TNE PANCRÉAS : TRAITEMENT ADJUVANT

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30 Juin 2022-Réunion de formation RENATEN LIMOUSIN

GUIDELINES ??

NO ADJUVANT THERAPY !!

POURQUOI UN TRAITEMENT ADJUVANT ?

- Patients jugés à risque significatif de récidive.
- Absence de résidu macroscopiquement décelable.
- Mais résidu microscopique probable.
- Augmenter le taux de survie sans récidive ET la Survie globale.

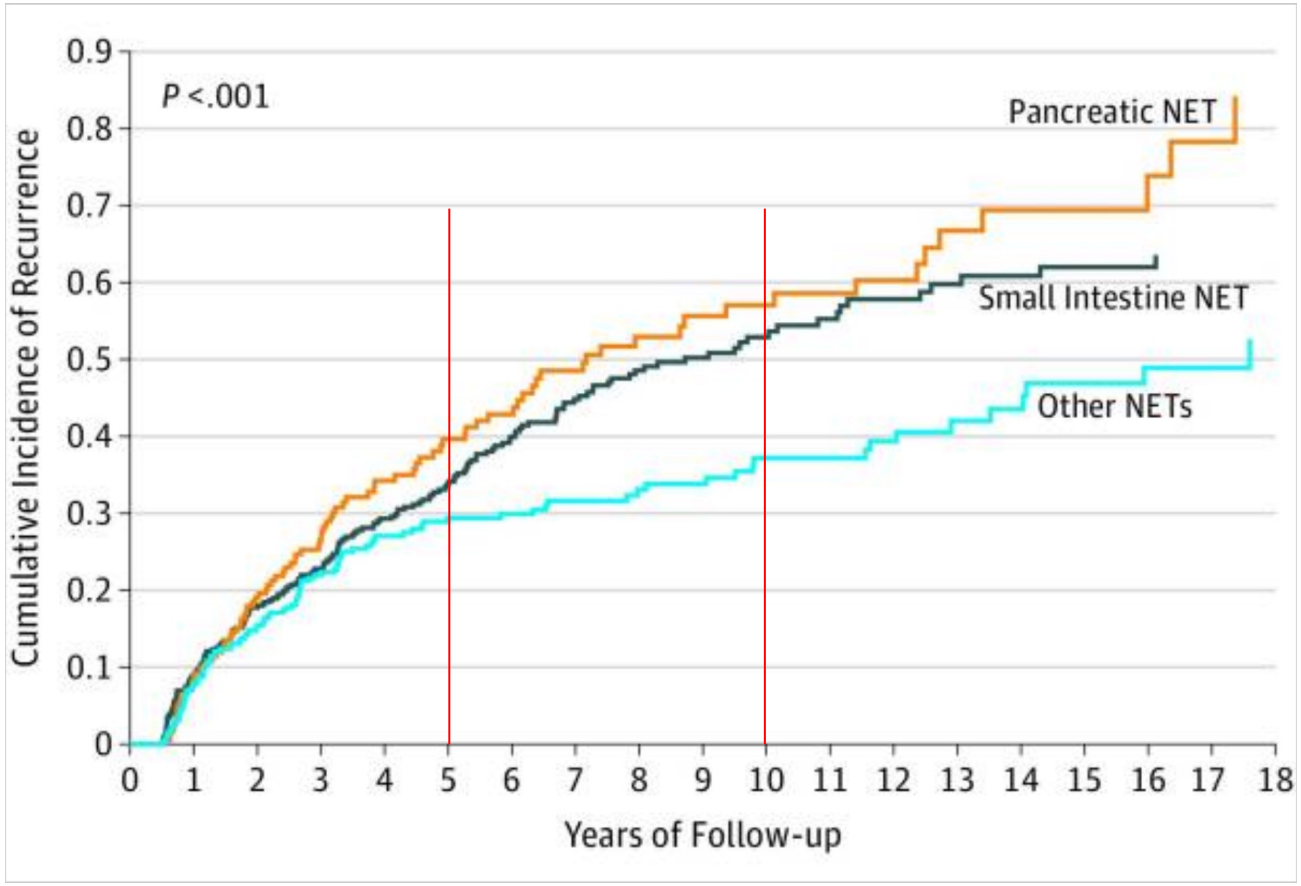
- Admis et reconnu pertinent dans de nombreuses tumeurs solides.

QUEL TAUX DE RÉCIDIVE ?

