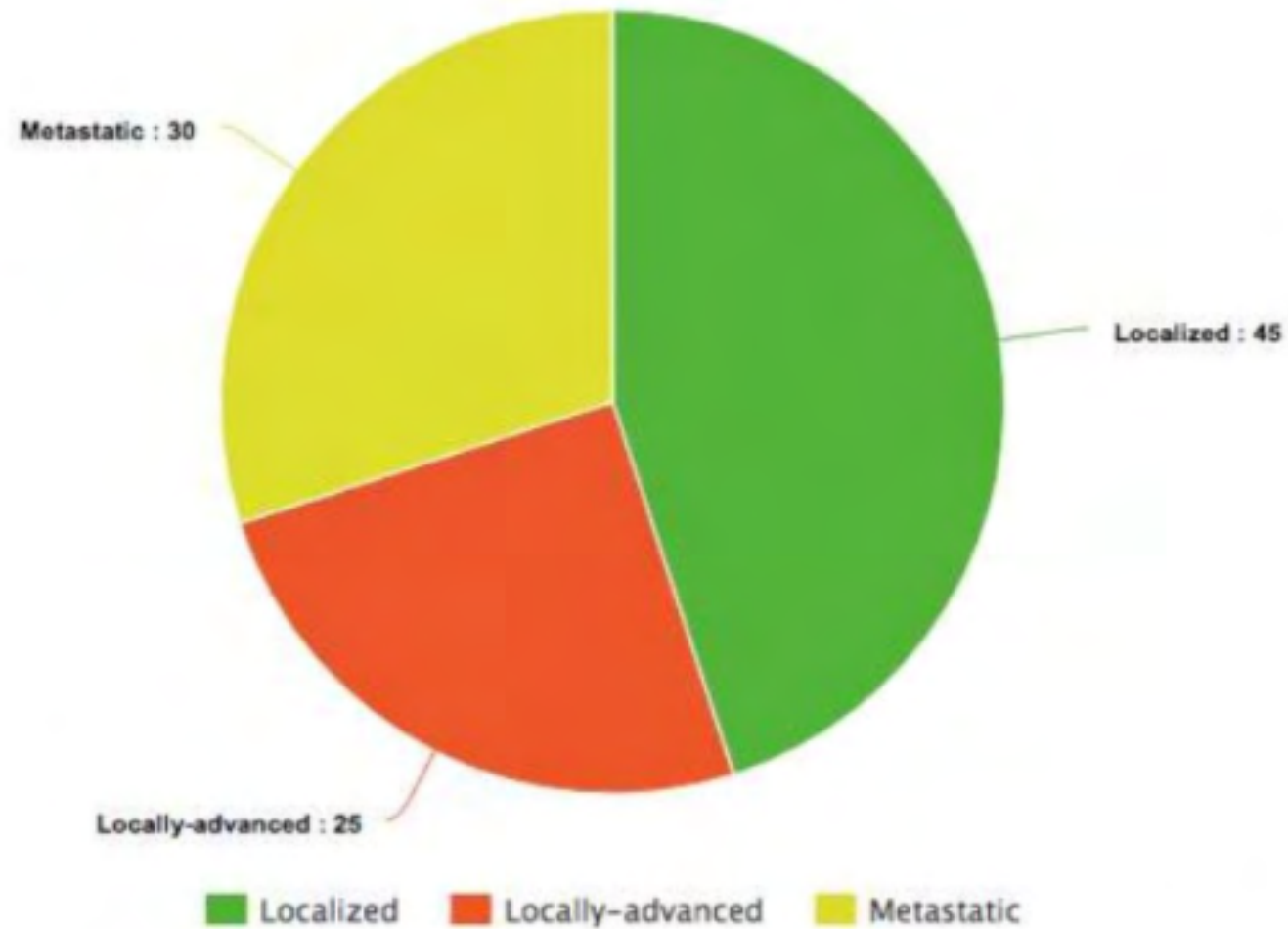


REUNION PATIENTS REIN 2022

Faut il un traitement après l'ablation de la tumeur du rein?

