Actualités Cancers du Pancréas 2023

onco Bretagne

Journée scientifique
Oncologie Digestive

VENDREDI 17 NOVEMBRE 2023
Palais des Congrès – SAINT-BRIEUC

Dr Jérôme MARTIN-BABAU

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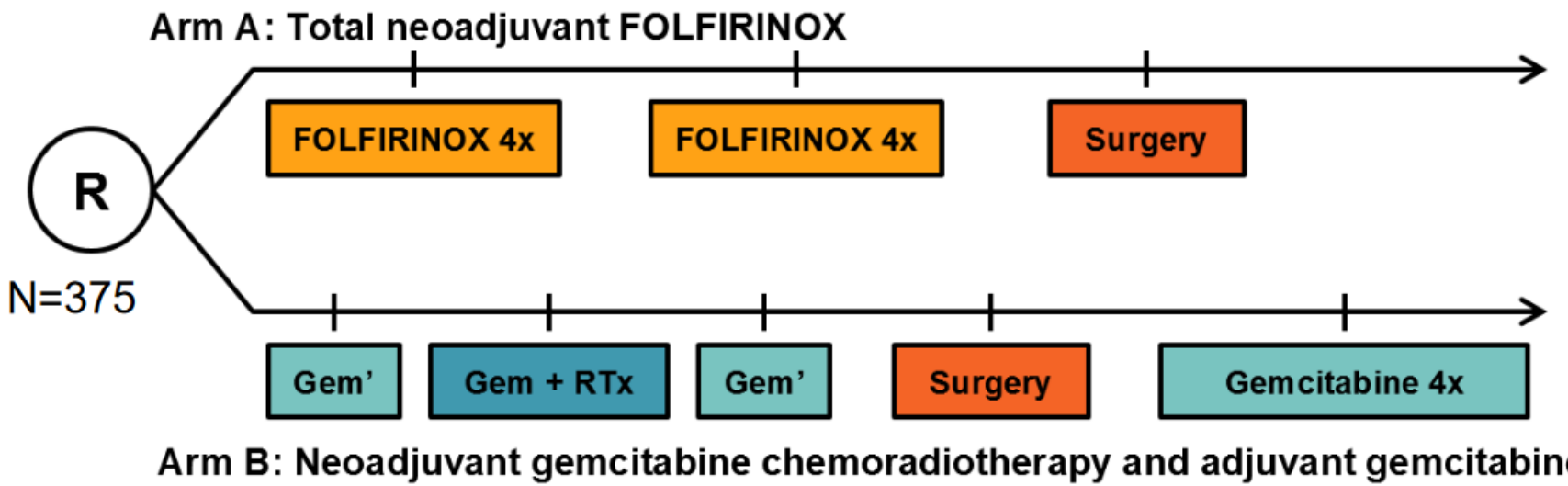
GROUPE MUTUALISTE

Résécables/localement avancé

PREOPANC-2 STUDY DESIGN

Koerkamp et al. (LBA83)

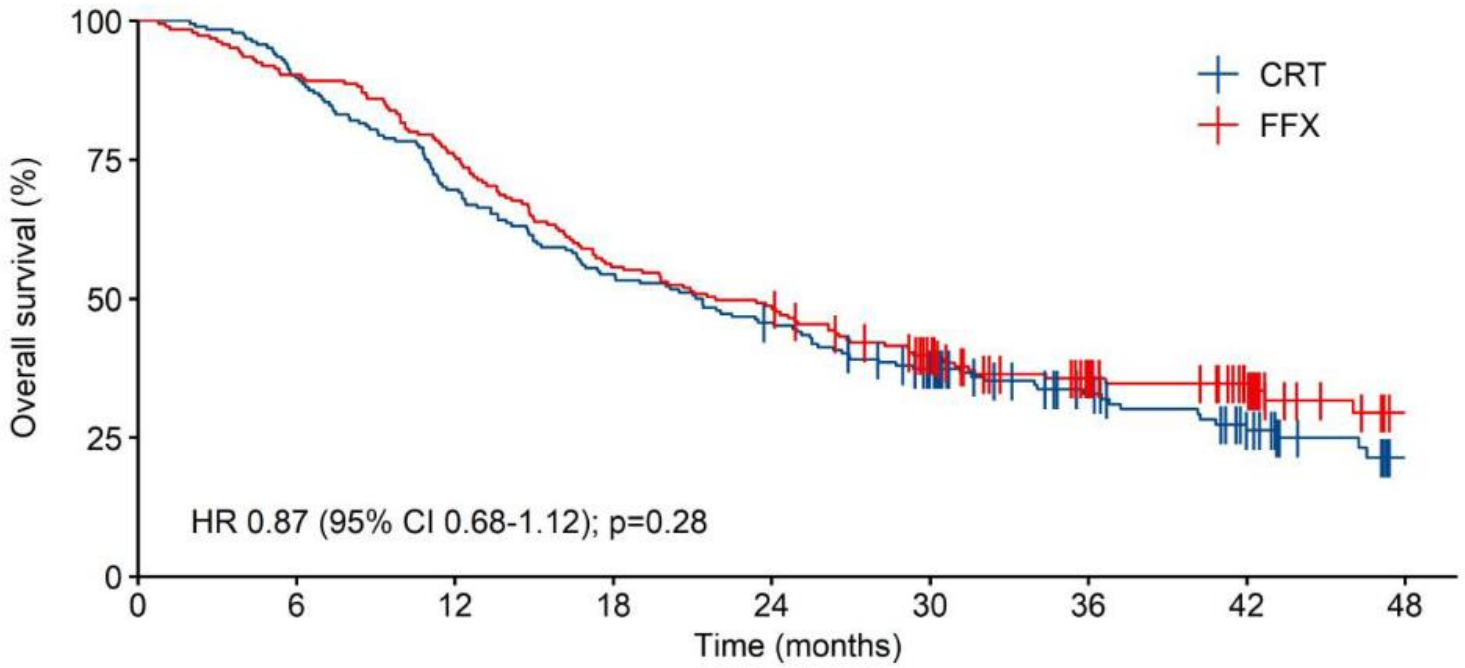
Comparison of 2 different neoadjuvant strategies for (borderline) resectable pancreatic cancer



1o endpoint: OS
2o endpoints: inc. R0 resection rate, path response

OVERALL SURVIVAL

Koerkamp et al (LBA 83)



Number at risk

CRT	184	165	128	100	83	61	39	24	7
FFX	185	167	140	103	90	64	43	28	9

Median OS	
FFX	21.9 (17.7-27.0)
CRT	21.3 (16.8-25.5)

1-year OS	
FFX	75.7%
CRT	69.6%

2-year OS	
FFX	48.6%
CRT	45.7%

3-year OS	
FFX	35.6%
CRT	32.8%

DPCG
Dutch Pancreatic Cancer Group

STUDY TREATMENT

	FOLFIRINOX	GEM-CRT	P-value
Completed neoadjuv rx	62%	88%	<0.001
>=4 cycles	81%	-	
Resection rate	77%	75%	0.7
R1 resection	39%	33%	0.28
ypN0	47%	58%	<0.01
ypN1 ypN2	33% 20%	35% 7%	
Pathologic complete response	11%	5%	0.26
Toxicity Gr 3-4 diarrhea Gr 3-4 febrile neutropenia	 23% 6%	 0% 1%	 <0.001 0.02

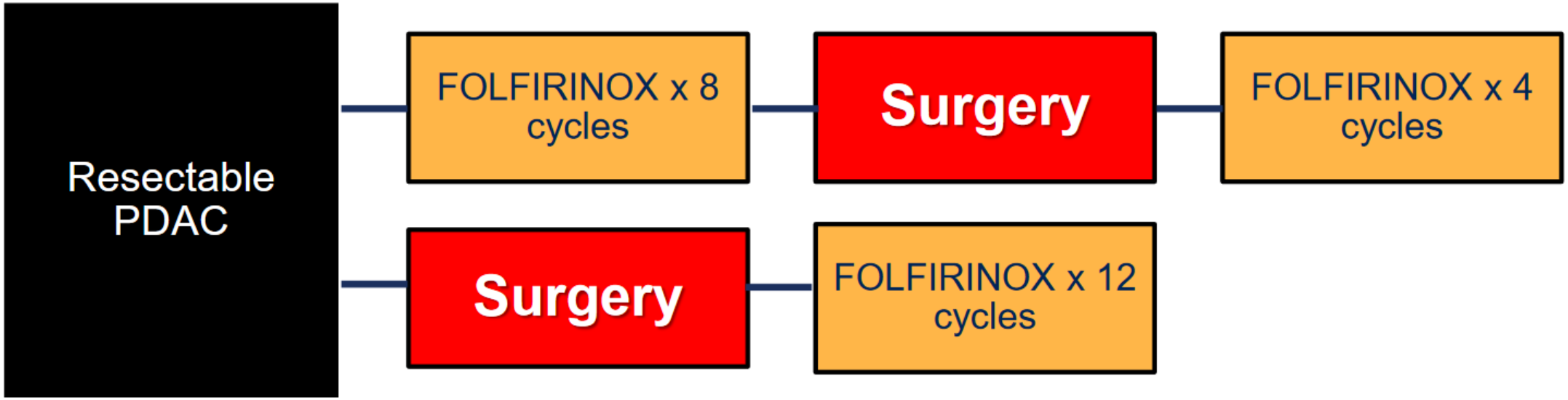
PREOPANC-2 : Conclusions

- Différences significatives entre les 2 schémas en matière de taux de complétion du traitement et des toxicités
- Taux de résection similaire
- Différences mineures au niveau pathologique (plus de ypN0 avec GemRx ; plus grand nb de R0 avec FOLFIRINOX..)
- **Malgré un effort majeur d'inclusions PAS DE DIFF de l'OS entre les 2 bras …!**

- Pour les lésions Borderline l'usage d'une NACT+/- Rx est commun mais la sélection et le type de traitement NA est encore discutable

- Pour les lésions résécables d'emblée : comme les 2 bras de cette étude comportaient une NACT, pour moi la question d'une NACT-RX vs chirurgie d'emblée pour patients résécables reste ouverte et non résolue…(même si je suis persuadé que cela soit justifié notamment CA19.9 élevé..)