Covariates	5 years				10 years			
	Developed metastasis	Alive and no metastasis observed	Dead and no metastasis observed	*P*	Developed metastasis	Alive and no metastasis observed	Dead and no metastasis observed	*P*
Primary site				<0.001				<0.001
Appendix	12 (13.79%)	26 (29.89%)	49 (56.32%)		13 (14.94%)	Masked[a]	70 (80.46%)	
Colon	13 (11.30%)	56 (48.70%)	46 (40.00%)		13 (11.30%)	21 (18.26%)	81 (70.43%)	
Larynx, bronchus, lung, trachea and other respiratory organs	162 (17.94%)	372 (41.20%)	369 (40.86%)		177 (19.60%)	75 (8.31%)	651 (72.09%)	
Others	54 (20.00%)	101 (37.41%)	115 (42.59%)		57 (21.11%)	25 (9.26%)	188 (69.63%)	
Pancreas	26 (23.85%)	30 (27.52%)	53 (48.62%)		33 (30.28%)	Masked[a]	72 (66.06%)	
Rectum	Masked[a]	101 (54.30%)	76 (40.86%)		Masked[a]	50 (26.88%)	126 (67.74%)	
Small intestine and cecum	93 (13.36%)	258 (37.07%)	345 (49.57%)		98 (14.08%)	58 (8.33%)	540 (77.59%)	

Shen et al, Annals of Oncology, 2017

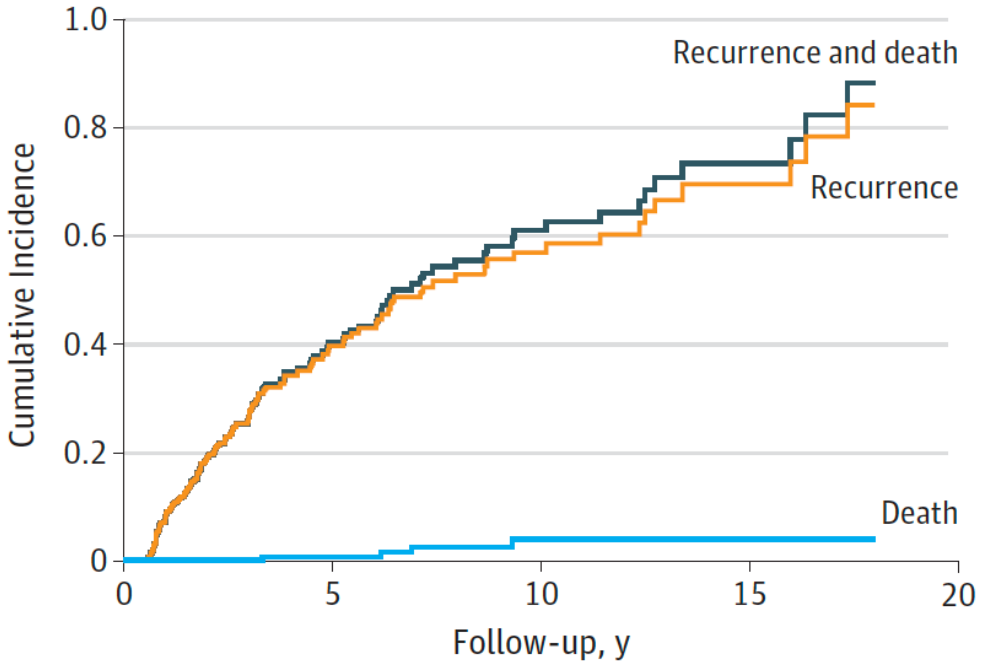
QUEL TAUX DE RÉCIDIVE ?



Singh et al, JAMA Oncol, 2018

RÉCIDIVE & SURVIE GLOBALE ?

A Patients with pancreatic neuroendocrine tumors



No. at risk	187	77	27	9
No. who had event (recurrence or death prior to current time)	0	68	88	94

Shen et al, Annals of Oncology, 2017

CHIRURGIE… QUEL SUIVI ?

- Suivi des patients opérés non standardisé.
- Risque de récidive surestimé par les centres experts.