Gwenaëlle Gravis
Oncologue médicale
Institut Paoli-Calmettes
Marseille
12/01/2022

REPARTITION DES STADES AU DIAGNOSTIQUE

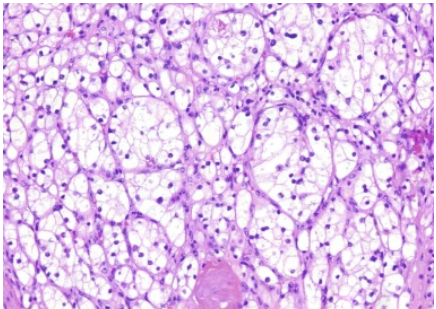
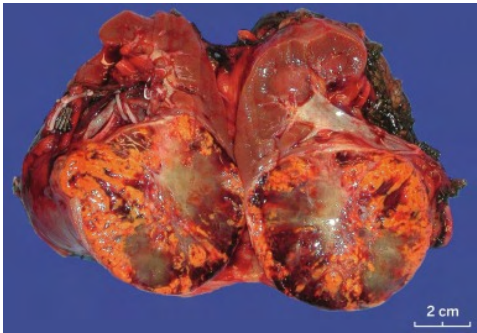
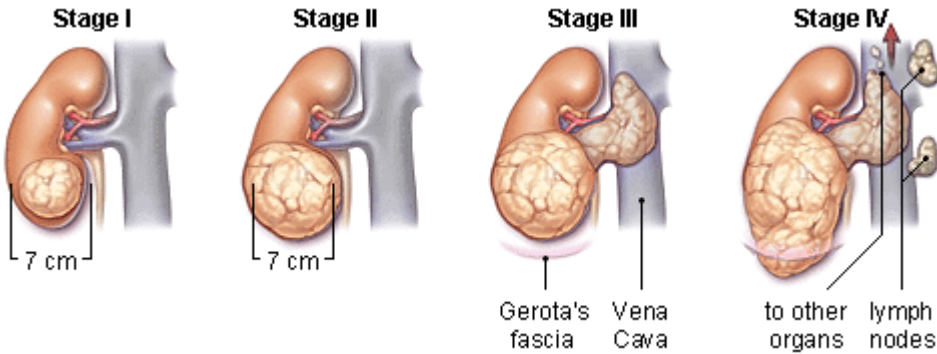


1. National Cancer Institute. SEER cancer statistics fact sheet: cancer of the kidney and renal pelvis. Accessed 2009;
2. Flanigan RC et al. Curr Treat Options Oncol 2003;4:385–90.

