

Développement de signatures transcriptomiques prédictives dans les cancers du pancréas

Recherche translationnelle et cohorte Pancréas

Partie 2

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Sorbonne Université

Liens d'intérêt

- Honoraires : Amgen, Abbvie, AstraZeneca, Bayer, Merck Serono, Pierre Fabre, Roche, Sanofi, Servier, Takeda
- Conseiller : Amgen, Acobiom, Bayer, BMS, GSK, Incyte, Merck Serono, MSD, Pierre Fabre, Servier, Takeda

SIGNATURE TRANSCRIPTOMIQUE

Tissu tumoral



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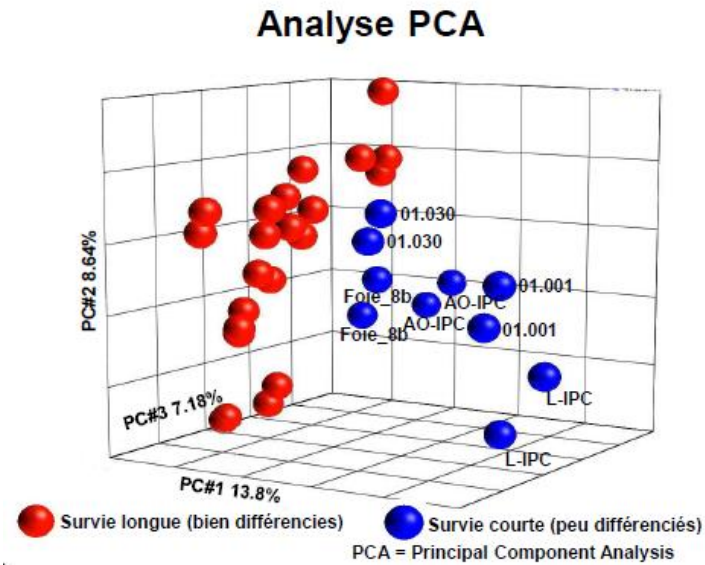
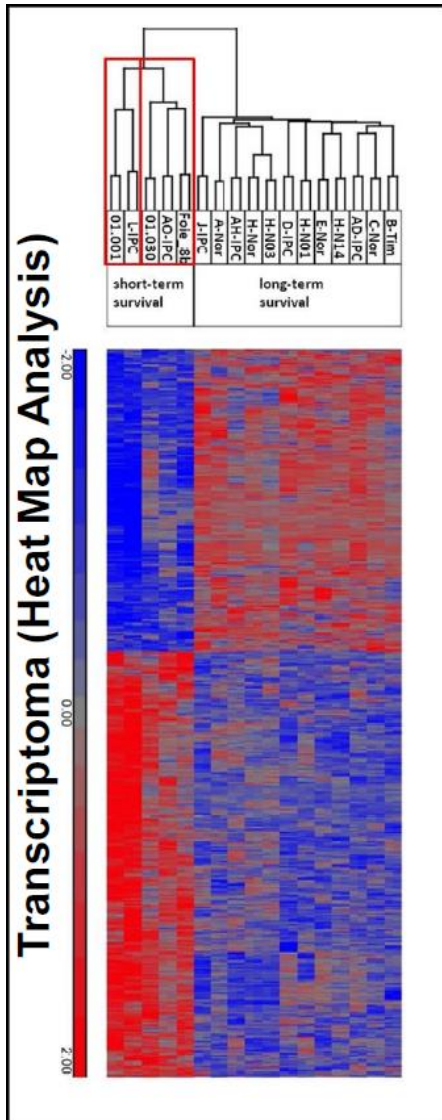
J. Augustin



Perspectives - OMIC analysis

- **But** : développer une médecine individualisée
- **Méthodologie** : analyses OMIC
 - Lignée cellulaires et modèles de xenogreffe
 - Analyse transcriptomique
 - Carte de sensibilité à la chimiothérapie

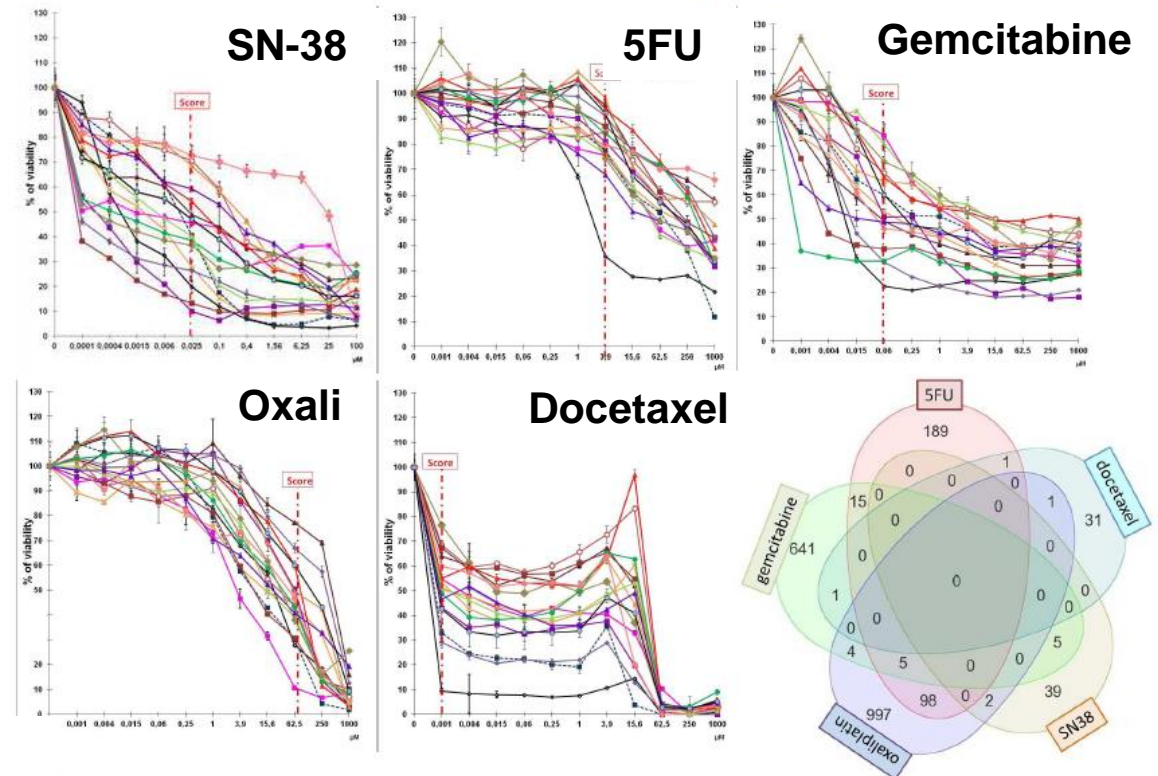
Résultats préliminaire (17 patients)