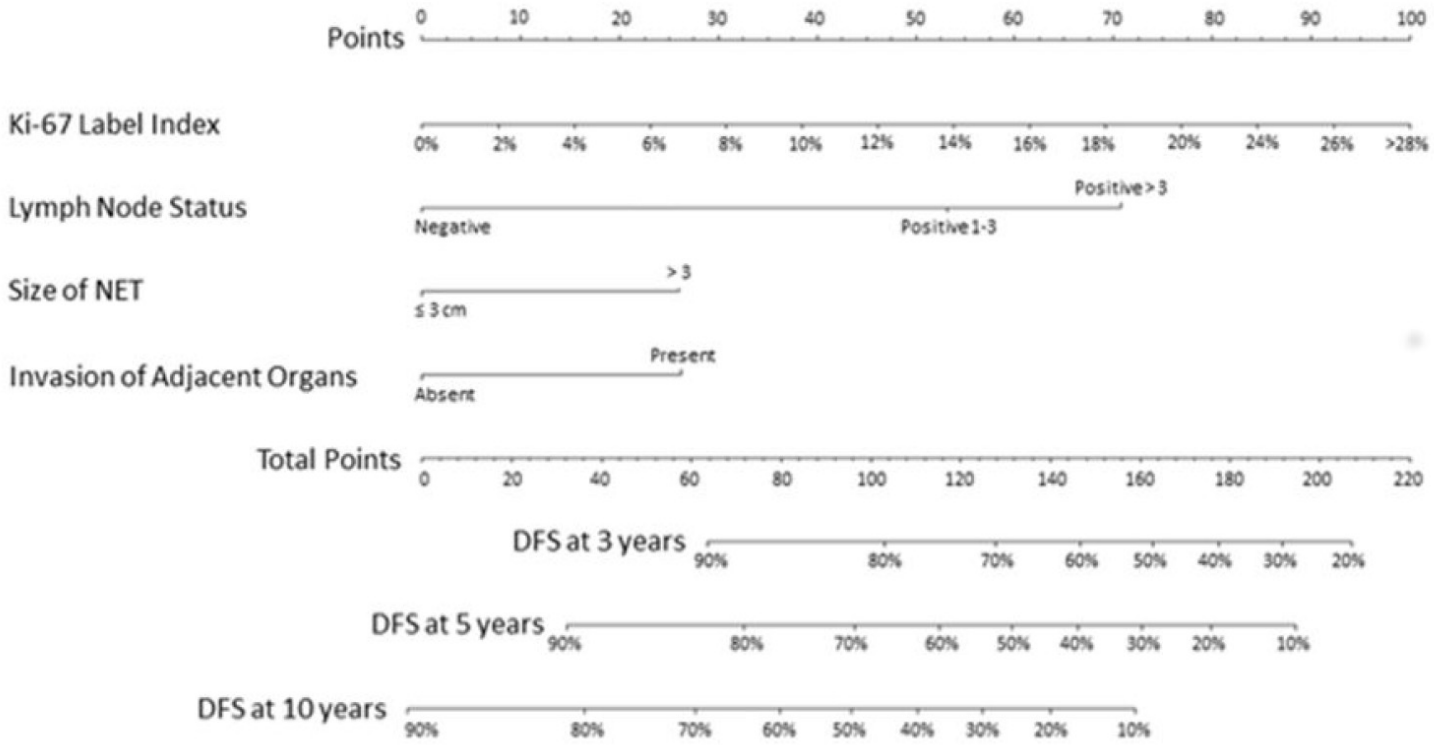
FOLLOW-UP : QUELLES RECOMMANDATIONS ?

Table 2. Summary of Recommended Follow-up After NET Resection

Organization	Recommendations for SBNET	Recommendations for panNET	Groups Not Requiring Follow-up
NCCN[1]	Clinical review at 3-12 mo with biomarkers and CT or MRI as clinically indicated; then review every 6-12 mo for maximum of 10 y.	Clinical review at 3-12 mo with biomarkers and CT or MRI as clinically indicated; then review every 6-12 mo for maximum of 10 y.	Appendiceal NET <2 cm completely resected by appendicectomy "as clinically indicated"; rectal NET <1 cm with negative margins
ENETS[2,31]	Grade 1: US, CT, or MRI at 6 and 12 mo, then yearly or longer; octreoscan (or gallium-68-based PET) at baseline and every 2 y. Grade 2-3: US, CT, or MRI every 3 mo indefinitely; octreoscan (or gallium-68-based PET) at 3 mo and yearly.	Grade 1: US, CT, or MRI at 6 and 12 mo, then yearly or longer; octreoscan (or gallium-68-based PET) at baseline and every 2 y. Grades 2-3: US, CT, or MRI every 3 mo indefinitely; octreoscan (or gallium-68-based PET) at 3 mo and yearly.	Appendiceal NET <1 cm completely resected by appendicectomy; appendiceal NET >1 cm completely resected by right hemicolectomy without LN involvement; completely resected rectal NETs <1 cm
ESMO[3]	Grades 1-2: biochemistry and CT or MRI every 3-6 mo. Grade 3: every 2-3 mo. Octreoscan after 18-24 mo if SRS positive.	Grades 1-2: biochemistry and CT or MRI every 3-6 mo. Grade 3: every 2-3 mo. Octreoscan after 18-24 mo if SSTR positive.	Not listed
NANETS[32,33]	Stages I-III: long-term surveillance (at least 10 y); imaging every 6 mo transitioning to annual imaging over time. No routine somatostatin-receptor imaging required.	CT or MRI 3-6 mo after resection, then every 6-12 mo for at least 7 y. Consider CgA or hormone markers if elevated levels at baseline, and nuclear imaging for suspected recurrence.	Stage I rectal NETs
CommNETs	Grade 1: CT every 12 mo for 3 y, then every 1-2 y for total of at least 10 y; no biochemistry.	Grade 1: CT every 12 mo for 3 y, then every 1-2 y for 10 y; no biochemistry.	Midgut: incidental grade 1, stage I tumors; pancreas: grade 1, node-negative, <2-cm tumors; rectal: grade 1, node-negative, T1 tumors; appendix: grade 1, <1-cm tumors

PRÉDIRE LE RISQUE DE RÉCIDIVE ?