EVALUATION DES RISQUES DE RECHUTE ET/OU DE DUREE DE VIE

Leibovich Risk Score

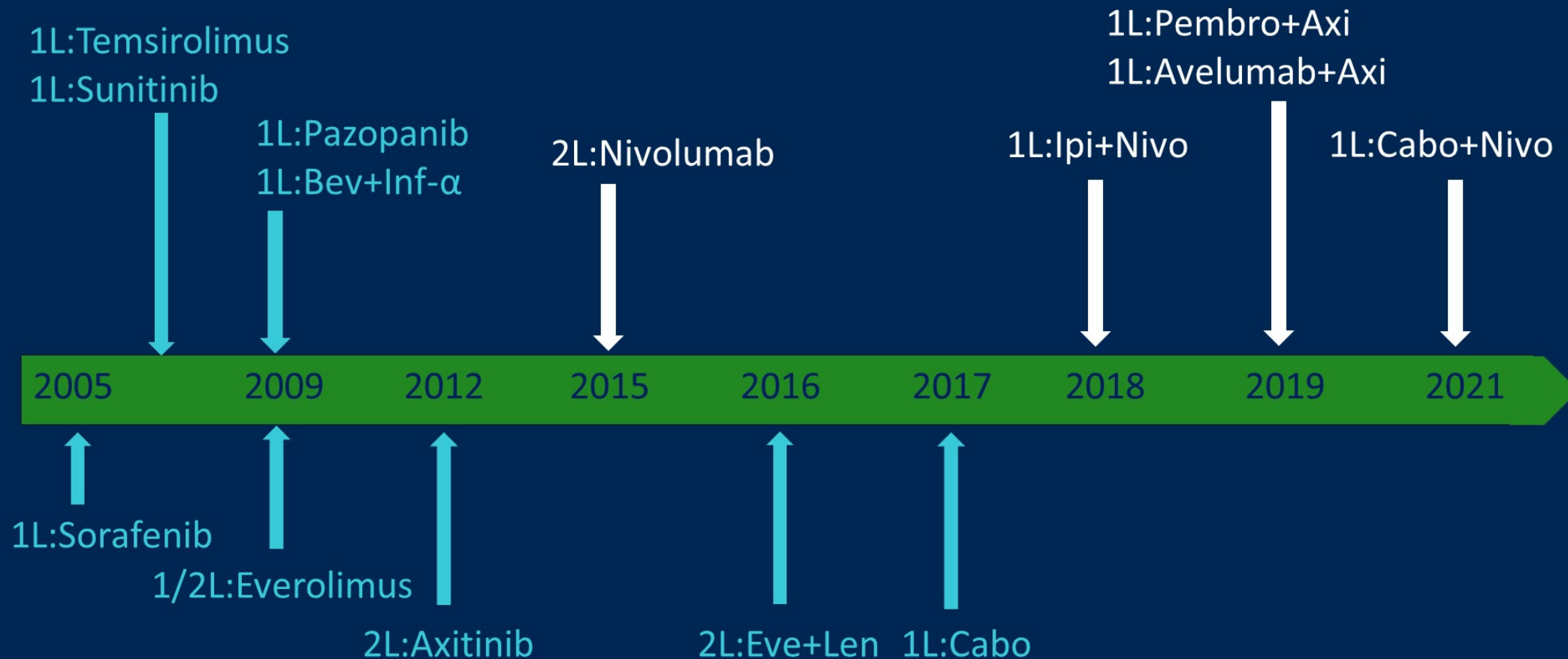
Scoring Algorithm to Predict Metastases After Radical Nephrectomy in Patients with ccRCC			
Primary Tumour Status (T)		Score	
pT1a		0	
pT1b		2	
pT2		3	
pT3a		4	
pT3b		4	
pT3c		4	
pT4		4	
Regional Lymph Node Status (N)		Score	
pNX		0	
pN0		0	
pN1		2	
pN2		2	
Tumour Size (cm)		Score	
<10		0	
≥10		1	
Nuclear Grade		Score	
1		0	
2		0	
3		1	
4		3	
Histologic Tumour Necrosis		Score	
No		0	
Yes		1	
Risk Groups			
Group		Score	
Low		0–2	
Intermediate		3–5	
High		≥6	
Estimated Metastasis-Free Survival Rate (%)			
Risk Group	Year One	Year Five	Year Ten
Low	99.5	97.1	92.5
Intermediate	90.4	73.8	64.3
High	57.7	31.2	23.6



UCLA Integrated Staging System (UISS)

UISS			
Risk Group	TNM Stage	Grade	ECOG
Low	I	1,2	0
Intermediate	I	1,2	≥1
	I	3,4	0
	I	3,4	≥1
	II	Any	Any
	III	I	0
	III	I	≥1
High	III	>I	0
	IV	Any	Any
OS (%)			
Risk Group	Year One	Year Three	Year Five
Low	97.5	90.5	83.8
Intermediate	95.4	81.6	71.9
High	84.4	55.5	44.0
Disease-Specific Survival (%)			
Risk Group	Year One	Year Three	Year Five
Low	100	94.9	91.1
Intermediate	97.2	87.7	80.4
High	89.0	63.7	54.7

LE CANCER DU REIN METASTATIQUE A CELLULES CLAIRES



1992: HD IL-2

Inf- α = Interferon α ; Bev = Bevacizumab; Ipi = Ipilimumab; Cabo = Cabozantinib

PRESENTED AT:

Genitourinary
Cancers Symposium

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PRESENTED BY: Stephanie Berg

#GU21

TRAITEMENT ADJUVANT

- Patients ayant un cancer du rein localisé opéré ayant un risque de rechute
- Objectifs :
 - Réduire les risque de rechute
 - Améliorer la durée de vie/ prise en charge standard
 - Ne pas sur traiter
 - Ne pas être trop toxique