Transcriptomes corrélés avec survie et type histo
Valeur pronostique

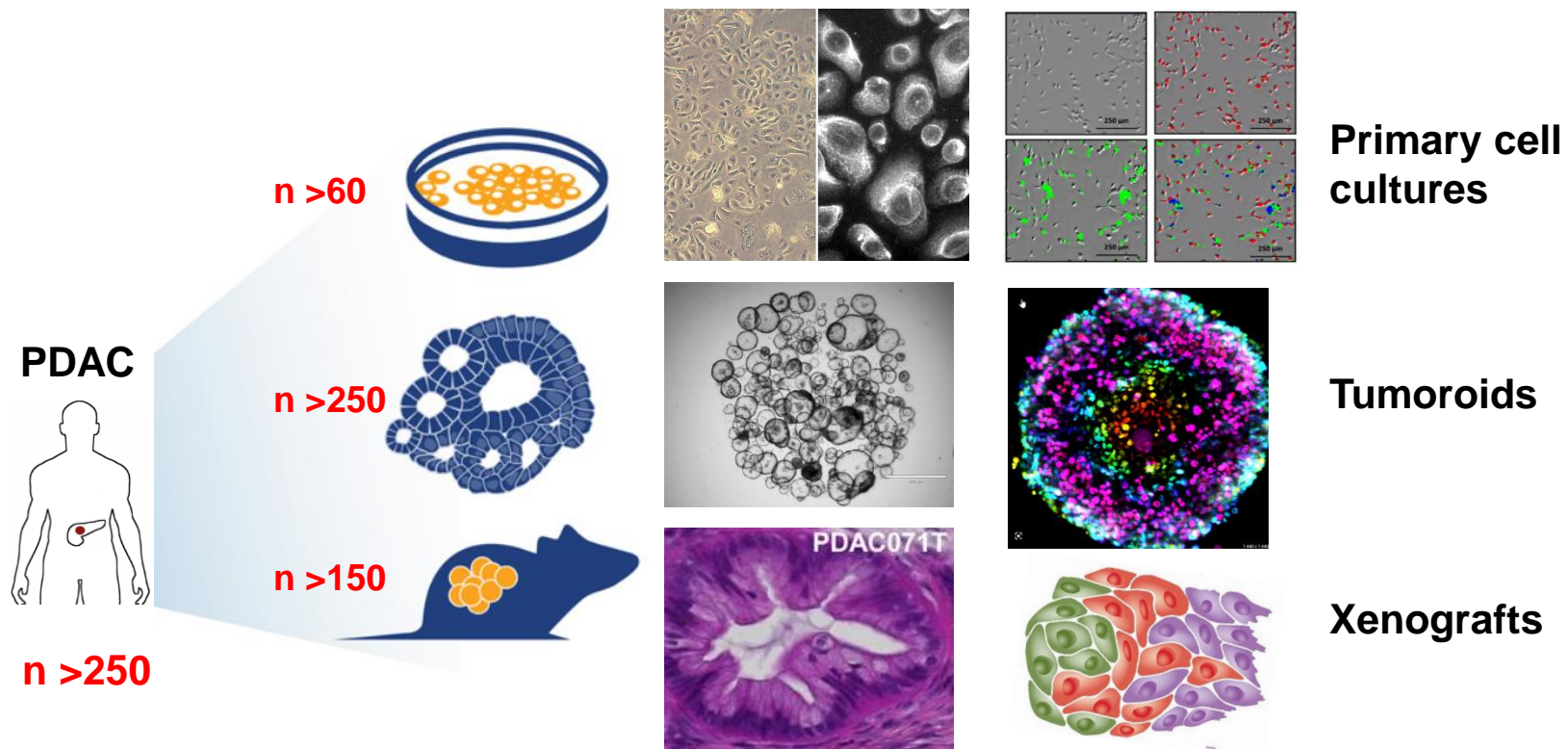
Transcriptomes corrélés avec la réponse / résistance
Valeur prédictive