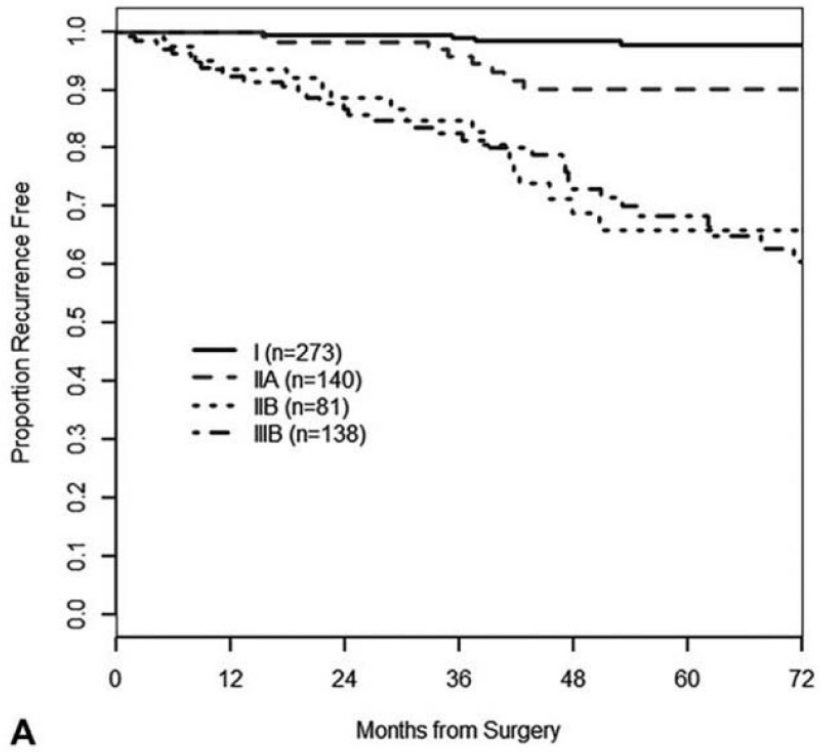
- Nombreux auteurs ont proposé l'élaboration de Nomogrammes
- Discrimination des risques de récidive.

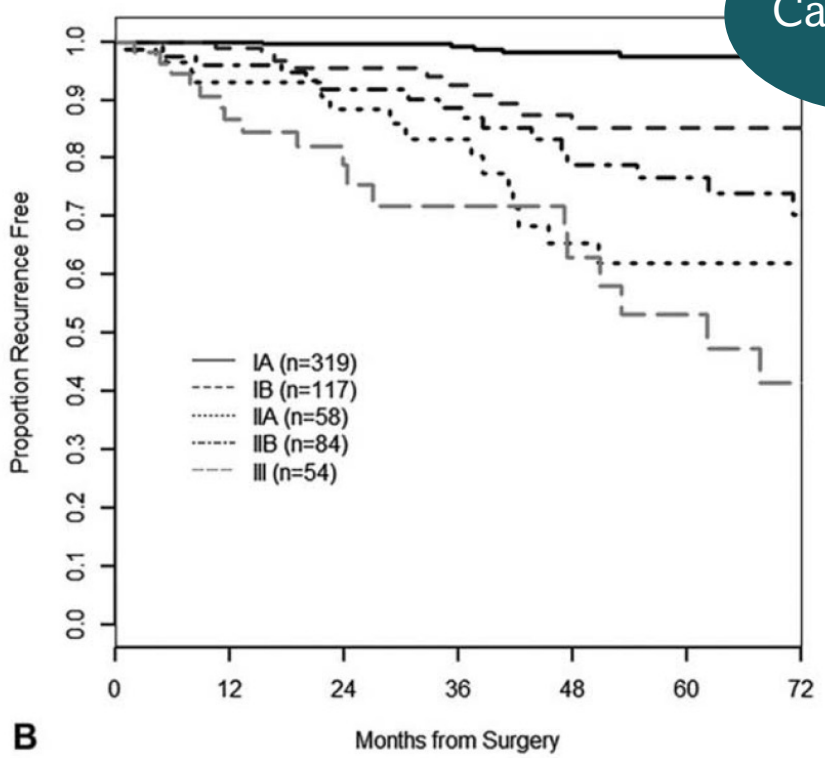


Merath et al, J Surg Oncol, 2019

PRÉDIRE LE RISQUE DE RÉCIDIVE ?