AVANT LES TKI

Study	N	Intervention	Primary Endpoint(s)	Outcome
Clark et al 2003 ²³	69	IL-2 vs observation	DFS	Closed early; interim analysis non-significant (P=0.73)
Messing et al 2003 ²⁴	283	IFN- α vs observation	OS	Non-significant (P=0.09)
Pizzocaro et al 2001 ²⁵	247	IFN- α 2b vs observation	OS, EFS	Non-significant (P=0.86 for OS, 0.11 for EFS)
Passalacqua et al 2014 ²⁶	303	IL-2 + IFN- α vs observation	RFS	Non-significant (P=0.44)
Atzpodiën et al 2005 ²⁷	203	IL-2 + IFN- α 2a + 5-FU vs observation	RFS	Non-significant (P=0.24)
Aitchison et al 2014 ²⁸	309	IL-2 + IFN- α 2a + 5-FU vs observation	DFS	Non-significant (P=0.23)
Kjaer et al 1987 ⁸⁶	65	Radiotherapy vs observation	RFS, OS	Non-significant (P>0.05)
Pizzocaro et al 1987 ⁸⁷	120	Medroxyprogesterone acetate vs observation	RFS	Non-significant (P not presented)
Naito et al 1997 ⁸⁸	66	UFT (tegafur and uracil 1:4) vs observation	NRR, RCC-specific survival rate	Non-significant (P not presented)
Adler et al 1987 ²⁹	43	Autologous irradiated tumour cells + hormonal therapy vs hormonal therapy alone	PFS	Non-significant (P<0.1)
Jocham et al 2004 ³¹	379	Autologous irradiated tumour cells vs observation	PFS	Significant, favouring vaccine group (P=0.02)
Galligioni et al 1996 ³⁰	120	Autologous irradiated tumour cells vs observation	DFS, OS	Non-significant (P=0.21 for DFS, 0.28 for OS)
Wood et al 2008 ³²	818	Autologous, tumour-derived heat-shock protein (glycoprotein 96)-peptide complex therapeutic vaccine vs observation	RFS	Non-significant (P=0.51)
Chamie et al 2017 ³³	864	Girentuximab vs placebo	DFS, OS	Non-significant (P=0.74 for DFS, 0.94 for OS)

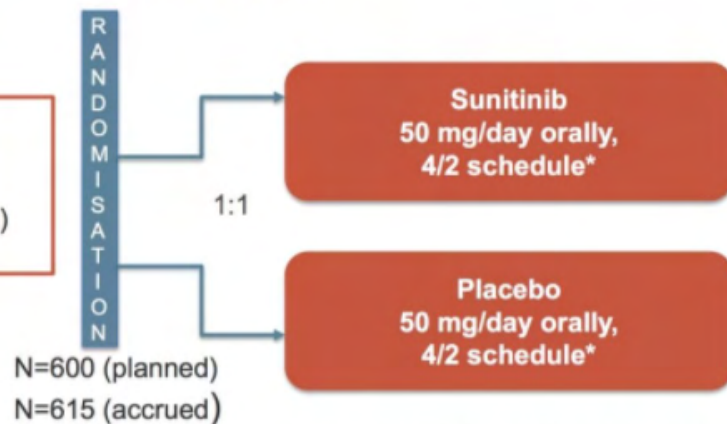
ETUDES DE PHASE III DE TKI EN ADJUVANT

Trial	Arms	Years	N	Primary Endpoint	Clear Cell Only	Eligibility	Hazard Ratio Confidence Interval
ASSURE (Haas, Lancet, 2016)	Sunitinib vs. Sorafenib vs. Placebo*	1	1943	DFS	No	pT1bG3-4N0, pT2-4GxN0, TxGxN+	Sunitinib – 1.02 (97.5% CI 0.85-1.23) Sorafenib – 0.97 (97.5% CI 0.80-1.17)
STRAC (Ravaud, NEJM, 2016)	Sunitinib vs. Placebo	1	615	DFS	Yes	pT3-4GxN0-x, TxGxN1-2	0.76 (95% CI 0.59-0.98)
PROTECT (Motzer, JCO, 2017)	Pazopanib vs. Placebo*	1	1538	DFS	Yes	pT2G3-4N0, pT3-4N0, pTxN1	0.86 (95% CI 0.70-1.06)
ATLAS (Gross-Goupil, Ann Oncol, 2018)	Axitinib vs. Placebo	1-3	724	DFS	Yes	pT2-4GxN0, pTxN1	0.870 (95% CI 0.66-1.147)
SORCE (Eisen, JCO, 2020)	Sorafenib vs. Placebo)*	1-3	1711	DFS	No	Leibovich score 3-11	1.01 (95% CI 0.83-1.23)
EVEREST	Everolimus vs. Placebo	1	1545	RFS	No	pT1bG3-4N0, pT2-4N1	Pending