Futurs essais à suivre pour questionner la place de la NACT chez les patients résécables



ClinicalTrials.gov NCT04340141 (Alliance), NCT04927780 (PREOPANC-3)

PRODIGE 29 - UCGI 26 - NEOPAN: Quality of life results of a Phase III randomised trial comparing chemotherapy with Folfirinox (FFX) or gemcitabine (gem) in locally advanced pancreatic carcinoma (LAPC)

M.P. Ducreux[1], R. Desgrippes[2], Y. Rinaldi[3], F. Di Fiore[4], R. Guimbaud[5], L. Evesque[6], J-B Bachet[7], P. Vanelslander[8], T. Lecomte[9], O. Capitain[10], A. Parzy[11], M. Bolliet[12], P-L Etienne[13], J. Forestier[14], F. El Hajbi[15], A-L Bignon[16], V. Lebrun-Ly[17], N. De Sousa Carvalho[18], M. Texier[19], O. Bouche[20]

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ESMO 2023, Madrid
1617P

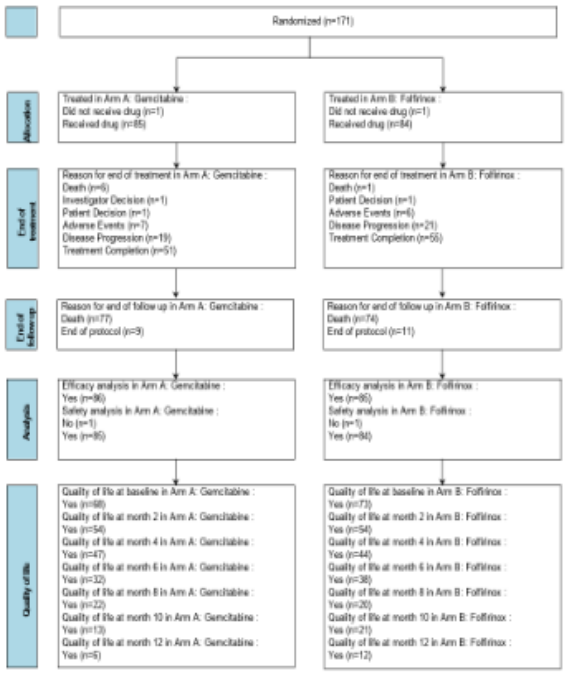
BACKGROUND

Pancreatic cancer (PC) is an aggressive malignancy and the 4th cause of all cancer deaths worldwide. More than 30% of patients with PC are unresectable because of the local extension with a median overall survival (OS) of less than one year.

The PRODIGE 24 study results showed that FFX is superior to gem in adjuvant therapy of resected PC, in terms of disease-free survival and OS. Though most clinician have shifted to FFX in unresectable LAPC, the superiority of FFX vs gem remains to be proven and the standard of care remains gem alone for unresectable LAPC.

The NEOPAN study addressed this question by comparing FFX to gem in unresectable locally advanced PC, in terms of Progression-Free Survival (primary objective) and Overall Survival (secondary objective).

CONSORT DIAGRAM



POPULATION DESCRIPTION

		Arm A: Gemcitabine N=86	Arm B: Folfirinox N=85	Total N=171
Sex	Male / Female	40 (47%) / 46 (53%)	45 (53%) / 40 (47%)	85 (50%) / 86 (50%)
Age (yr)	Mean	66	66	66
	Median	68	68	68
	Range	43 ; 81	42 ; 84	42 ; 84
ECOG PS 0 vs 1	0 / 1	38 (45%) / 47 (55%)	37 (44%) / 48 (56%)	75 (44%) / 95 (56%)
	Missing	1	0	1
Head of Pancreas	Yes / No	49 (57%) / 37 (43%)	44 (52%) / 41 (48%)	93 (54%) / 78 (46%)
Diagnosis	Histological / Cytological	40 (47%) / 46 (53%)	55 (65%) / 30 (35%)	95 (56%) / 76 (44%)
Histological type of disease	Adenocarcinoma / Adenosquamous carcinoma	85 (99%) / 1 (1%)	85 (100%) / 0	170 (99%) / 1 (1%)
cT	3 / 4 / X	1 (1%) / 85 (99%) / 0	2 (2%) / 82 (96%) / 1 (1%)	3 (2%) / 167 (98%) / 1 (1%)
cN	0 / 1 / X	38 (44%) / 16 (19%) / 32 (37%)	23 (27%) / 16 (19%) / 46 (54%)	61 (36%) / 32 (19%) / 78 (46%)
Type of vascular invasion	Superior mesenteric artery	45 (52%)	37 (44%)	82 (48%)
	Celiac trunk	42 (49%)	43 (51%)	85 (50%)
	Portal vein	18 (21%)	24 (28%)	42 (25%)
	Mesenteric vein	34 (40%)	34 (40%)	68 (40%)
Biliary bypass	Yes / No	24 (28%) / 62 (72%)	25 (29%) / 60 (71%)	49 (29%) / 122 (71%)
Digestive bypass	Yes / No	4 (5%) / 82 (95%)	0 (0%) / 85 (100%)	4 (2%) / 167 (98%)

RESULTS

Compliance

End of treatment reason	Gem Arm (N= 86)	FFX arm (N= 85)
End of protocol	51 (60%)	55 (65%)
Disease Progression	19 (22%)	21 (25%)
EI	7 (8%)	6 (7%)
Death	6 (7%)	1 (1%)
Investigator decision	1 (1%)	/
Patient decision	1 (1%)	1 (1%)

Subsequent Treatment

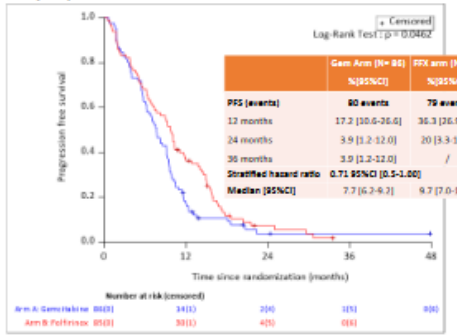
	Gem Arm (N= 86)	FFX arm (N= 85)
Before PD		
. Chemotherapy (CT)	28 (33%)	33 (39%)
. Radiotherapy (RT)	10 (12%)	15 (18%)
. CT-RT	10 (12%)	14 (16%)
. Surgery	4 (5%)	5 (6%)
After PD		
. CT	44 (51%)	56 (66%)
. RT	4 (5%)	7 (8%)
. CT-RT	2 (2%)	1 (1%)

In arm A, after progression with gem :
- 15 patients received FFX (17%)
- 11 patients received FOLFOX (13%)
- 6 patients received FOLFIRI (7%)

Safety—Patient with at least one AE

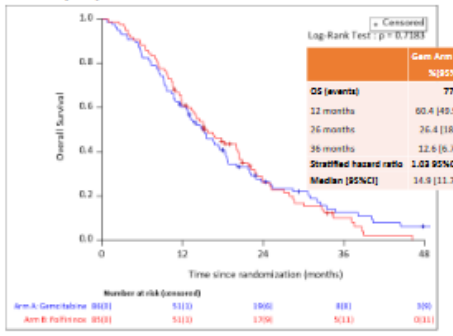
Grade	Gem Arm (N= 85) Nb of patient (%)	FFX arm (N= 84) Nb of patient (%)
1	85 (100%)	82 (98%)
2	81 (95%)	81 (96%)
3	60 (71%)	72 (86%)
4	19 (22%)	17 (20%)
5	7 (8%)	1 (1%)

PFS (ITT)



	Gem Arm (N= 86) %[95%CI]	FFX arm (N= 85) %[95%CI]
PFS (events)	80 events	79 events
12 months	17.2 [10.6-26.0]	36.3 [26.9-47]
24 months	3.9 [1.2-12.0]	20 [3.3-15.7]
36 months	3.9 [1.2-12.0]	/
Stratified hazard ratio	0.71 95%CI [0.5-1.00]	
Median [95%CI]	7.7 [6.2-9.2]	9.7 [7.0-11.7]

OS (ITT)



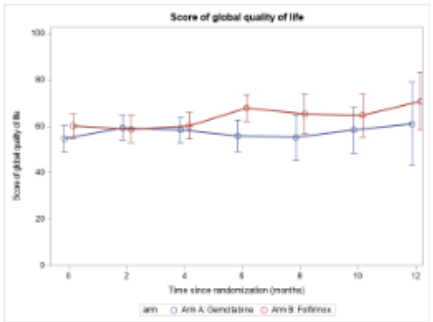
	Gem Arm (N= 86) %[95%CI]	FFX arm (N= 85) %[95%CI]
OS (events)	77	74
12 months	60.4 [49.9-70.1]	61.1 [50.4-70.7]
26 months	26.4 [18-37.1]	26.0 [17.4-37.1]
36 months	12.6 [6.7-22.4]	10.2 [4.9-20.0]
Stratified hazard ratio	1.03 95%CI [0.73-1.46]	
Median [95%CI]	14.9 [11.7-18.13]	15.7 [6.9-20.0]

Safety—Toxicities

AE (% of patient)	Gem Arm (N= 85)				FFX arm (N= 84)			
	G1	G2	G3	G4	G1	G2	G3	G4
Nausea	20%	20%	5%	/	37%	35%	12%	/
Vomiting	21%	12%	5%	/	20%	21%	10%	1%
Anemia	40%	44%	5%	/	51%	21%	12%	/
Neutropenia	11%	16%	22%	11%	12%	21%	12%	1%
Febril neutropenia	1%	/	1%	/	/	1%	2%	/
Thrombopenia	45%	16%	5%	/	55%	10%	5%	1%
Fatigue	38%	47%	5%	/	26%	35%	18%	/
Fièvre	16%	4%	2%	/	10%	5%	2%	/
Diarrhea	31%	12%	4%	/	43%	19%	14%	4%