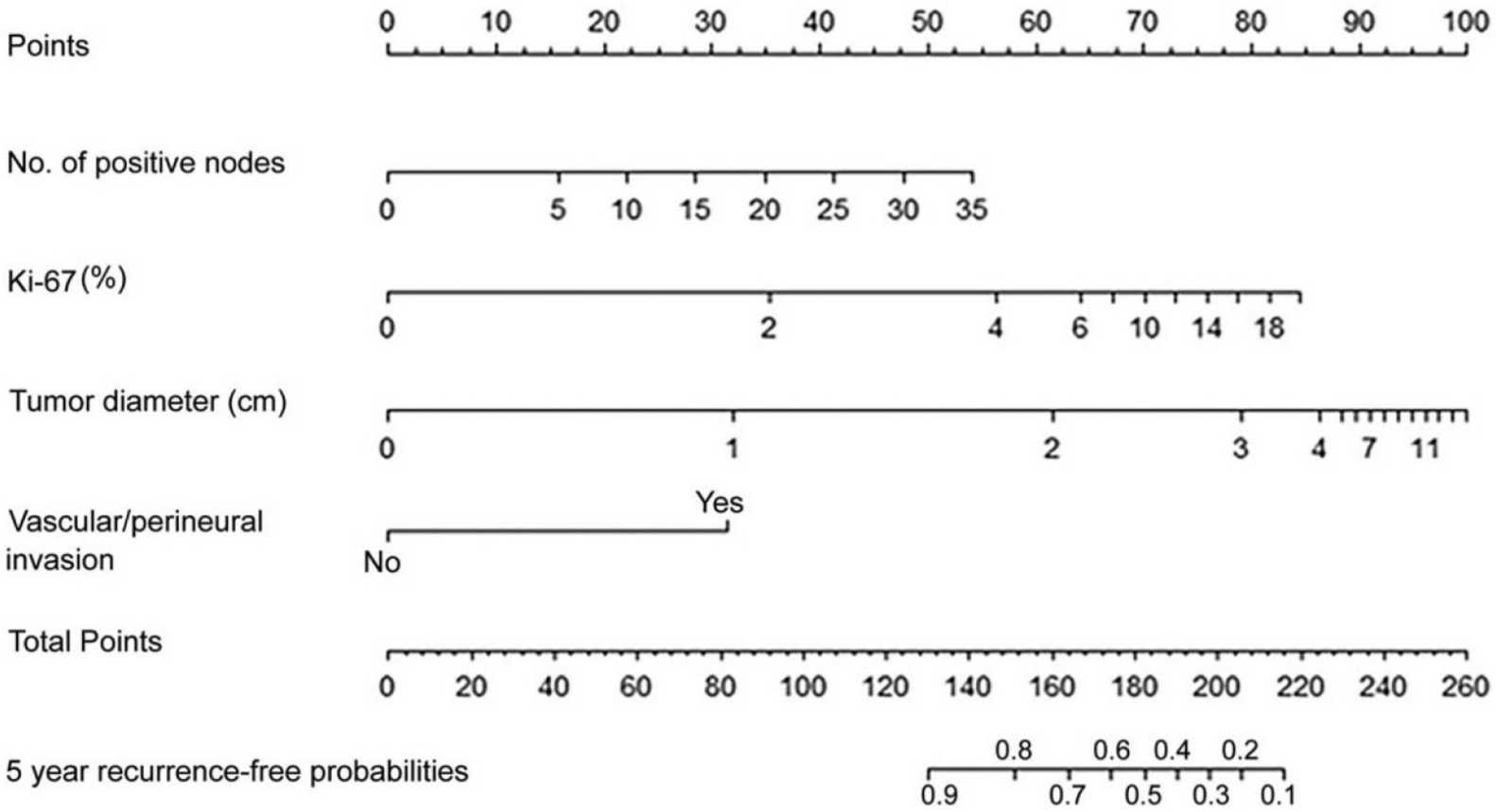
Carcinome





Pulvirenti et al, Annals of Surgery, 2021

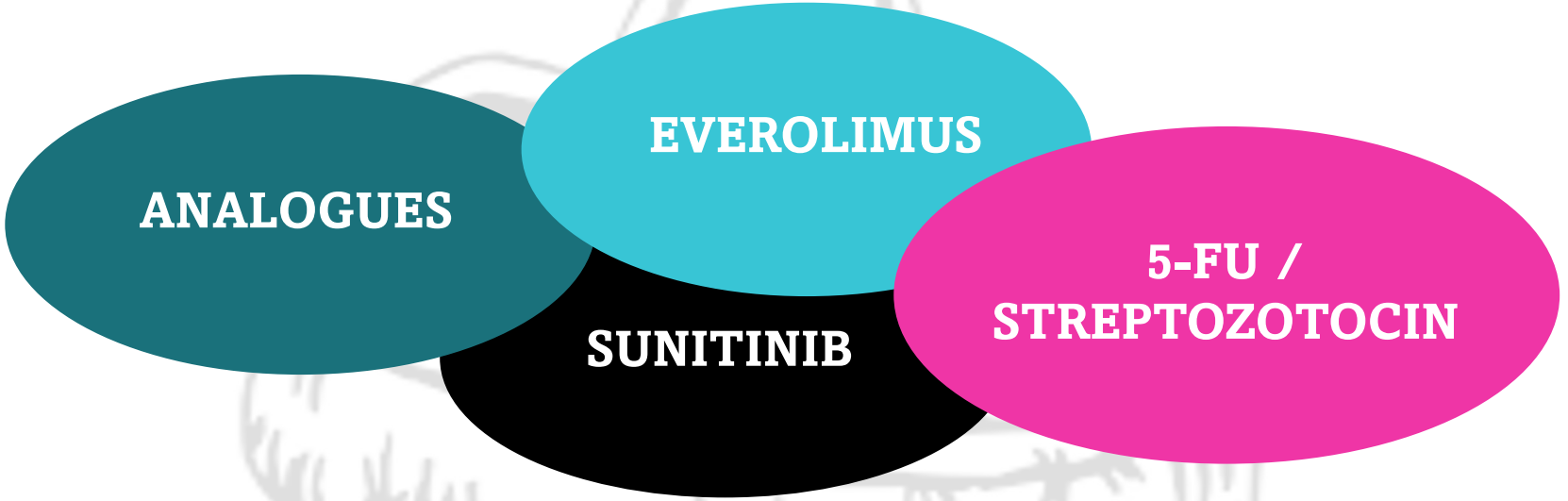
PRÉDIRE LE RISQUE DE RÉCIDIVE ?