Study Design

Clear Cell RCC

- Stratified by
- UISS risk groups
 - ECOG PS (<2 vs.2)
 - Country

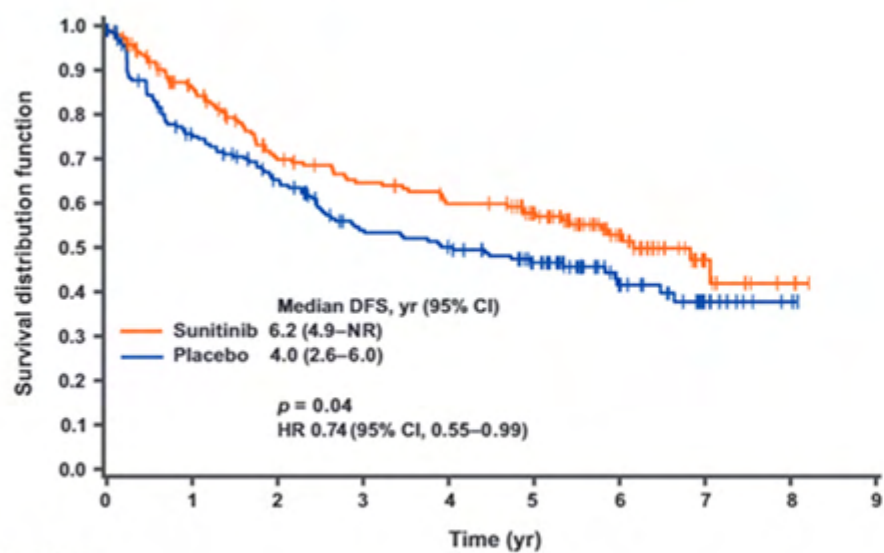


*Dose reduction only to 37.5 mg/day allowed

Ravaud A, S-TRAC, NEJM, 2016

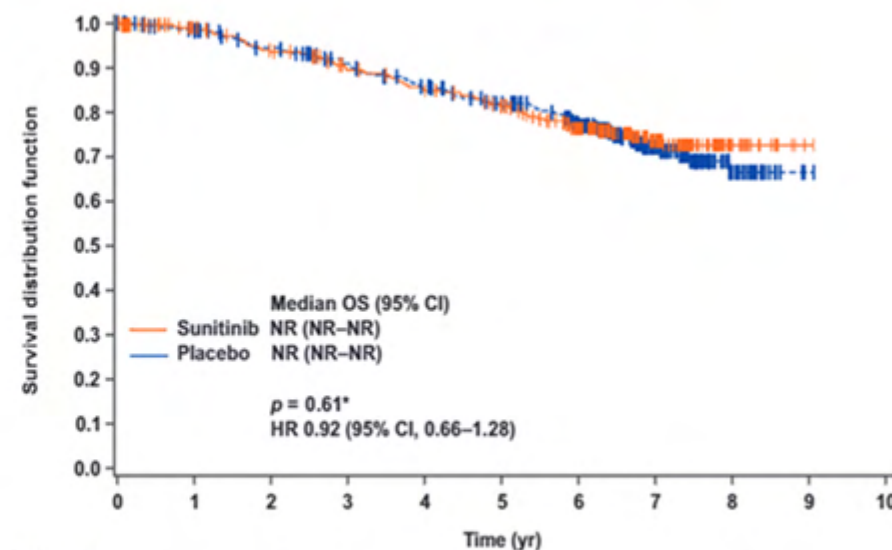
ETUDE STRAC

Disease-Free Survival



No. at risk									
Sunitinib	194	143	109	98	89	75	40	10	3
Placebo	194	134	110	83	76	60	28	10	2

Overall Survival



No. at risk										
Sunitinib	309	278	258	236	222	205	160	82	16	1
Placebo	306	289	269	250	231	210	172	82	23	1