Chimiogramme

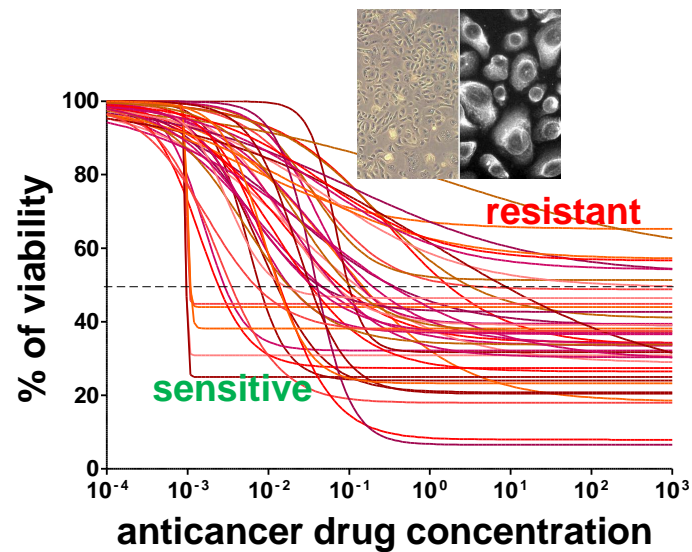


Profil de sensibilité spécifique de chaque drogue
=> Score de sensibilité

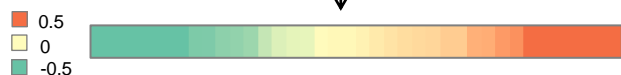
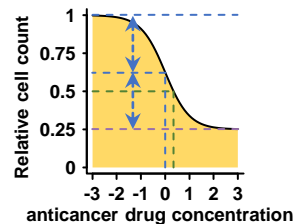
Modèles précliniques



Culture primaire de cellules



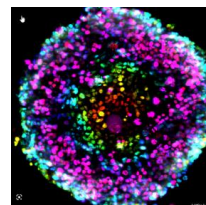
Integration of primary cell models



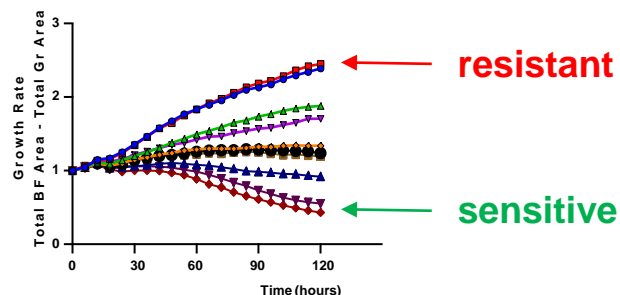
Anticancer drug sensitivity score
gemcitabine, 5FU, paclitaxel, oxaliplatin and irinotecan

Organoïdes

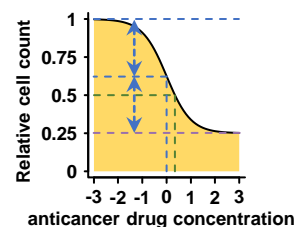
Tumoroïdes



Imaging Systems

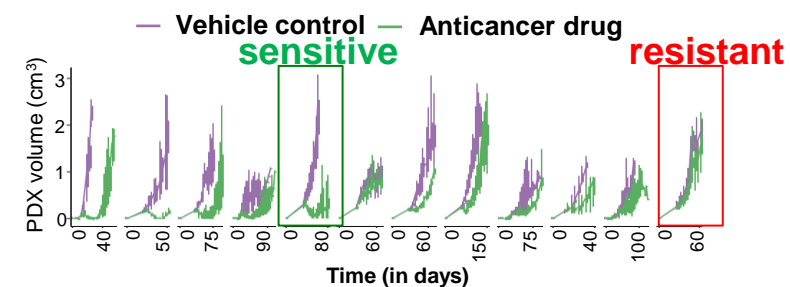


Integration of organoids models

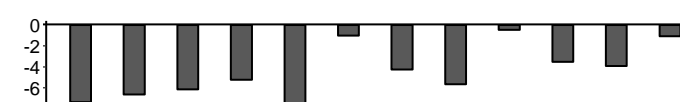


Anticancer drug sensitivity score
gemcitabine, 5FU, paclitaxel, oxaliplatin and irinotecan