Pulvirenti et al, Annals of Surgery, 2021

Reference	Merath 2018	Pulvirenti 2019	Zaidi 2019	Zou 2020	Sho 2019
N	1477 GEP NET (60% panNET)	960 Sporadic PAnNET	1006 PanNET NFct	245 PanNET	140 PanNET
Recurrences	207 (14%)	(12%)	130 (13%)	20 (8%)	23 (16%)
% of patients > 20% risk					
Parameter single	Ki67>6% N1	Ki67>4% T≥2 cms	Ki67>20%	Grade 2	Ki67>20%
Parameter combination	T≥3 cms + 1 other T4 + 1 other	N1 + 1 other AI/PNI + 1 other	Ki67>3%+1-2 others T>2cms + 1 other N1+ 1-2 others Symptoms+1-2 others	N1+Size>5	Ki67>8% +1 other N1+1 other Size > 5+1 other

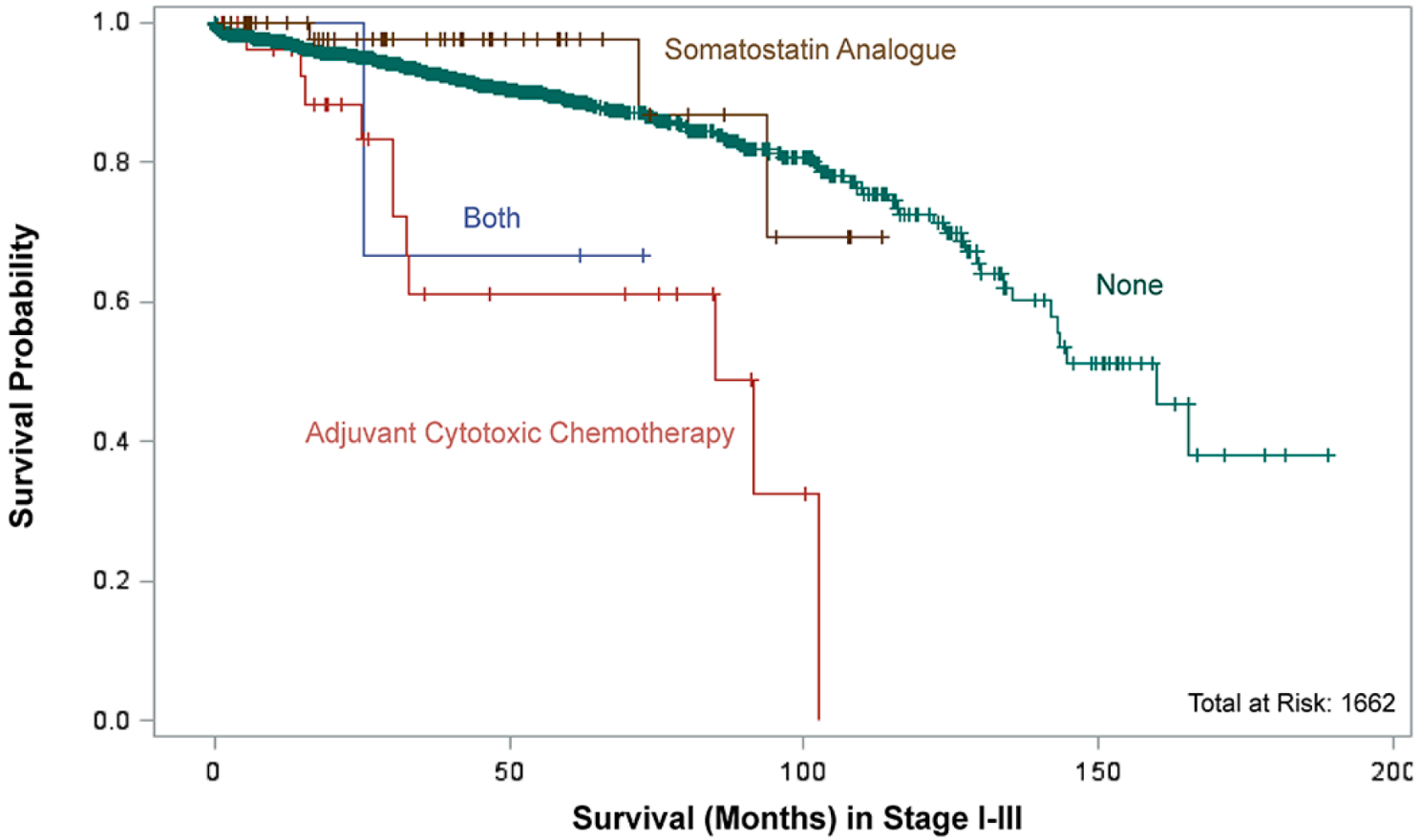
QUEL TRAITEMENT ADJUVANT?