Quality of Life (No parameter was statistically significant except for diarrhea and dyspnea which was at the limit of significativty)

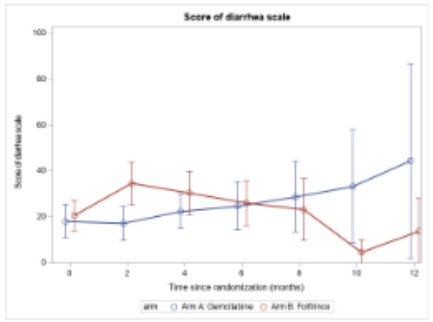
Global Health Status



Time (in months)	Gem Arm (N= 86) %[95%CI]	FFX arm (N= 85) %[95%CI]
3 months	80.5 [68.4-88.8]	71.5 [58.5 ; 81.7]
6 months	58.5 [44.3-71.3]	49.7 [36.6 ; 62.8]
12 months	37.1 [22.6-54.2]	44.2 [31.1 ; 58.2]

p=0.73

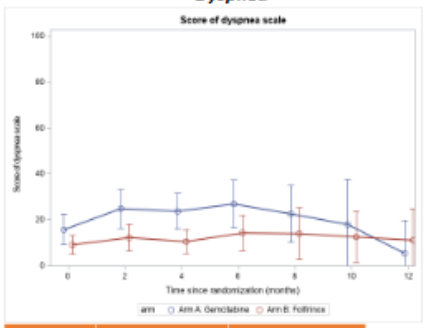
Diarrhea



Time (in months)	Gem Arm (N= 86) %[95%CI]	FFX arm (N= 85) %[95%CI]
3 months	89.3 [78.5 ; 95]	50.4 [37.6 ; 63.2]
6 months	63.2 [48.3 ; 76]	37.8 [25.9 ; 51.5]
12 months	37.1 [21.2 ; 56.3]	20.1 [10.3 ; 35.6]

p=0.002

Dyspnea



Time (in months)	Gem Arm (N= 86) %[95%CI]	FFX arm (N= 85) %[95%CI]
3 months	72.8 [59.8 ; 82.8]	82.6 [70.8 ; 90.3]
6 months	52.1 [38.2 ; 65.8]	70.8 [57.6 ; 81.2]
12 months	39.3 [25.4 ; 55.1]	56.9 [41.3 ; 71.3]

p=0.052

Conclusion

- NEOPAN is one of the largest phase III trials involving LAPC.
- The trial met its primary endpoint: PFS was significantly longer with FFX
- FFX was well tolerated, but no significant difference in OS was observed
- Quality of life was not adversely affected by FFX excepted for diarrhea which was increased with FFX

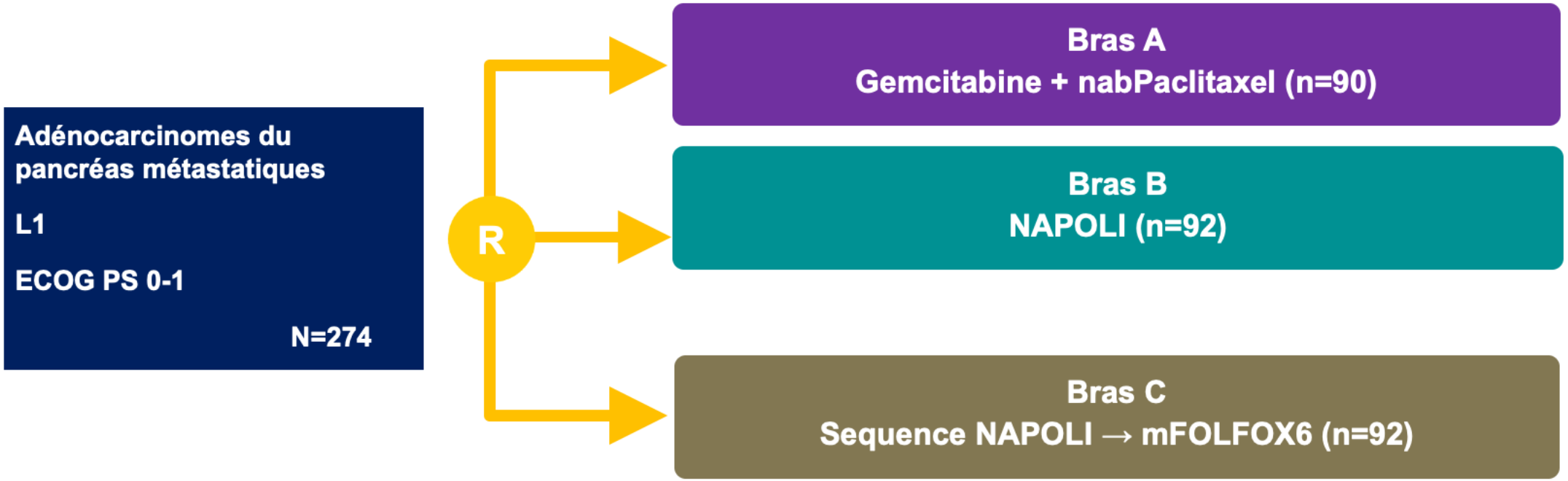
Acknowledgment

We thank the patients and their families for participating in the study. We are also indebted to all the participating centers.

For additional information, please contact Prof. Michel DUCREUX , study coordinator: Michel.DUCREUX@gustaveroussy.fr

Métastatiques

FOOTPATH : Irinotécan liposomal + 5FU-acide folinique (NAPOLI) vs NAPOLI séquentiel et mFOLFOX6 vs gem+nabP en L1 cancers du pancréas métastatique



- **Objectif principal** : Survie sans progression
- **Objectifs secondaires** : Survie globale, Taux de réponse tumorale & contrôle de la maladie, Durée de traitement, Toxicité

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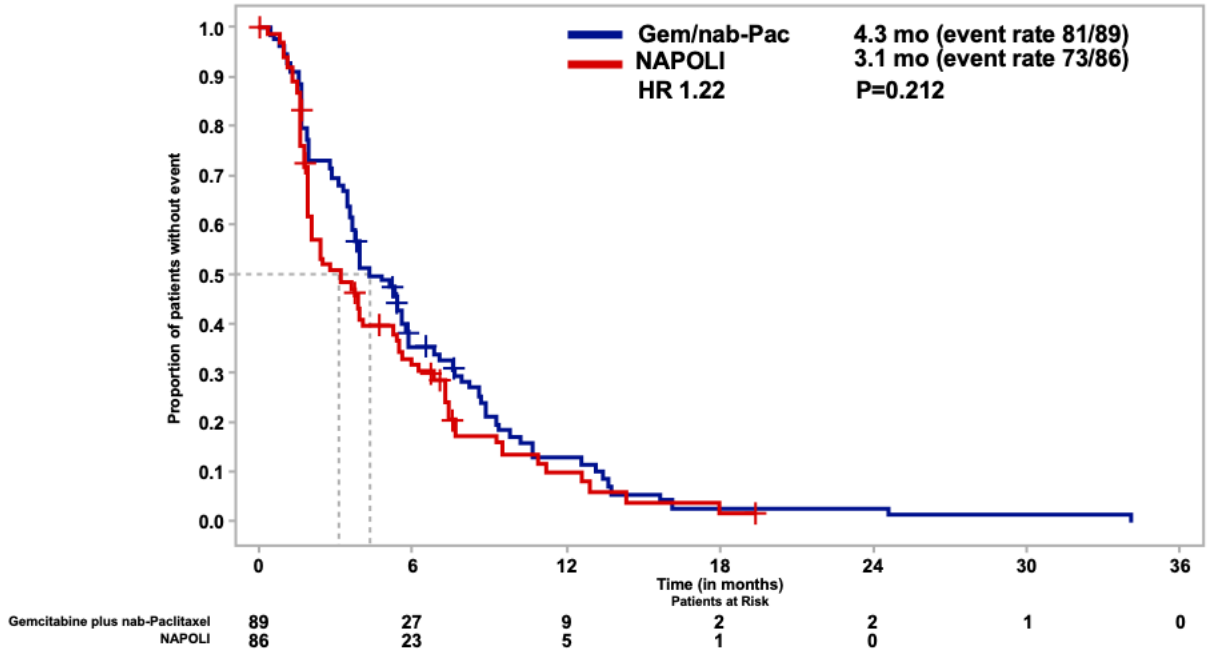
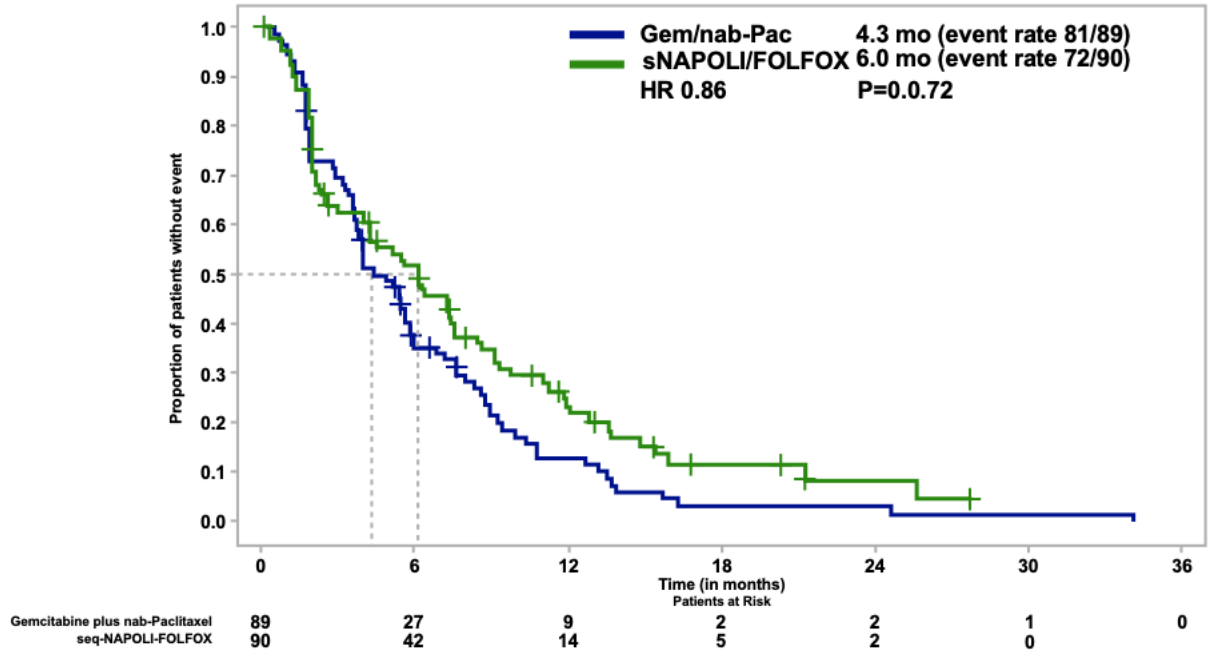
FOOTPATH : Survie sans progression