Xenogrefe

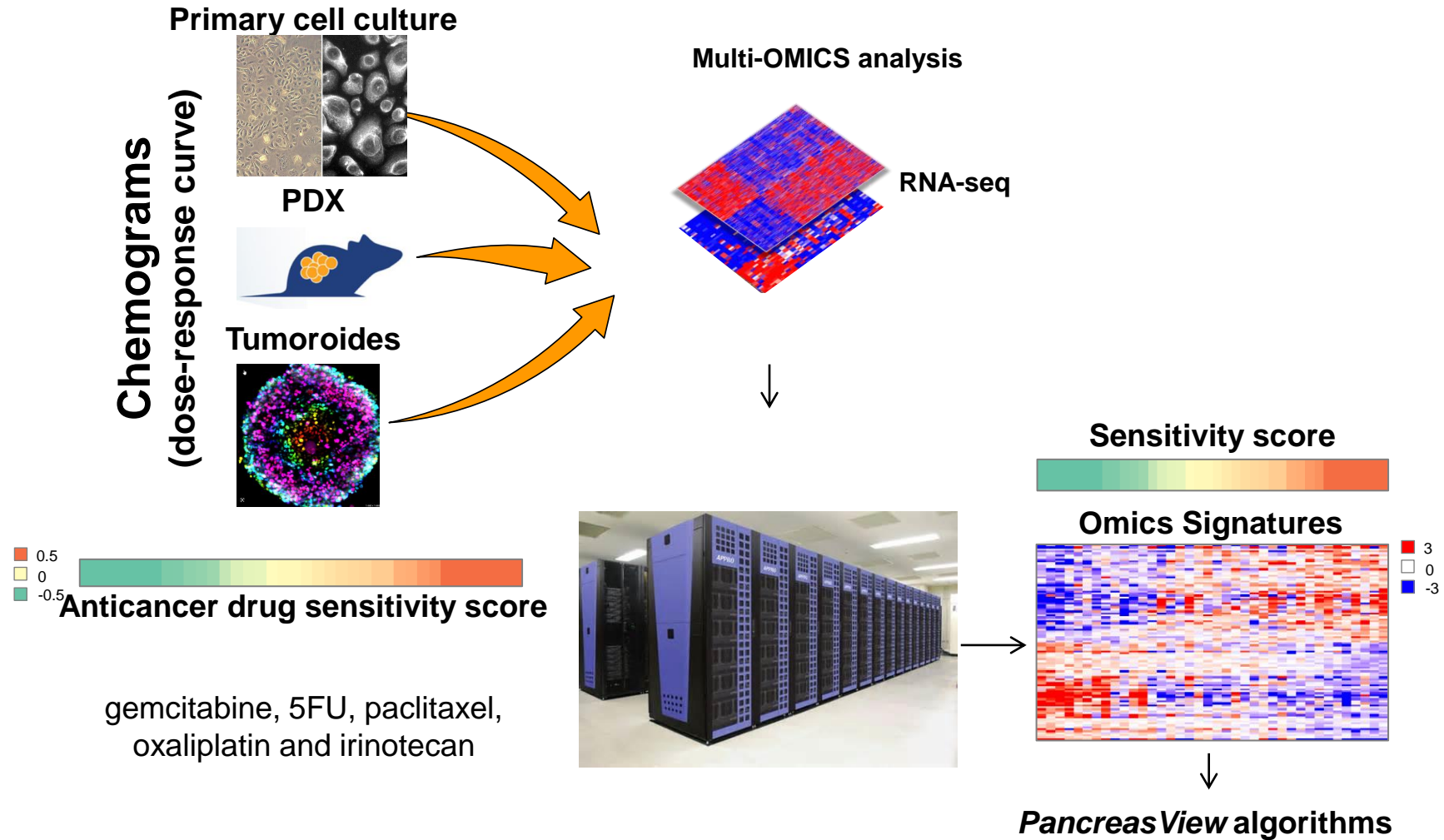


Normalized volume difference of PDX

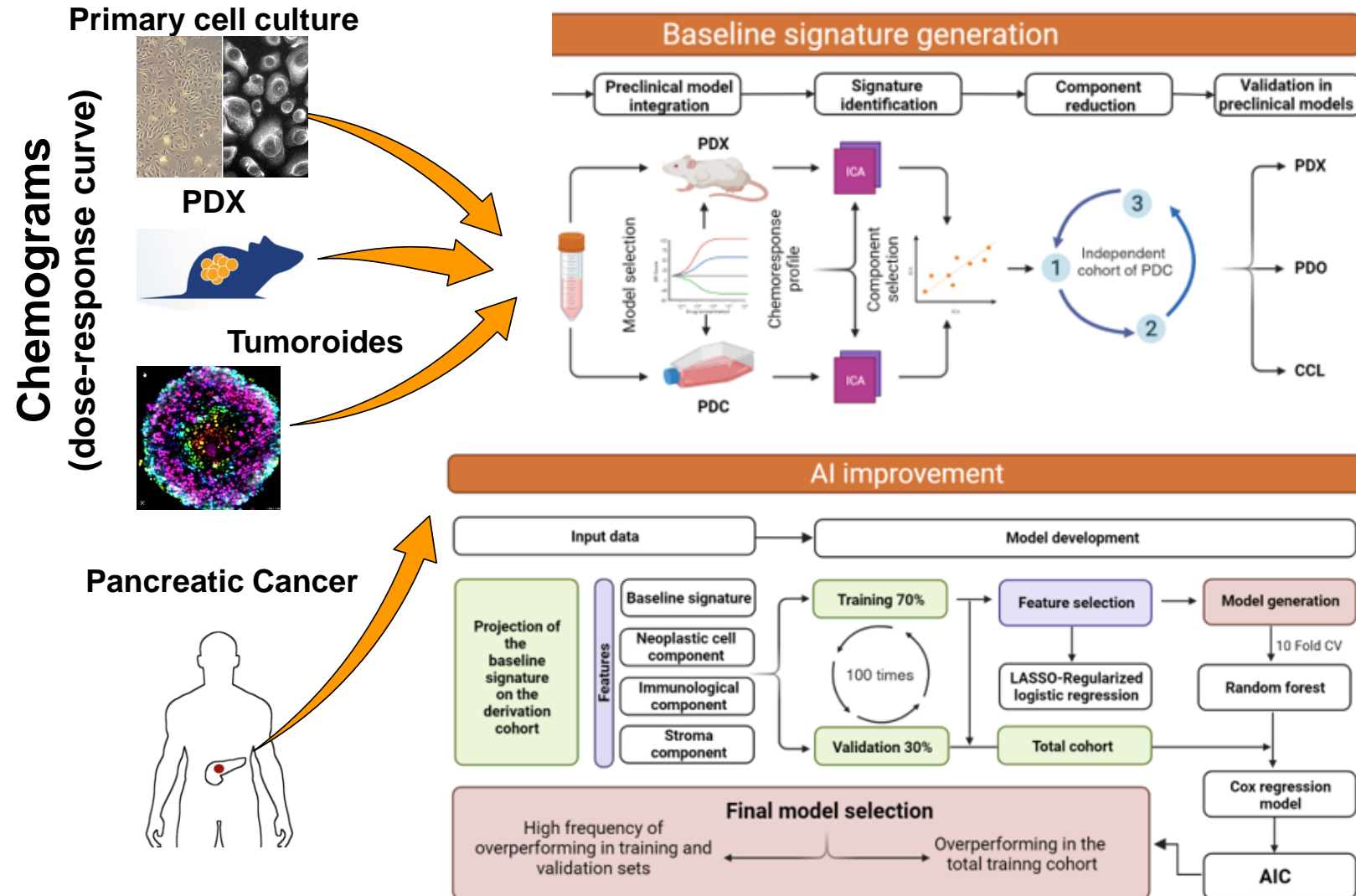


Anticancer drug sensitivity score
gemcitabine, 5FU, paclitaxel, oxaliplatin and irinotecan