QUE SAIT-ON ?

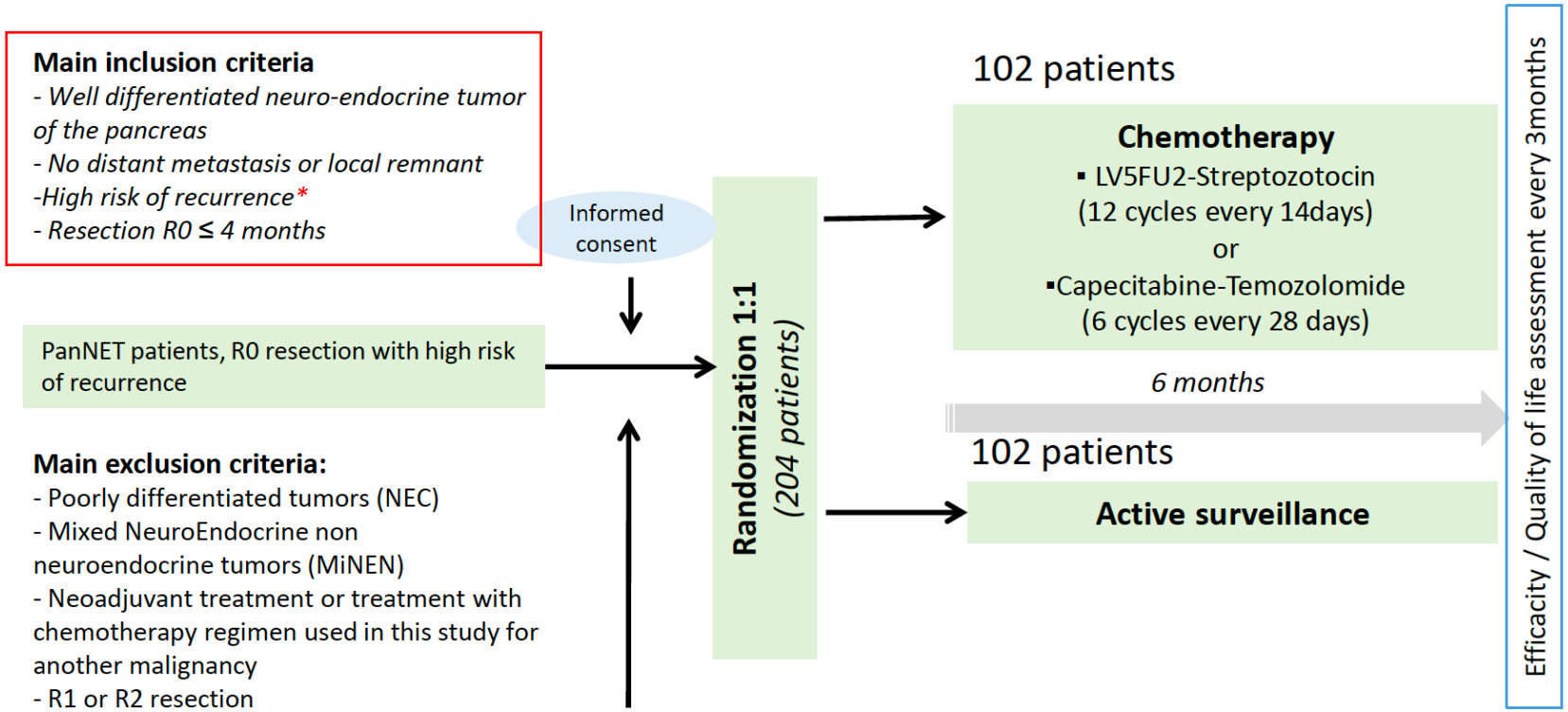
- Etude Rétrospective.
- Multicentrique.
- TNE pancréatiques opérées.
- Stades I-III.
- Exclusion des patients R2.

- Etude négative.