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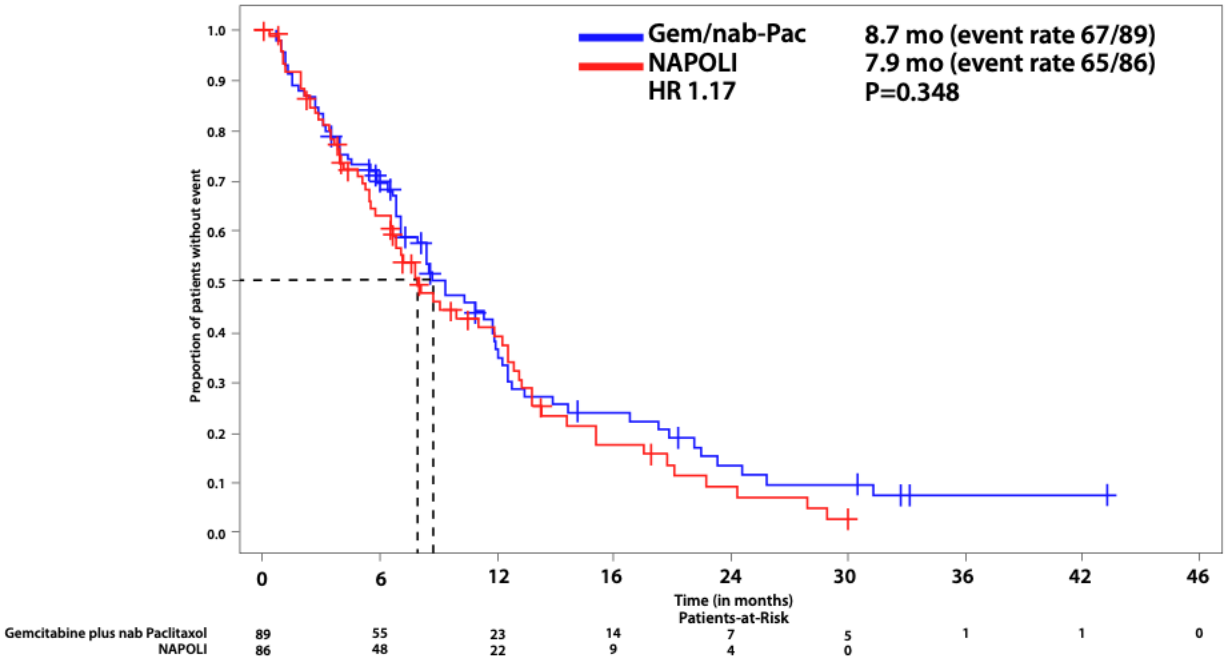
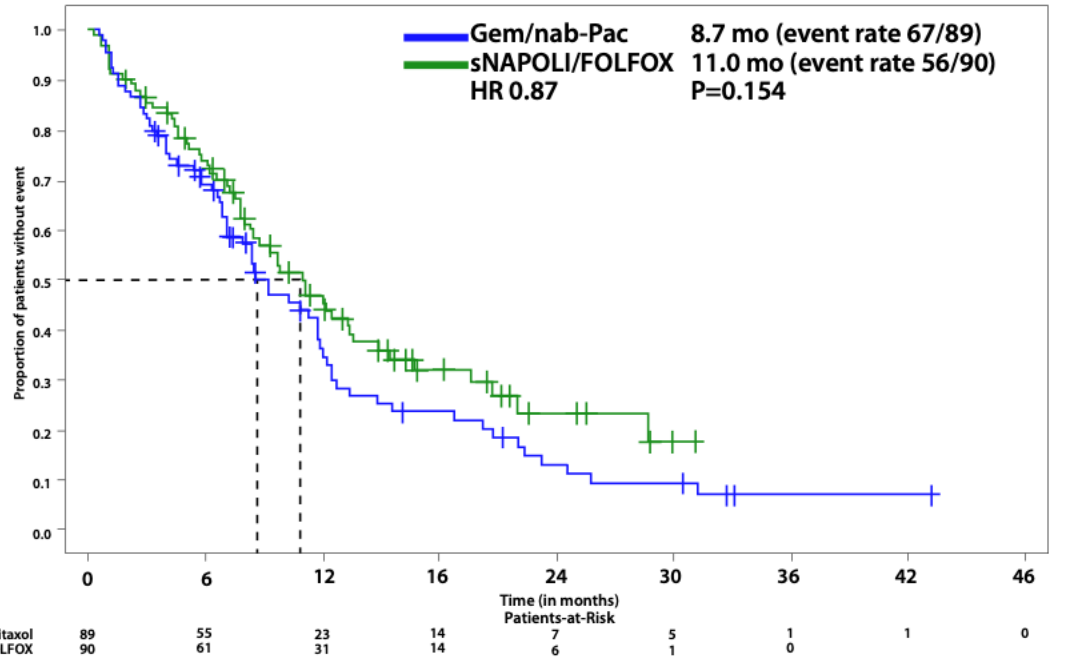
FOOTPATH : Survie globale





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FOOTPATH : Conclusions

- Cette étude n'a pas démontré la supériorité de NAPOLI ni de la séquence NAPOLI/mFOLFOX6 par rapport au traitement standard par gem/nab-pac
- Le standard de première ligne est le FOLFIRINOX pour les patients en bon état général
- Ces données actuelles soutiennent l'hypothèse que l'alternance NAPOLI/mFOLFOX6 pourrait être aussi efficace en termes de SG, mais moins toxique, que le mFOLFIRINOX
- Plusieurs essai en cours testent des stratégies séquentielles :
  - Prodige 61 Fungemax : (Gem/NabPac vs Naliri-5FU vs Gem/NabPac - Naliri-5FU)
  - Gabrinox 2 (Gem/NabPac-FOLFIRINOX vs FOLFIRINOX)

NAPOLI 3 : Résultats à 18 mois du NALIRIFOX vs Gem-NabP en L1 pour mPDAC

- **ADK pancréatiques Métastatiques**
- **Metastases≥1**
- **Diag ≤ 6 semaines**
- **ECOG PS 0 ou 1**
- **L1**

N=770

R

NAL-IRI >50mg/m
5FU 2400 mg/
LV 400 mg/
Oxaliplatine 60 mg/
J1-15/28

Stratification : EGOG PS 0/1, Région, Métastases hépatiques

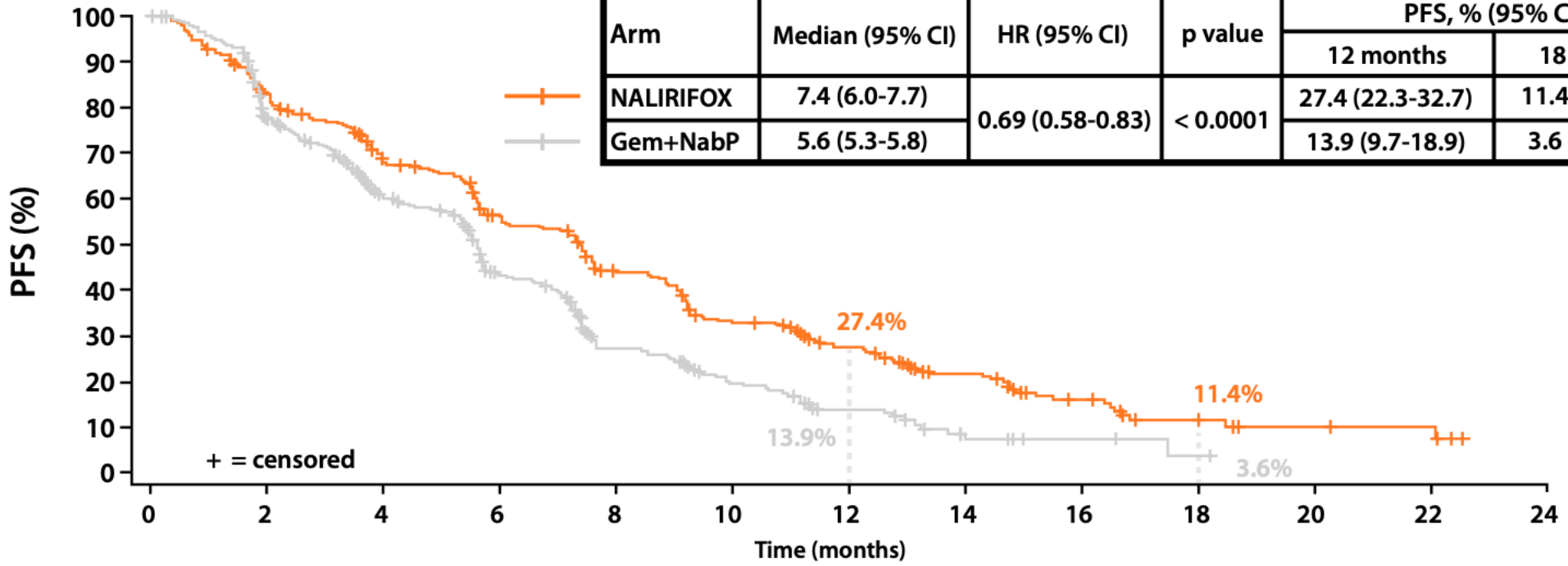
GEM 1000mg/m² + NabP 125 mg/m²
J1-8-15/28