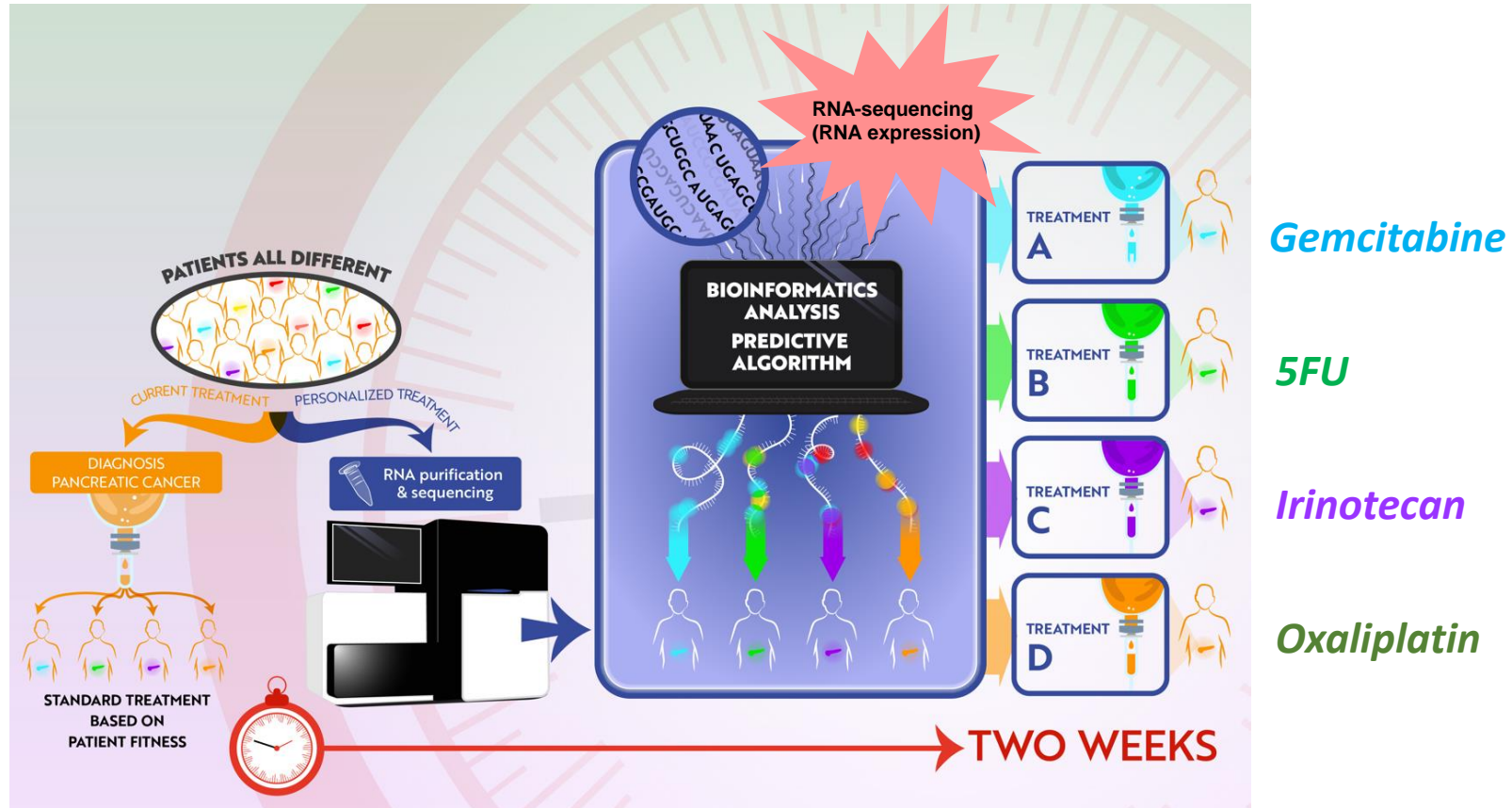
Synergistic In Vivo and In Vitro Model Power