Median follow-up 6.6 years in the sunitinib arm and 6.7 years in the placebo arm

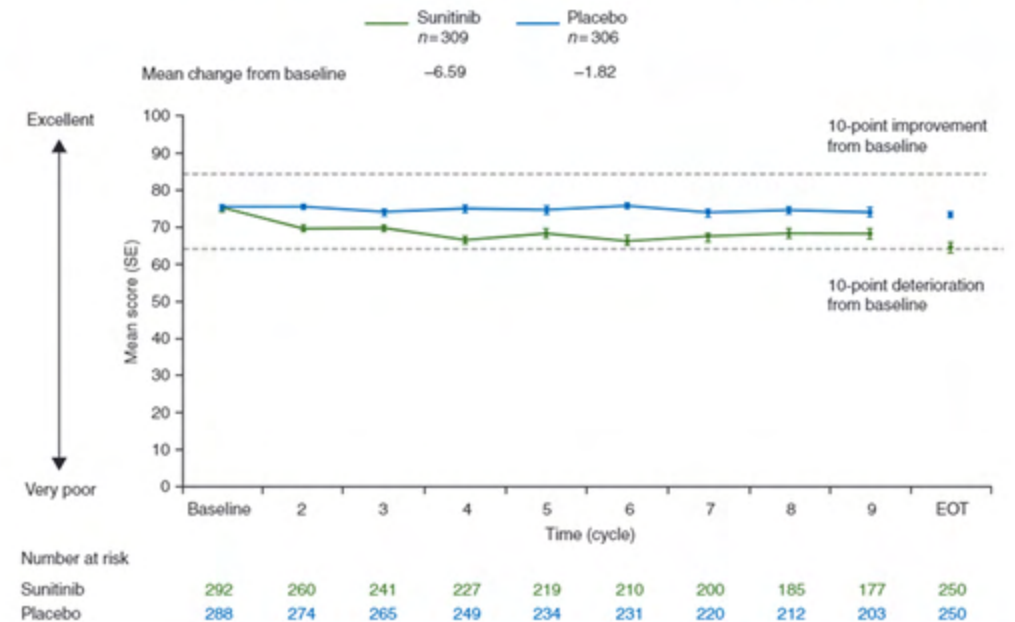
Ravaud A et al NEJM 2016

Motzer B et al Europ Urol 2018

STRAC toxicités et qualité de vie du SUTENT vs Placebo

Toxicity Parameter	Sunitinib Arm
Any Attribution Grade 3 AE	48%
Any Attribution Grade 4 AE	12%
Dose Reduction	34%
Dose Interruption	46%
Completed 1-year of Therapy	56%
Treatment DC due to AE	28%

EORTC QLQ-C30: Global Health Status Domain



Ravaud A et al NEJM 2016

Staelher et al Annal Oncol 2018

PLUSIERS ETUDES INTERNATIONALE D'IMMUNOTHERAPIE EN COURS

Trial	Sample Size	Inclusion Criteria	Treatment	Primary Endpoint	Expected Results
IMmotion010	778	pT2G4, pT3aG3-4, pT3b-T4Gx, pTxN1, pTxNxM1 (resected to NED*); clear cell	Atezolizumab vs. placebo	DFS	1/2022
CheckMate 914	1600	pT2aG3-4N0, pT2b-T4GxN0, pTxGxN1; clear cell	Nivolumab + ipilimumab vs. nivolumab + placebo vs. placebo	DFS	1/2023
Prosper	766	T2Nx, TxN1, TxNxM1 (resected to NED); any RCC histology	Nivolumab vs. observation	EFS	11/2023
RAMPART	1750	Leibovich score 3-11; any RCC histology	Durvalumab + tremelimumab vs. durvalumab vs. observation	DFS, OS	7/2024

*Metachronous pulmonary, lymph node, or soft tissue recurrence >12 months from nephrectomy; CPI=Checkpoint inhibitors; RCC=Renal cell carcinoma; NED=No evidence of disease; DFS=Disease-free survival; EFS=Event-free survival; OS=Overall survival.