- **Objectif principal** : Survie globale (SG)
- **Objectifs secondaires** : Survie sans progression & taux de réponse/ investigateurs, tolérance

O'Reilly E et al, ASCO 2023 Abstract 4006

NAPOLI 3 : Survie sans progression (ITT/investigateurs)

Arm	Median (95% CI)	HR (95% CI)	p value	PFS, % (95% CI)	
				12 months	18 months
NALIRIFOX	7.4 (6.0-7.7)	0.69 (0.58-0.83)	< 0.0001	27.4 (22.3-32.7)	11.4 (7.1-16.9)
Gem+NabP	5.6 (5.3-5.8)			13.9 (9.7-18.9)	3.6 (0.5-12.3)



No. at risk:													
NALIRIFOX	383	271	210	164	122	87	61	39	20	9	5	4	0
Gem+NabP	387	267	182	112	60	38	19	6	3	1	0	0	0

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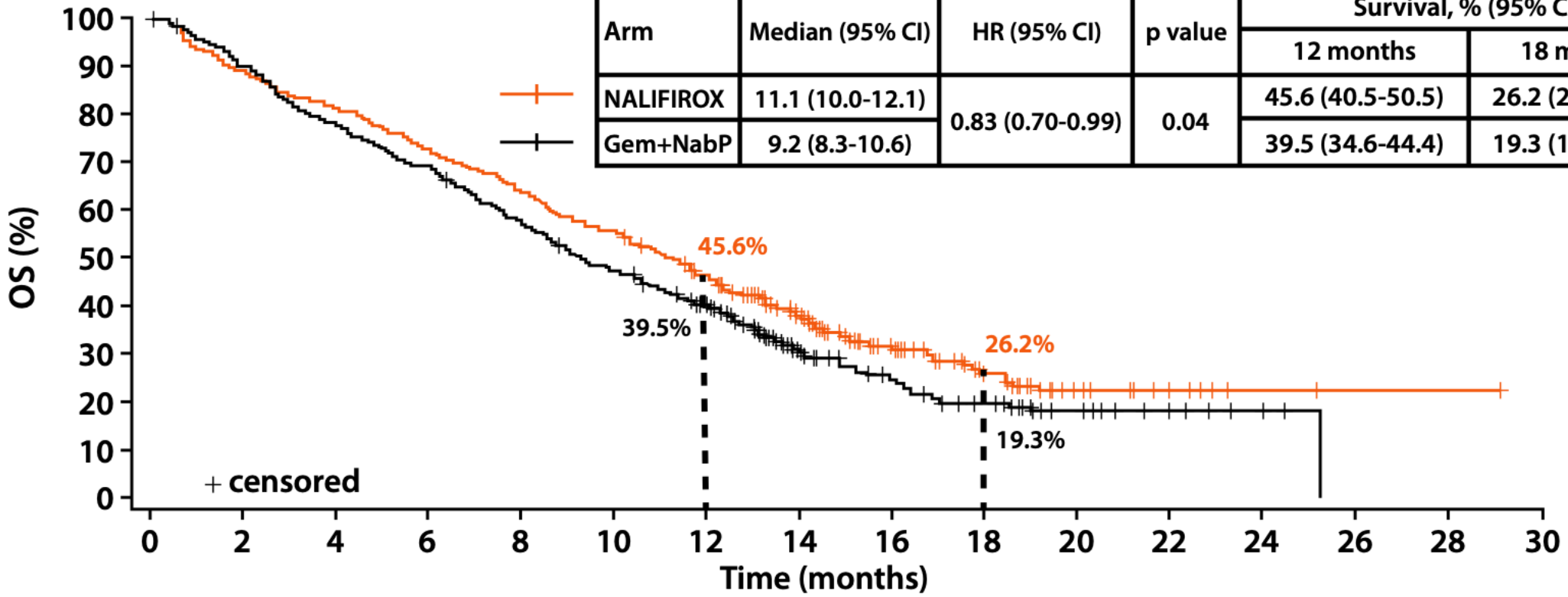
NAPOLI 3 : Survie globale (ITT)

Arm	Median (95% CI)	HR (95% CI)	p value	Survival, % (95% CI)	
				12 months	18 months
NALIFIROX	11.1 (10.0-12.1)	0.83 (0.70-0.99)	0.04	45.6 (40.5-50.5)	26.2 (20.9-31.7)
Gem+NabP	9.2 (8.3-10.6)			39.5 (34.6-44.4)	19.3 (14.8-24.2)



No. at risk:																
NALIRIFOX	383	337	308	274	241	209	162	98	59	32	13	7	2	1	1	0
Gem+NabP	387	345	298	261	218	179	140	80	50	28	15	10	3	0	0	0

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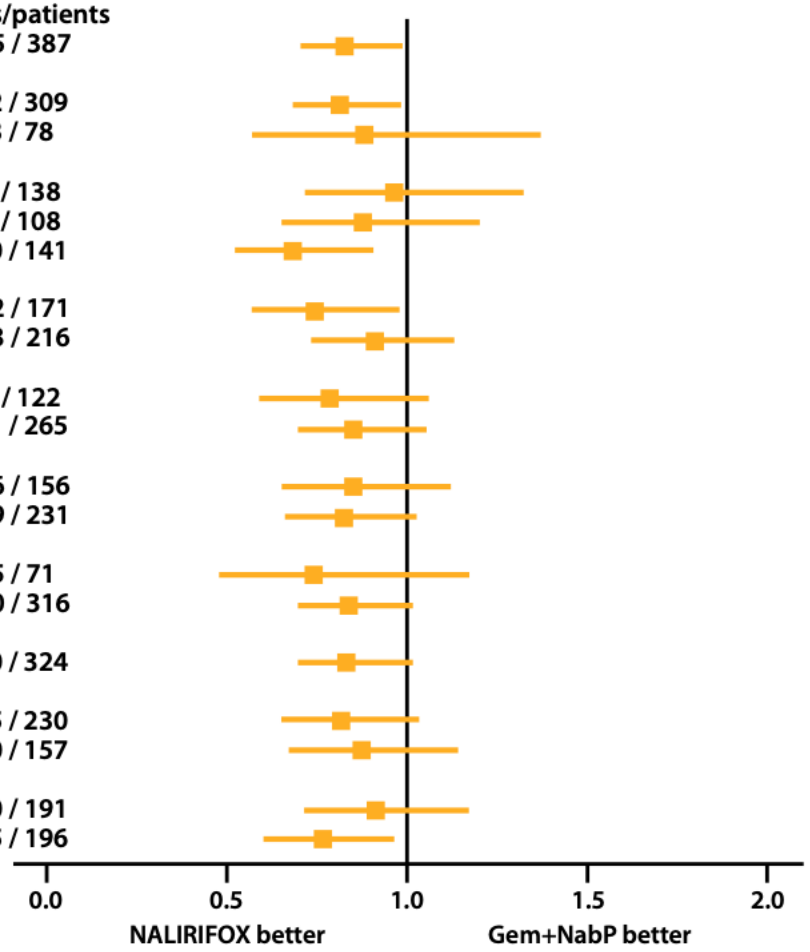
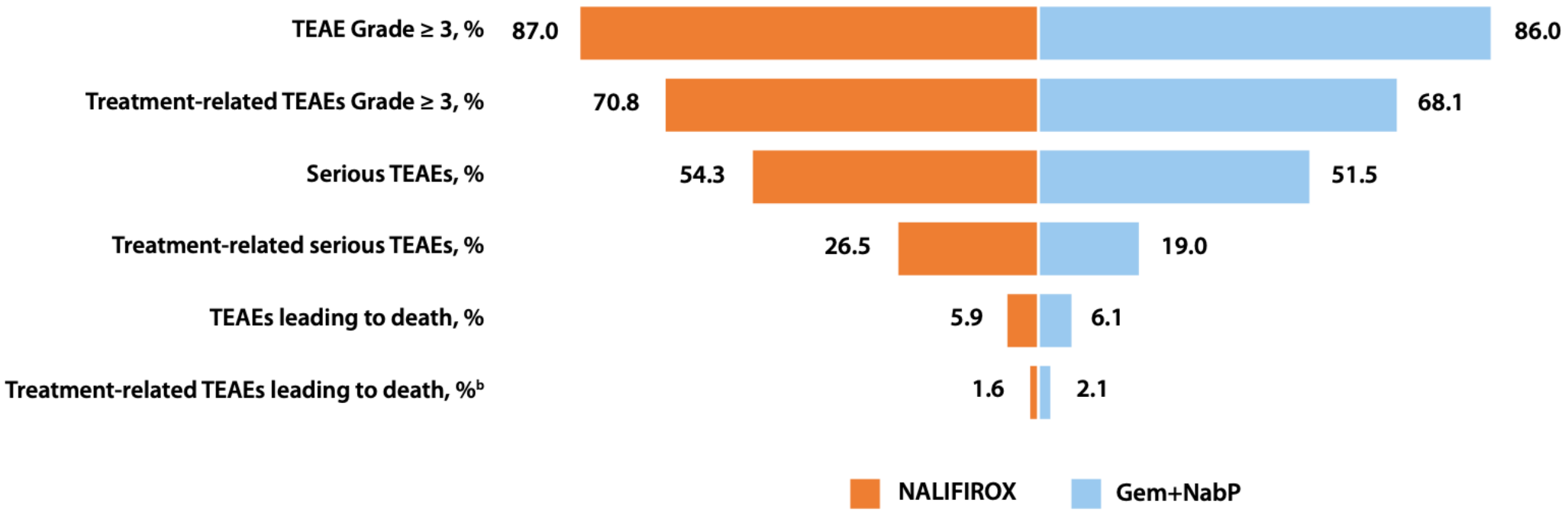
NAPOLI 3 : Survie globale /sous groupes (ITT)