Synergistic In Vivo and In Vitro Model Power



“PancreasView” Plateforme transcriptomique predictive



Clinical validation

Personalized treatments
Avoiding toxicity
Optimizing treatments

Signature transcriptomique prédictive

GEMPRED

Sensibilité à la gemcitabine

1/ 38 lignées cellulaires

2/ 27 organoïdes

Signature transcriptomique prédictive

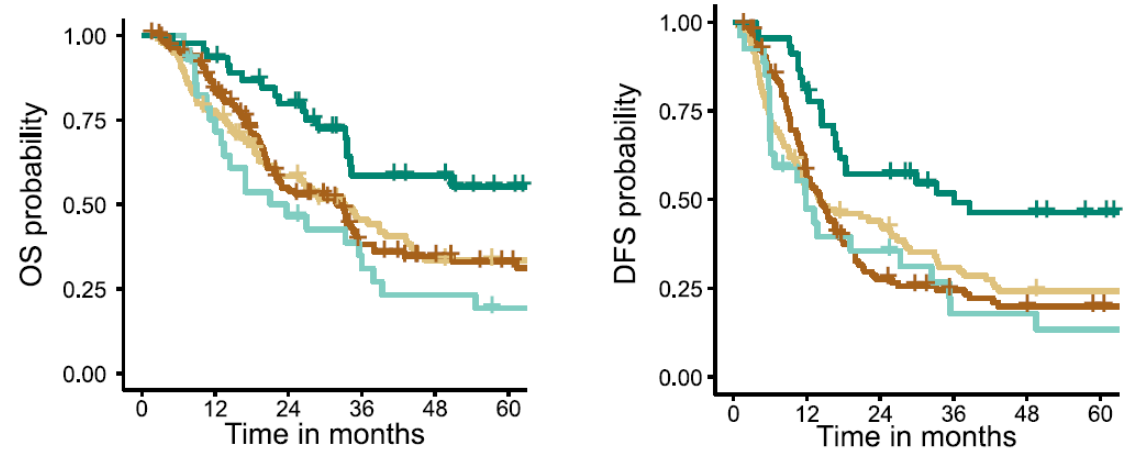
GEMPRED

Sensibilité à la gemcitabine

1/ 38 lignées cellulaires

2/ 27 organoïdes

300 patients avec PDAC réséqué

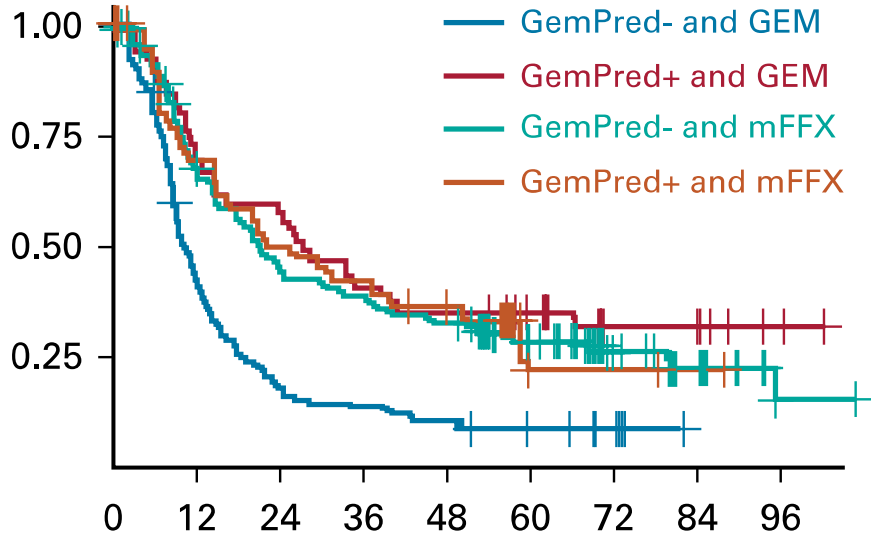


		Number at risk								Number at risk					
<i>GemPred</i>								<i>GemPred</i>							
-	w/gem	99	76	52	38	28	26	-	w/gem	97	52	41	28	22	21
	w/gem	124	96	56	32	24	19		w/gem	117	62	28	21	17	15
+	w/gem	29	20	13	9	6	4	+	w/gem	27	12	9	4	4	3
	w/gem	46	43	35	21	19	14		w/gem	45	37	25	19	17	14

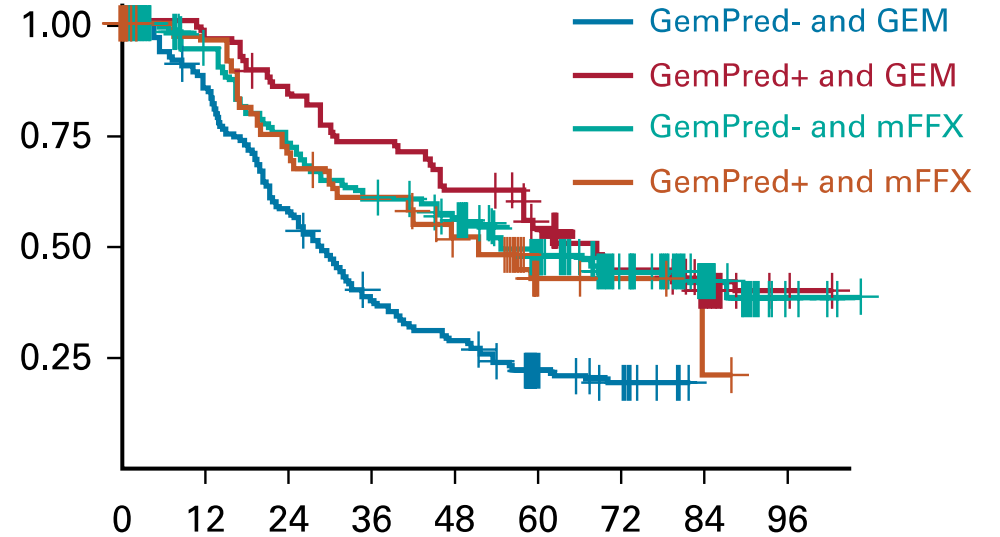
b		HR (95% CI)	p-value	d		HR (95% CI)	p-value
<i>GemPred</i> +	w/gem	1.36 (0.847-2.19)	0.202	<i>GemPred</i> +	w/gem	1.25 (0.777-2.02)	0.357
	w/gem	1 (0.717-1.39)	0.998		w/gem	1.1 (0.807-1.5)	0.547
<i>GemPred</i> +	w/gem	0.336 (0.167-0.678)	0.00234	<i>GemPred</i> +	w/gem	0.385 (0.2-0.739)	0.00415

PRODIGE24

Survie sans récurrence



Survie globale



Subgroup analysis	No. of Events/No. of Patients		sHR (95% CI)	P Value int.
	mFFX	GEM		
Overall	126/183	136/167	0.619 (0.482-0.795)	.008
GemPred+	26/39	33/50	1.05 (0.602-1.83)	
GemPred-	100/144	103/117	0.45 (0.336-0.603)	