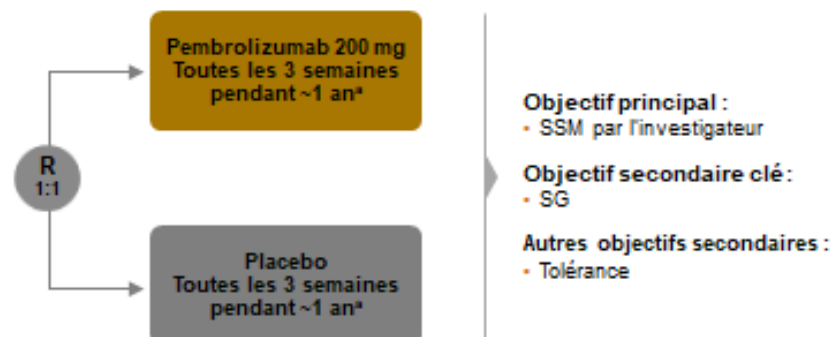
KEYNOTE-564 Schéma de l'étude

Principaux critères d'éligibilité

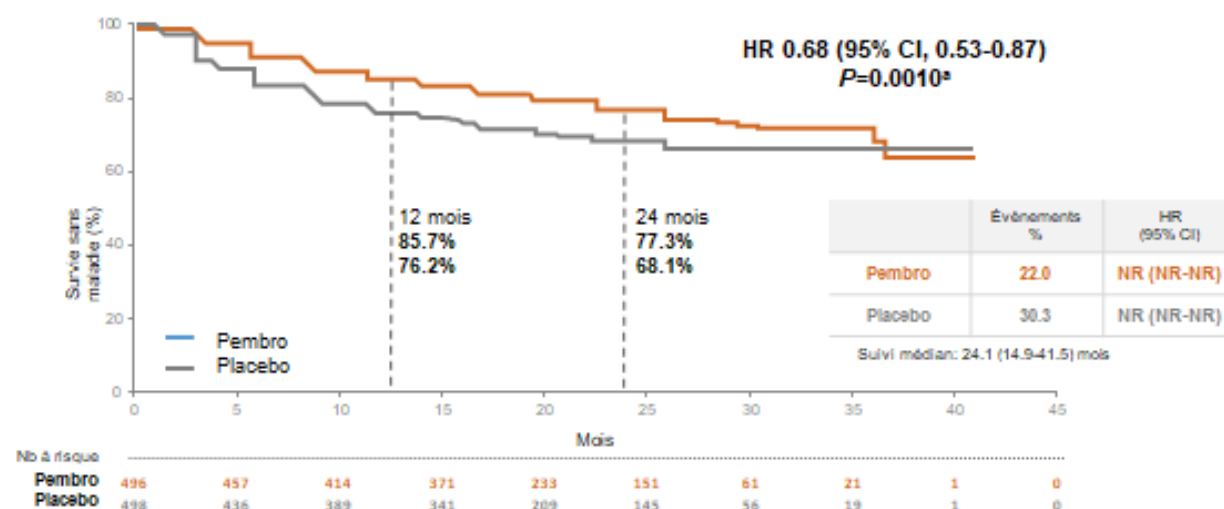
- Diagnostic histopathologique de carcinome renal à cellules claires
- Néphrectomie et/ou métastasectomie ≤12 semaines avant la randomisation
- Pas de traitement systémique antérieur
- ECOG PS 0 ou 1
- Echantillon de tissu disponible pour évaluation du statut PD-L1

Facteurs de stratification :