Subgroup	NALIRIFOX, events/patients	Gem+NabP, events/patients	HR (95% CI)
Overall	259 / 383	285 / 387	0.83 (0.70, 0.99)
Presence of liver metastases at baseline			
Yes	220 / 309	242 / 309	0.82 (0.68, 0.98)
No	39 / 74	43 / 78	0.89 (0.57, 1.37)
Number of metastatic sites			
1	75 / 114	92 / 138	0.98 (0.72, 1.32)
2	87 / 120	83 / 108	0.89 (0.65, 1.20)
≥3	97 / 149	110 / 141	0.69 (0.52, 0.90)
Baseline ECOG PS			
0	97 / 168	112 / 171	0.75 (0.57, 0.98)
1	162 / 215	173 / 216	0.91 (0.73, 1.13)
Region			
North America	85 / 120	94 / 122	0.79 (0.59, 1.06)
Rest of the world	174 / 263	191 / 265	0.86 (0.70, 1.05)
Main pancreatic tumor location			
Head	97 / 147	116 / 156	0.86 (0.65, 1.12)
Other	162 / 236	169 / 231	0.83 (0.67, 1.02)
Baseline CA 19-9			
< 37 U/mL	34 / 60	45 / 71	0.75 (0.48, 1.17)
≥ 37 U/mL	223 / 321	240 / 316	0.84 (0.70, 1.01)
Race			
White	218 / 315	240 / 324	0.84 (0.70, 1.01)
Sex			
Male	139 / 204	175 / 230	0.82 (0.66, 1.02)
Female	120 / 179	110 / 157	0.88 (0.68, 1.14)
Age			
< 65 years	127 / 193	130 / 191	0.92 (0.72, 1.17)
≥ 65 years	132 / 190	155 / 196	0.77 (0.61, 0.97)



O'Reilly E et al, ASCO 2023 Abstract 4006

NAPOLI 3 : Profils de toxicités



Median (range) duration of treatment was 24.3 (0.4-100.9) weeks with NALIFIROX and 17.6 (0.7-81.7) weeks with Gem+NabP

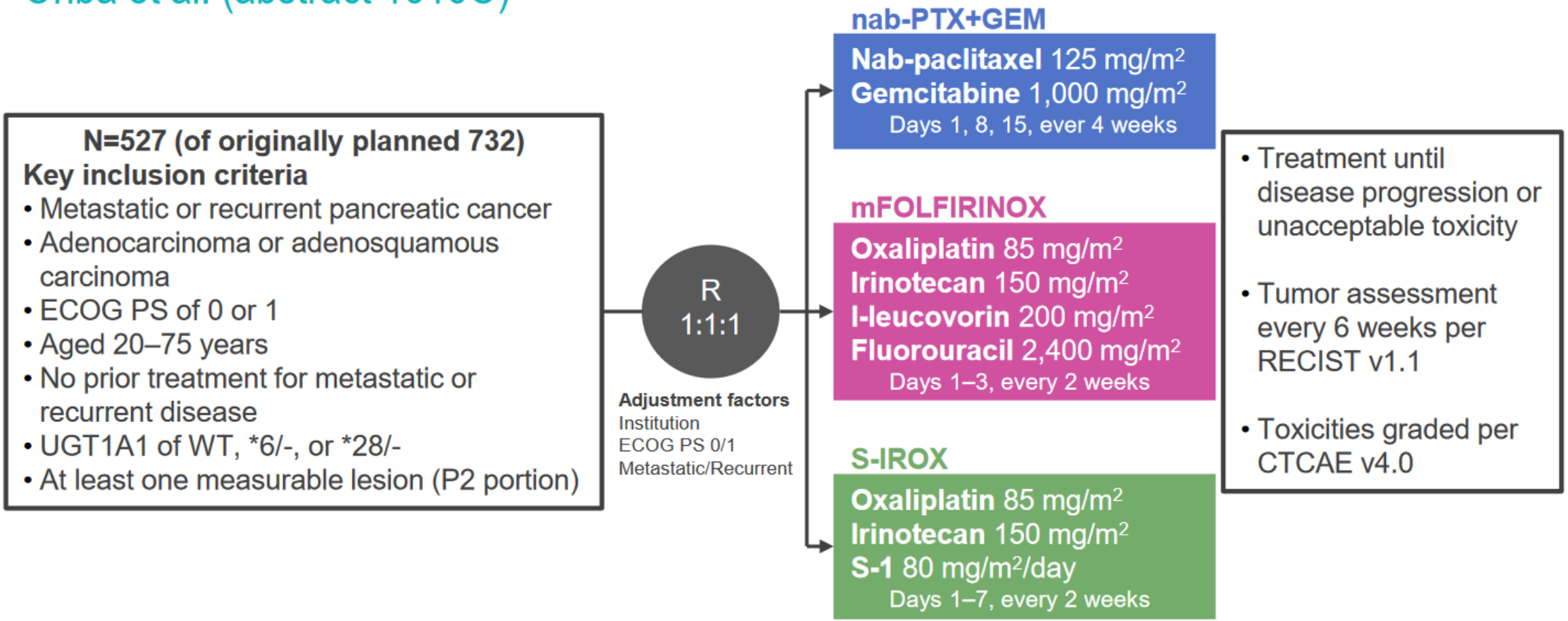
O'Reilly E et al, ASCO 2023 Abstract 4006

NAPOLI 3 : Conclusions

- Le traitement de L1 des patients atteints d'adénocarcinomes pancréatiques métastatiques par rapport au schéma gemNabP, NALIRIFOX a démontré une amélioration significative :
  - SG médiane 9,2 vs 11,1 mois ; HR 0,83 [IC95% 0,7045-0,9881] p-0,0355
  - SSP médiane 5,6 vs 7,4 mois ;HR 0,69 [IC95% 0,5786-0,8334] p<0,0001
- Tous les sous groupes de patients semblent en bénéficier
- Le profil de tolérance du NALIRIFOX était attendu
- Le régime NALIRIFOX s'ajoute aux traitements utilisables en première ligne métastatiques pour ces cancers
- Il faudrait pouvoir comparer ce nouveau régime au FOLFIRINOX

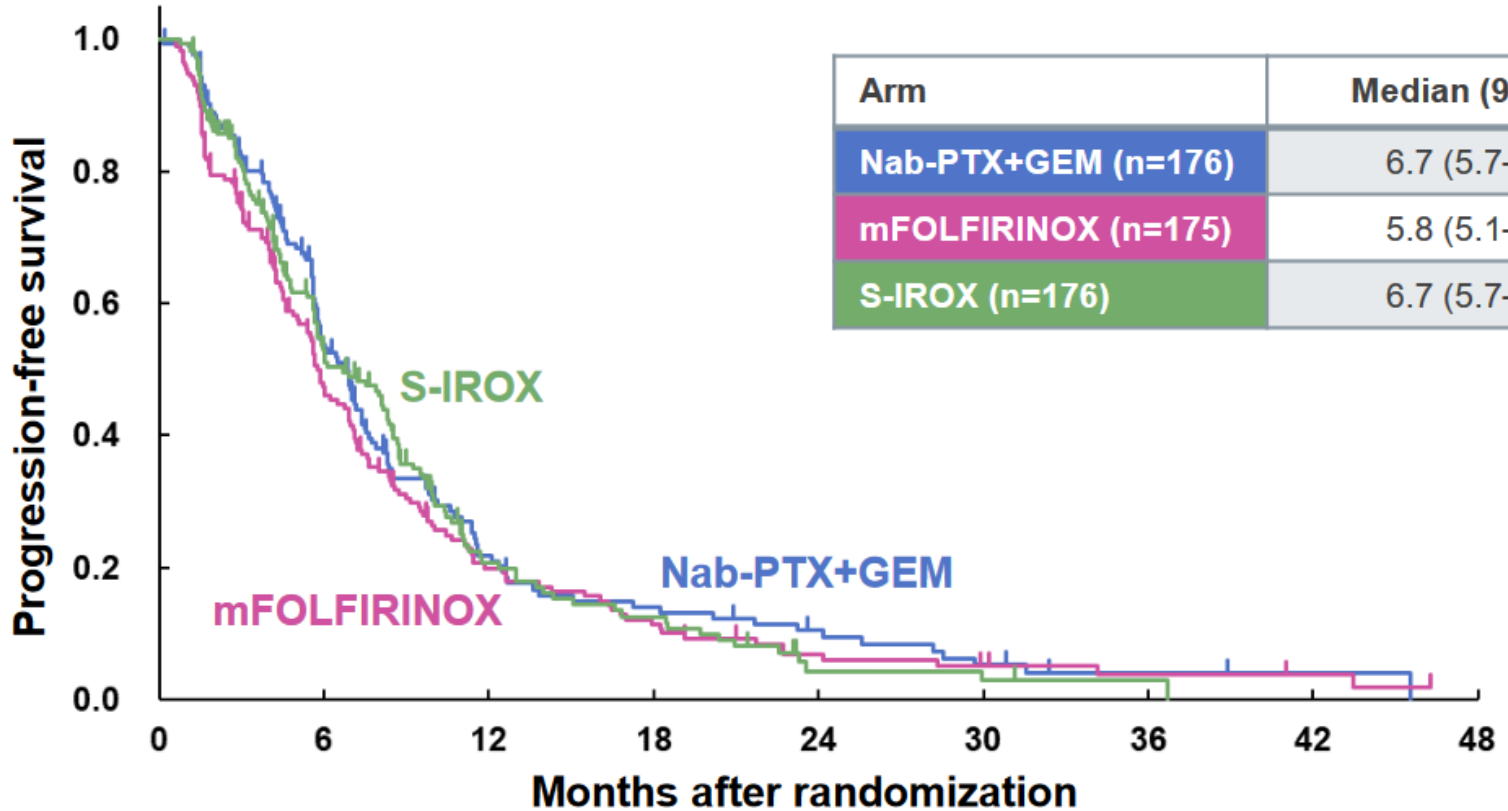
JCOG1611 (GENERATE): Trial Design

Ohba et al. (abstract 1616O)