Subgroup analysis	No. of Events/No. of Patients		sHR (95% CI)	P Value int.
	mFFX	GEM		
Overall	92/183	114/167	0.624 (0.471-0.826)	.004
GemPred+	20/39	26/50	1.22 (0.649-2.3)	
GemPred-	72/144	88/117	0.464 (0.335-0.642)	

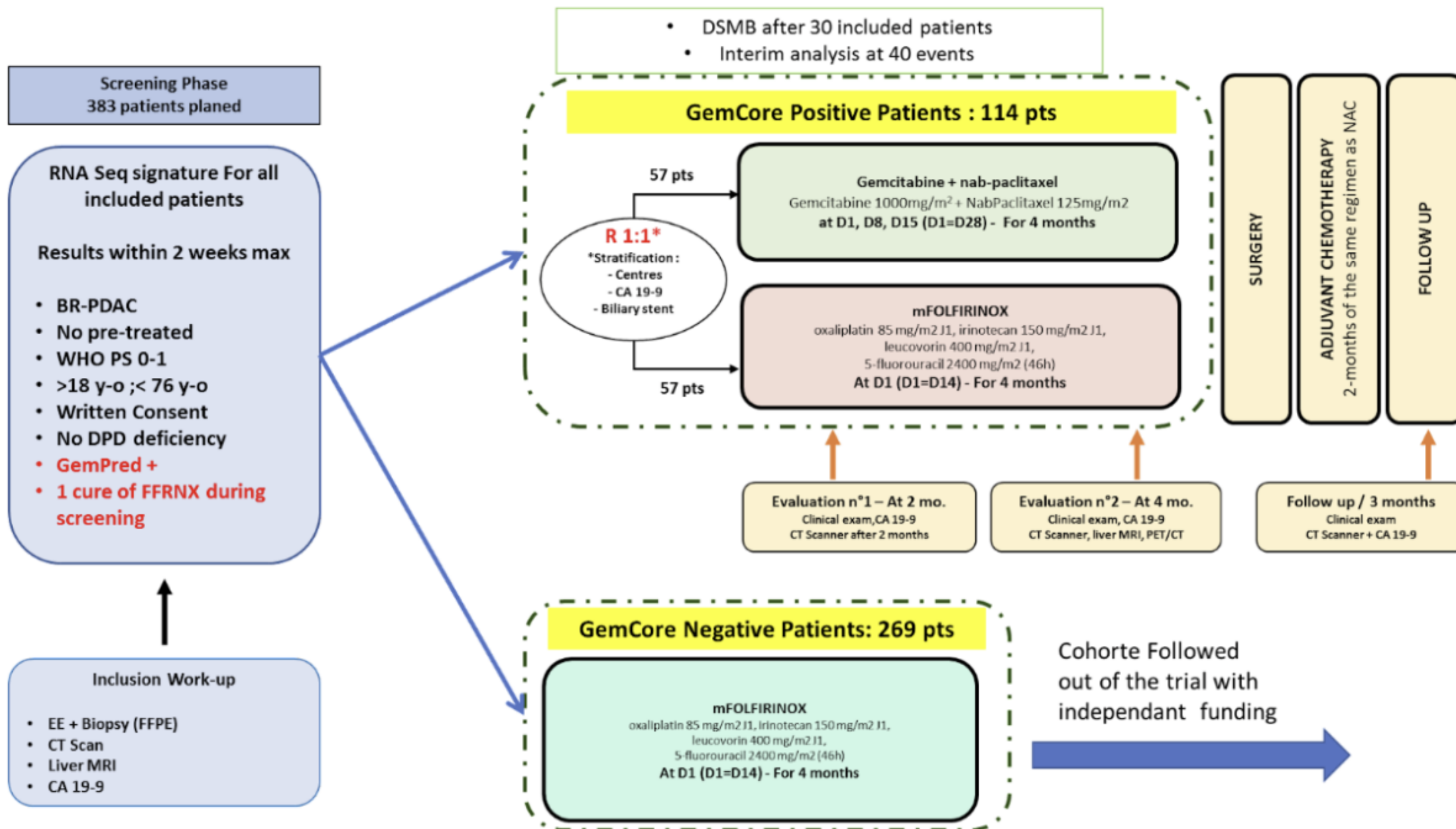
350 patients ; Gempred+ 25,5%

Nicolle R et al, J Clin Oncol 2023

Conclusion

- Données robustes et très prometteuses
- Évaluation des signatures en cours à partir de cohortes de patients avec PDAC avancé
- Essais thérapeutiques prospectifs en projet
- Faisabilité à terme en routine ?
Délai, remboursement...

NEOPREDICT



SIGNATURE TRANSCRIPTOMIQUE

Plasma

Cohortes rétrospectives

164 patients BACAP-NCT02818829 et GEMCIPANC- NCT03599154

- 66 PDAC localement avancé
- 98 PDAC métastatique

Traitement par FOLFIRINOX (n=89) ou gemcitabine (n=72)

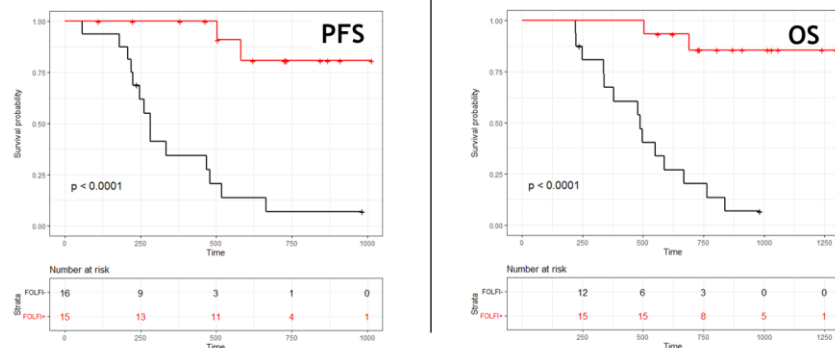
Prélèvement sanguin avant tout traitement : Sang Total, Tube PAXgene