- M0 vs M1 NED
- Stratification du groupe M0 :
 - ECOG PS 0 vs 1
 - US vs non-US



Survie sans maladie

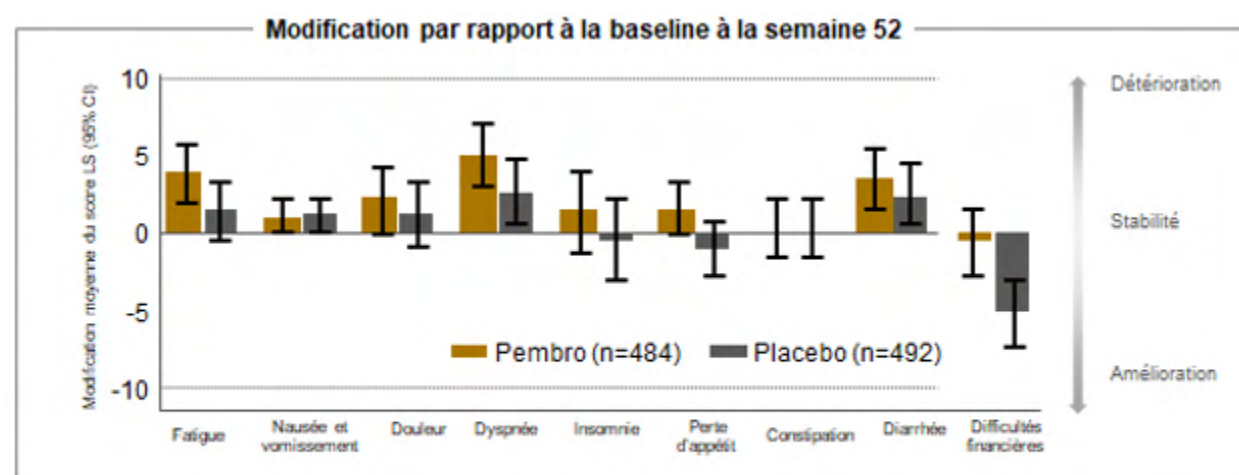
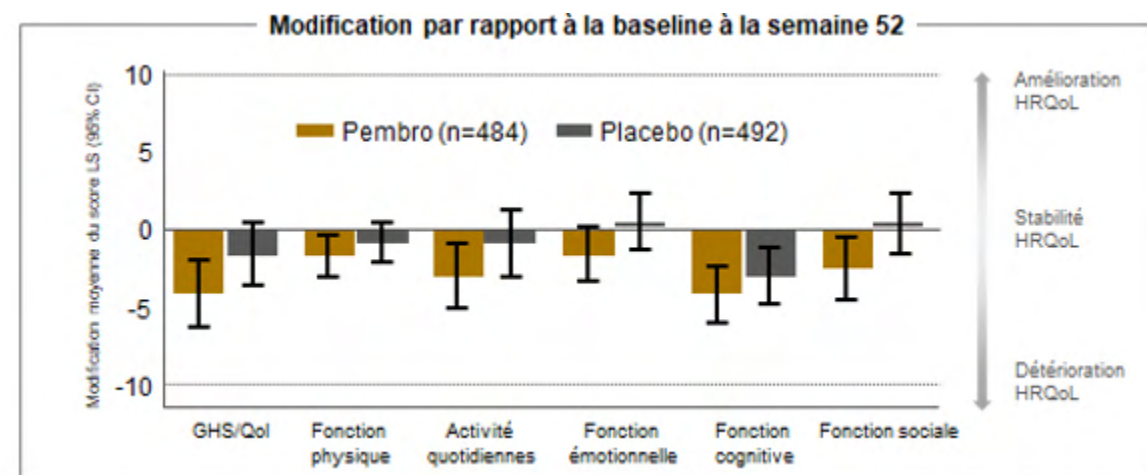


TOLERANCE

Participants avec 1EI, n (%)	Pembro N = 488	Placebo N = 496
Els de toutes causes	470 (96.3)	452 (91.1)
Grade 3-5	158 (32.4)	88 (17.7)
Responsable d'un arrêt de traitement	101 (20.7)	10 (2.0)
Responsable du décès	2 (0.4)	1 (0.2)
Els graves de toutes causes	100 (20.5)	56 (11.3)
Responsable d'un arrêt de traitement	49 (10.0)	5 (1.0)
Els reliés au traitement	386 (79.1)	265 (53.4)
Grade 3-5	92 (18.9)	6 (1.2)
Responsable d'un arrêt de traitement	86 (17.6)	3 (0.6)
Responsable du décès	0	0

* Els graves sont acutés, nettement en jeu le pronostic vital, nécessitent une hospitalisation, responsable du décès ou d'un handicap permanent, ou jugé grave par l'investigateur.
La durée médiane de traitement était de 11.1 (0.0-11.1) mois avec le pembro et 11.1 (0.0-11.1) mois avec le placebo.

Scores de qualité de vie QLQ-C30 Auto évaluation patient



- Les scores n'ont pas atteint le seuil de significativité clinique par rapport à la baseline (ligne pointillée) dans les 2 bras de traitements et les intervalles de confiance se superposent

Le traitement adjuvant dans le cancer du rein

- Pas de traitement adjuvant validé actuellement en FRANCE
- Le standard est la surveillance
- Les études sont en cours (à l'IPC) :
 - CHECKMATE 914
 - RAMPART

