20.0)	5(11.1)	12(26.7)	7(15.6)	7(15.6)	4(8.9)	12(26.7)
Anemia n(%)	5(11.1)	5(11.1)	1(2.2)	7(15.6)	9(20.0)	3(6.7)	1(2.2)	10(22.2)
Rash n(%)	4(8.9)	2(4.4)	0	6(13.3)	3(6.7)	1(2.2)	1(2.2)	4(8.9)
Fatigue n(%)	3(6.7)	3(6.7)	2(4.4)	5(11.1)	5(11.1)	2(4.4)	1(2.2)	6(13.3)
Fever n(%)	3(6.7)	2(4.4)	1(2.2)	5(11.1)	2(4.4)	0	0	2(4.4)

Summary & Conclusions

- Nimotuzumab combined with gemcitabine increases OS and PFS in patients with K-Ras wild-type locally advanced or metastatic pancreatic cancer, with an obvious good safety profile.
- NOTABLE study showed a breakthrough in treatment of advanced pancreatic cancer.
- NOTABLE study lightened a new era of target treatment of enriched pancreatic cancer population based on biomarker.
- Addition of Nimotuzumab to current treatment regimen will provide benefit and great value to pancreatic cancer patients.



Retrospective Real-World Study of Nimotuzumab Combined with Chemotherapy for Advanced Pancreatic Cancer

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Background:

Existing treatment options including gemcitabine-based therapy and 5FU-based chemotherapy have limited prognostic impact in advanced pancreatic cancer (APC): the median overall survival (mOS) was 6-11 months for 1st line therapy and 4-9 months for 2nd line therapy.

Nimotuzumab (nimo), anti-EGFR monoclonal antibody, had been shown to be more effective against APC in two previous studies, PCS07 (a phase II study in Germany) and NOTABLE study (a phase III study in China).

Although the NOTABLE study obtained an encouraging result in China, it focused on a narrow population, KRAS wild-type patients.

This study aimed to explore the efficacy and safety of nimo in the real-world population with APC.

Methods:

In this retrospective observational study, patients with APC were treated with nimo and followed up in a real-world clinical setting.

Demographic and clinical data of these patients were collected from electronic medical records of First Affiliated Hospital of Xi'an Jiaotong University from April 2018 to June 2022.

The primary efficacy endpoint was overall survival.

Results:

A total of 104 patients (median age was 60.5 years, range 34-84) treated with nimo and chemotherapy were analyzed.

Among them, 11 (10.6%) were in stage II (AJCC 8th edition), 23 (22.1%) were in stage III, and 70(67.3%) were in stage IV.

The treatment regimen included gemcitabine plus nab-paclitaxel (AG, 80.77%), gemcitabine plus S-1 (GS, 10.58%) and others.

The dosage of nimo was 200-400mg weekly, of which above 50% of patients received nimo 400 mg weekly.

About 66 (63.5%) patients received nimo as 1st line therapy and 38 (36.5%) patients as 2nd line therapy.

Up to July 5, 2022, the median follow-up time was 8.12 months and the mOS was not reached.

The 1-year and 2- year OS rate were 80.2% and 74.4%, respectively.

Further subgroup analysis showed that the mOS was also not reached in 1st line treatment of nimo (median follow-up time 8.77 months) as well as the 2nd line treatment of nimo (median follow-up time 7.62 months), showing a potential survival benefit. No grade 3 or above toxicities were observed.

Conclusions:

AG regimen was the most common therapy in clinical practice in China. The real-world study displayed the addition of nimo would prolong the survival for APC, with a good safety profile.

Thank you