=> Analyses transcriptomiques

Résultats

FOLFIRINOX

Locally advanced



Patients with a **positive test** had a significantly longer **PFS (20.7 months vs. 7.7 months)**

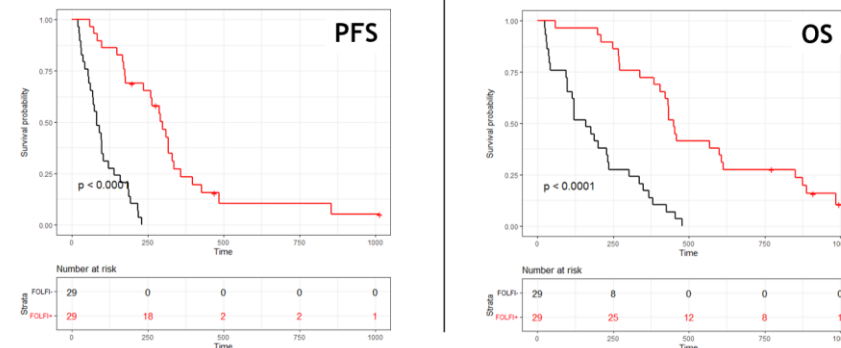
The log-rank test returned the following results for PFS (HR = 0.07 (95% CI: 0.02–0.32); $p < 0.0001$)

Patients with a **positive test** had a significantly longer **OS (26.9 months vs. 16.1 months)**

The log-rank test returned the following results for OS (HR = 0.07 (95% CI: 0.016–0.31); $p < 0.0001$)

FOLFIRINOX

Metastatic



Patients with a **positive test** had a significantly longer **PFS (9.9 months vs. 2.7 months)**

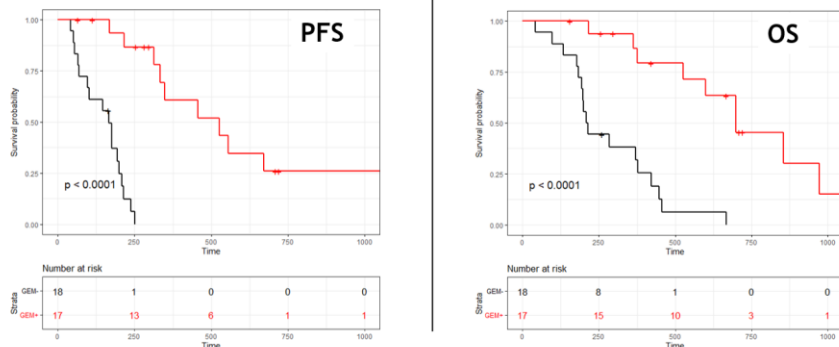
The log-rank test returned the following results for PFS (HR = 0.15 (95% CI: 0.07–0.31); $p < 0.0001$)

Patients with a **positive test** had a significantly longer **OS (14.9 months vs. 5.3 months)**

The log-rank test returned the following results for OS (HR = 0.19 (95% CI: 0.1–0.36); $p < 0.0001$)

gemcitabine

Locally advanced



Patients with a **positive test** had a significantly longer **PFS (17.5 months vs. 5.6 months)**

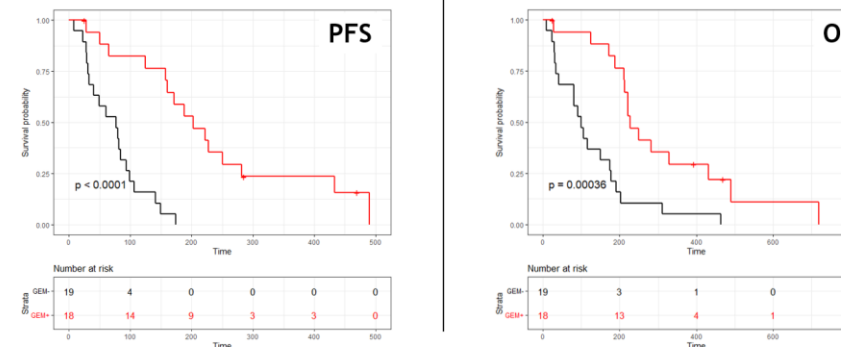
The log-rank test returned the following results for PFS (HR = 0.04 (95% CI: 0.01–0.2); $p < 0.0001$)

Patients with a **positive test** had a significantly longer **OS (23.3 months vs. 7.0 months)**

The log-rank test returned the following results for OS (HR = 0.12 (95% CI: 0.04–0.34); $p < 0.0001$)

gemcitabine

Metastatic



Patients with a **positive test** had a significantly longer **PFS (6.7 months vs. 2.6 months)**

The log-rank test returned the following results for PFS (HR = 0.14 (95% CI: 0.05–0.36); $p < 0.0001$)

Patients with a **positive test** had a significantly longer **OS (7.5 months vs. 3.3 months)**

The log-rank test returned the following results for OS (HR = 0.28 (95% CI: 0.13–0.58); $p < 0.0007$)

Conclusion

- Données préliminaires, valeur pronostique vs prédictive ?
- Problématiques de la disponibilité de cohortes de validation
- Analyse ancillaire prévue dans des essais en cours : GEMFOX, PANACH2

Merci de votre attention

Remerciement Nelson Dusetti pour les slides