- **Primary endpoint of phase 3 = OVERALL SURVIVAL**

Progression-free Survival

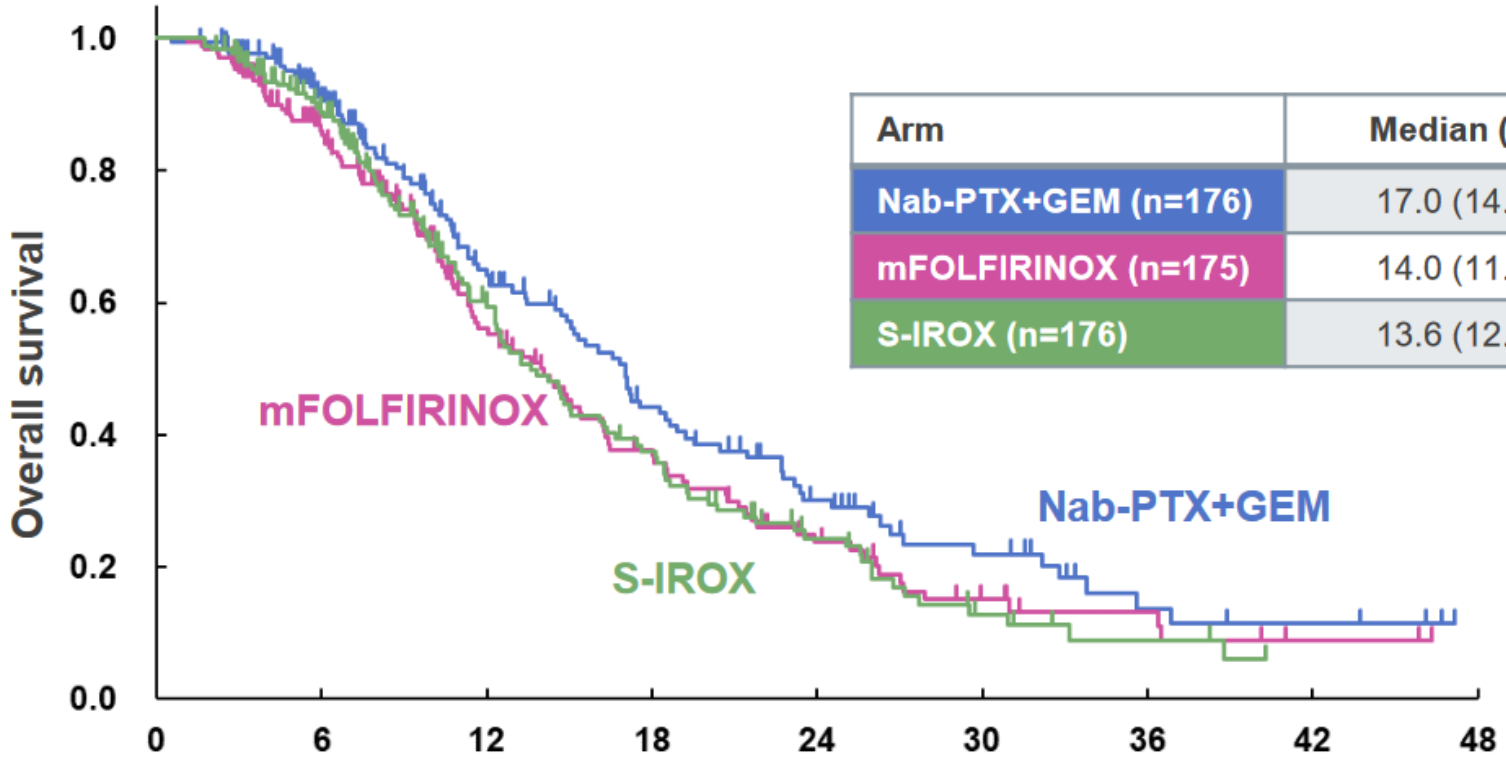


Arm	Median (95% CI)	HR (95% CI)
Nab-PTX+GEM (n=176)	6.7 (5.7–7.4)	–
mFOLFIRINOX (n=175)	5.8 (5.1–6.9)	1.15 (0.91–1.45)
S-IROX (n=176)	6.7 (5.7–8.3)	1.07 (0.84–1.35)

Patients at risk

Nab-PTX+GEM	176	78	26	16	10	5	2	1	0
mFOLFIRINOX	175	74	28	16	8	5	3	2	0
S-IROX	176	78	23	14	3	2	1	0	

Overall Survival (Updated: May 2023)



Arm	Median (95% CI)	HR (95% CI)*
Nab-PTX+GEM (n=176)	17.0 (14.5–18.9)	–
mFOLFIRINOX (n=175)	14.0 (11.4–16.3)	1.29 (0.98–1.70)
S-IROX (n=176)	13.6 (12.3–16.3)	1.29 (0.98–1.70)

* By stratified Cox regression model

Patients at risk									
Nab-PTX+GEM	176	135	76	47	27	15	6	4	0
mFOLFIRINOX	175	128	66	39	21	10	6	2	0
S-IROX	176	133	68	42	21	8	4	0	

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

JCOG 1611 (GENERATE) : Conclusions

- Essai clôturé précocement pour futilité du S-IROX vs Gem-NabP
- Les auteurs concluent que Gem-NabP est supérieur et devrait être le standard de 1ere ligne des mPDAC devant avantage en OS et meilleur profil de toxicité.
- Cependant ces résultats sont à pondérer devant les résultats récents de NAPOLI3
  - mFOLFIRINOX < NALIRIFOX (peu probable…)
  - Chimiosensibilité de la population asiatique PDAC différente (plus probable)
- Ces résultats challengent cependant le FOLFIRINOX de 1ère ligne
  - Pour ma pratique quotidienne pas de modification : FOLFIRINOX pour patients OMS 0-1
  - Cependant me permettent d'avoir moins de réticence à participer aux essais de 1ere ligne dans lesquels la chimiothérapie est très fréquemment Gem-NabP +/- drogue expérimentale

Quelques données pour être provocateur avec le FOLFIRINOX …!

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.

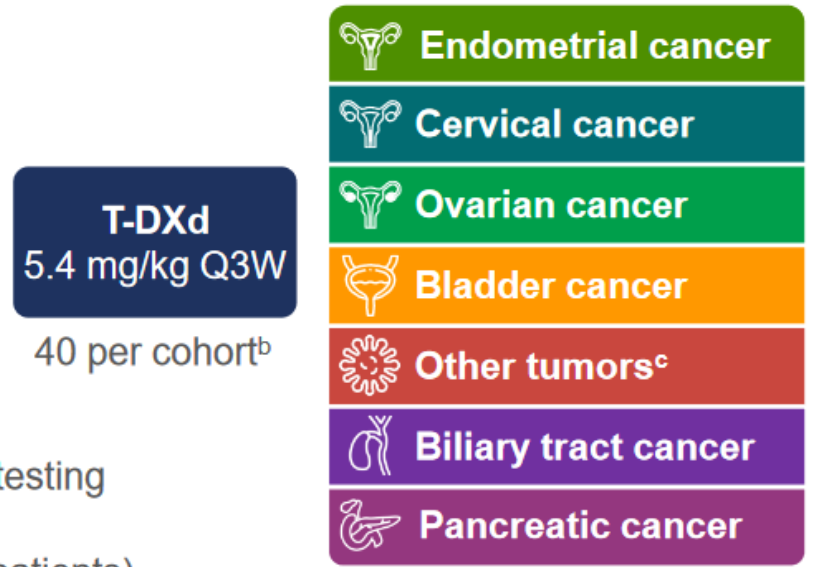
Des nouveautés … ??

DESTINY-PanTumor02: a Phase 2 study of T-DXd for HER2-expressing solid tumors

An open-label, multicenter study (NCT04482309)

Key eligibility criteria

- Advanced solid tumors not eligible for curative therapy
- 2L+ patient population
- HER2 expression (IHC 3+ or 2+)
  - Local test or central test by HercepTest if local test not feasible (ASCO/CAP gastric cancer scoring[1])[a]
- Prior HER2-targeting therapy allowed
- ECOG/WHO PS 0–1



Primary endpoint

- Confirmed ORR (investigator)

Secondary endpoints

- DOR, DCR, PFS, OS
- Safety

Exploratory analysis

- Subgroup analyses by HER2 status

Primary analysis
data cutoff: Jun 8, 2023
Median follow up: 12.75 mo

Baseline characteristics

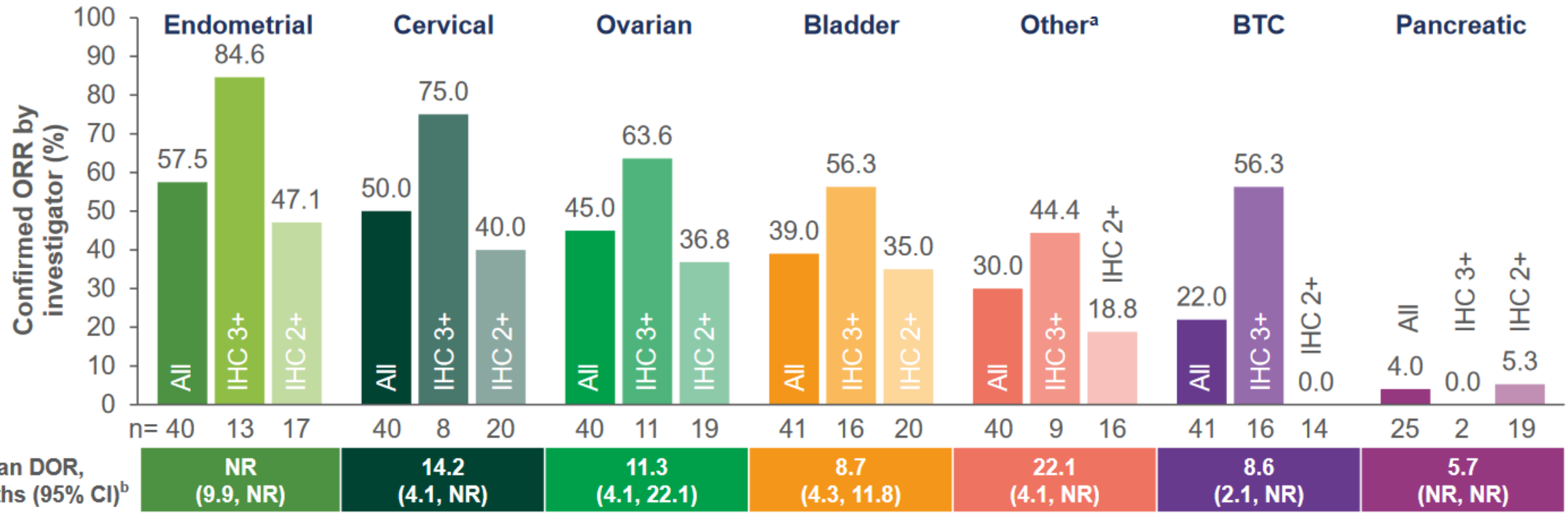
- 267 patients received treatment; 202 (75.7%) based on local HER2 testing
  - 111 (41.6%) patients were IHC 3+ based on HER2 test (local or central) at enrollment, primary efficacy analysis (all patients)
  - **75 (28.1%) patients were IHC 3+ on central testing**, sensitivity analysis on efficacy endpoints (subgroup analyses)
- Median age was 62 years (23–85) and **109 (40.8%) patients had received ≥3 lines of therapy**