ADJUPanNET-1: Study design

PanNET patients, Phase III, 204 patients with molecular companion study



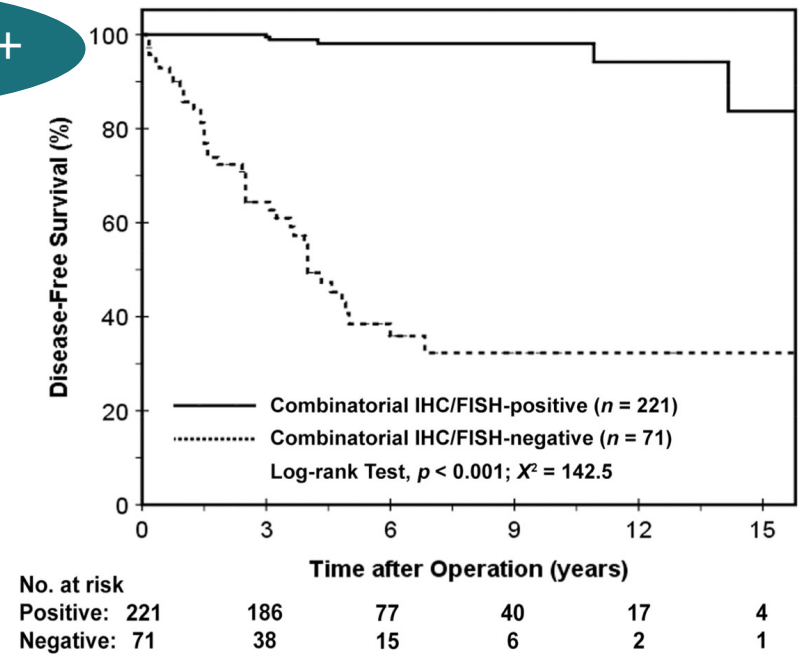
High risk of recurrence as defined by the following situations:

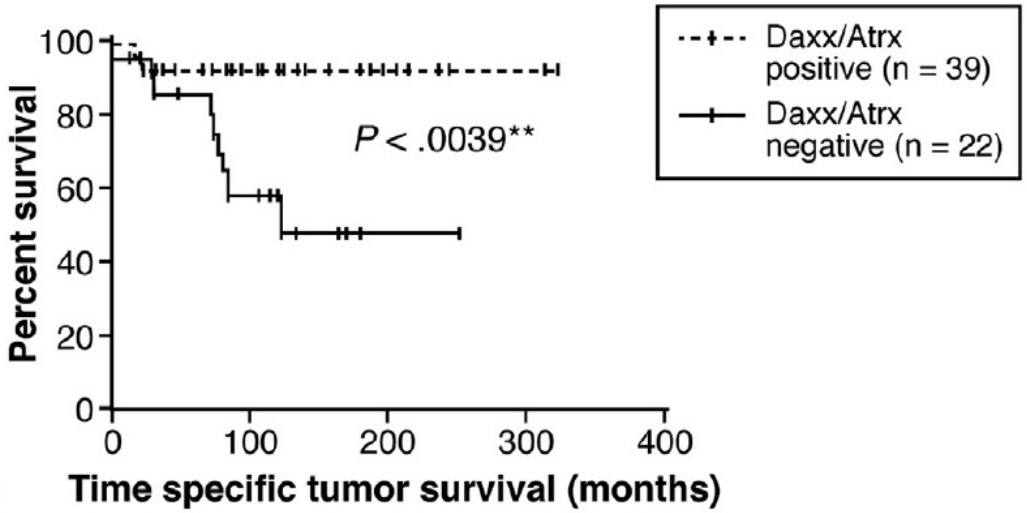
- Ki67 ≥ 10% (i.e. : Grade 3 or high Ki67 Grade 2)
- Ki67 5-9% combined with 1 pejorative prognostic parameter among:T size > 3 cm or Positive lymph node
- Ki67 > 3% combined with : -2 pejorative prognostic parameters among ,T Size > 3 cm, and Positive lymph node or ,3 pejorative prognostic parameter among, presence of angio-perineural invasion and or, tumor-related symptom and T Size > 3 cm, or Positive LN

L'AVENIR ?

- Marqueurs biologiques prédictifs de récidive.
- Mutations protéines :
  - **DAXX** (domaine de mort)
  - **ATRX** (réparation télomères)
- Corrélées avec augmentation risque de récidive et mortalité.

Rétrospectif sur M+





Marinoni et al, Gastroenterology, 2014

Roy et al, Gastroenterology, 2018

EN CONCLUSION

- Bénéfice probable d'un traitement adjuvant dans les Pan-NET.
- Nécessité de sélectionner les malades pouvant bénéficier de l'adjuvant.
- **Place des marqueurs moléculaires ?**

- Essai prochain du GTE : **ADJUPanNET-1**

Groupe d'étude des Tumeurs Endocrines

MERCI POUR VOTRE ATTENTION