[a]Patients were eligible for either test. All patients were centrally confirmed; [b]planned recruitment, cohorts with no objective responses in the first 15 patients were to be closed; [c]patients with tumors that express HER2, excluding tumors in the tumor-specific cohorts, and breast cancer, non-small cell lung cancer, gastric cancer, and colorectal cancer

2L, second-line; ASCO, American Society of Clinical Oncology; CAP, College of American Pathologists; DCR, disease control rate; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PS, performance status; Q3W, every 3 weeks; T-DXd, trastuzumab deruxtecan; WHO, World Health Organization

1. Hofmann M, et al. *Histopathology*. 2008;52:797–805

Objective response and duration of response



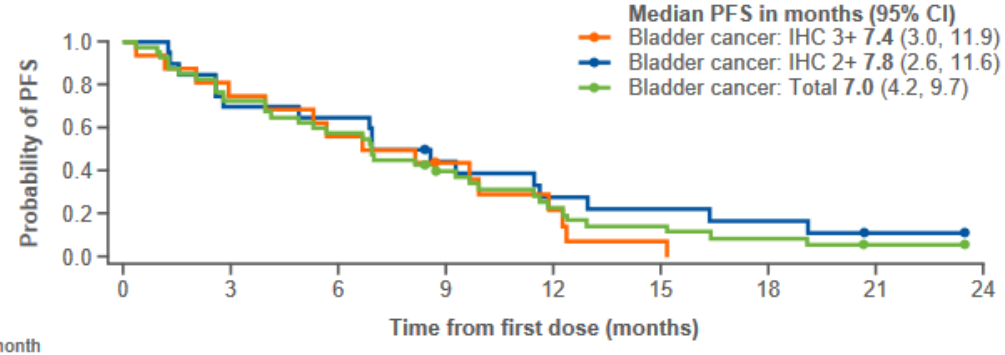
	All patients (N=267)	IHC 3+ (n=75)	IHC 2+ (n=125)
ORR, % (95% CI)	37.1 (31.3, 43.2)	61.3 (49.4, 72.4)	27.2 (19.6, 35.9)
Median DOR, months (95% CI)[b]	11.3 (9.6, 17.8)	22.1 (9.6, NR)	9.8 (4.3, 12.6)

Analysis of ORR by investigator was performed in patients who received ≥1 dose of T-DXd; all patients (n=267; including 67 patients with IHC 1+ [n=25], IHC 0 [n=30], or unknown IHC status [n=12] by central testing) and patients with centrally confirmed HER2 IHC 3+ (n=75) or IHC 2+ (n=125) status. Analysis of DOR was performed in patients with objective response who received ≥1 dose of T-DXd; all patients (n=99; including 19 patients with IHC 1+ [n=6], IHC 0 [n=9], or unknown IHC status [n=4] by central testing) and patients with centrally confirmed HER2 IHC 3+ (n=46) or IHC 2+ (n=34) status. [a]Responses in extramammary Paget's disease, head and neck cancer, oropharyngeal neoplasm, and salivary gland cancer; [b]includes patients with a confirmed objective response only

BTC, biliary tract cancer; CI, confidence interval; DOR, duration of response; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; NR, not reached; ORR, objective response rate; T-DXd, trastuzumab deruxtecan

Efficacy endpoint: PFS by HER2 status per cohort

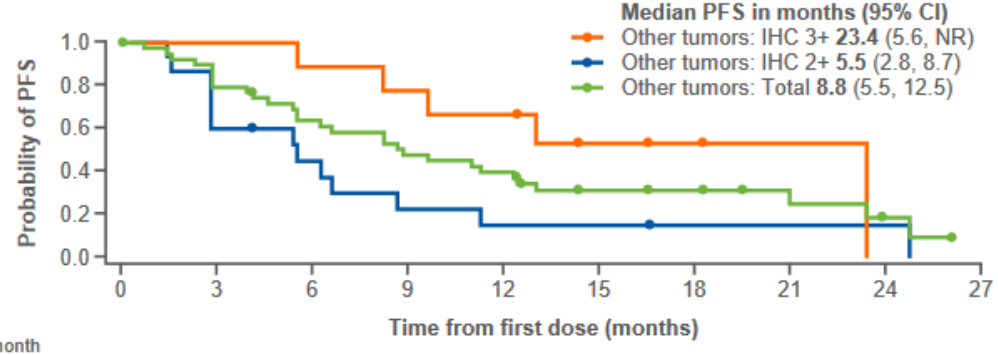
Bladder cancer



Number at risk, month

Bladder cancer: IHC 3+	16	12	9	6	3	1	0		
Bladder cancer: IHC 2+	20	14	13	8	5	4	3	1	0
Bladder cancer: Total	41	29	23	14	8	5	3	1	0

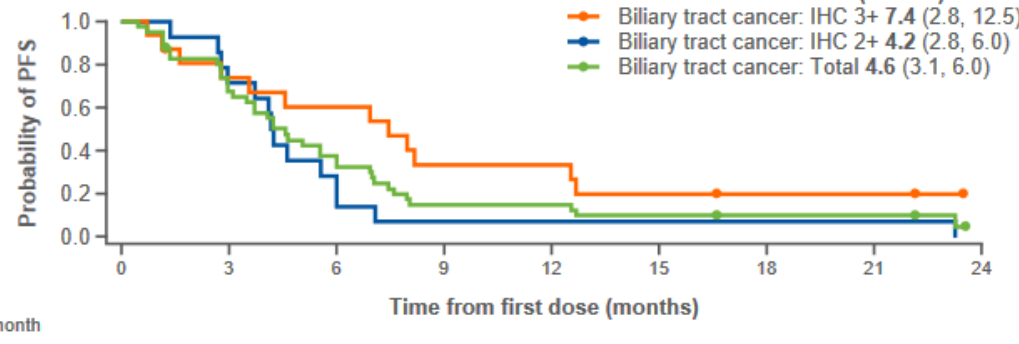
Other tumors



Number at risk, month

Other tumors: IHC 3+	9	9	8	7	6	3	2	1	0	
Other tumors: IHC 2+	16	9	6	3	2	2	1	1	1	0
Other tumors: Total	40	31	24	18	15	9	7	4	2	0

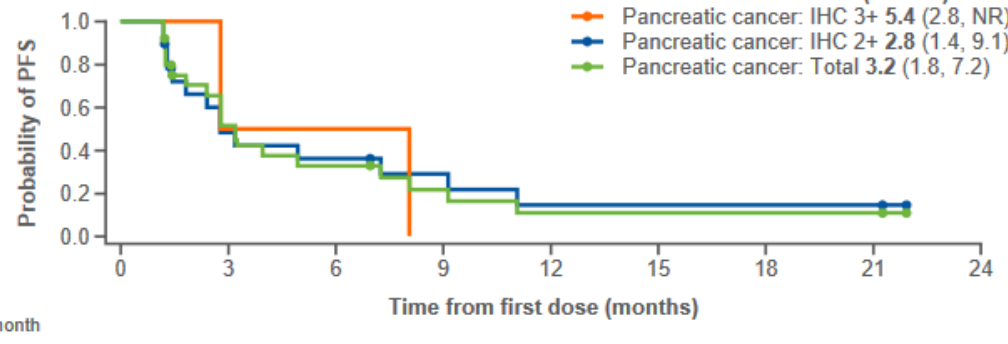
Biliary tract cancer



Number at risk, month

Biliary tract cancer: IHC 3+	16	11	9	5	5	3	2	2	0
Biliary tract cancer: IHC 2+	14	10	3	1	1	1	1	1	0
Biliary tract cancer: Total	41	27	14	6	6	4	3	3	0

Pancreatic cancer



Number at risk, month

Pancreatic cancer: IHC 3+	2	1	1	0					
Pancreatic cancer: IHC 2+	19	8	6	4	2	2	2	2	0
Pancreatic cancer: Total	25	11	7	4	2	2	2	2	0

Circle indicates a censored observation
CI, confidence interval; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; NR, not reached; PFS, progression-free survival

(Developmental therapeutics, Proffered Paper session)

Abstract 652O: Preliminary clinical activity of RMC-6236, a first-in-class, RAS-selective, tri-complex RAS-MULTI(ON) inhibitor in patients with KRAS mutant pancreatic ductal adenocarcinoma and non-small cell lung cancer (Arbour et al.)

- RMC-6236: Pan-RAS inhibitor
- N=46 patients with metastatic PDAC evaluable for efficacy (dose of 80 mg PO or higher)
- KRAS G12D and G12V mutations most common (G12C excluded)
- **ORR = 20%**
- Most common AEs: rash, nausea/vomiting, diarrhea

Merci de votre attention !