REUNION PATIENTS REIN 2022
Faut il un traitement après l'ablation de la tumeur du rein?

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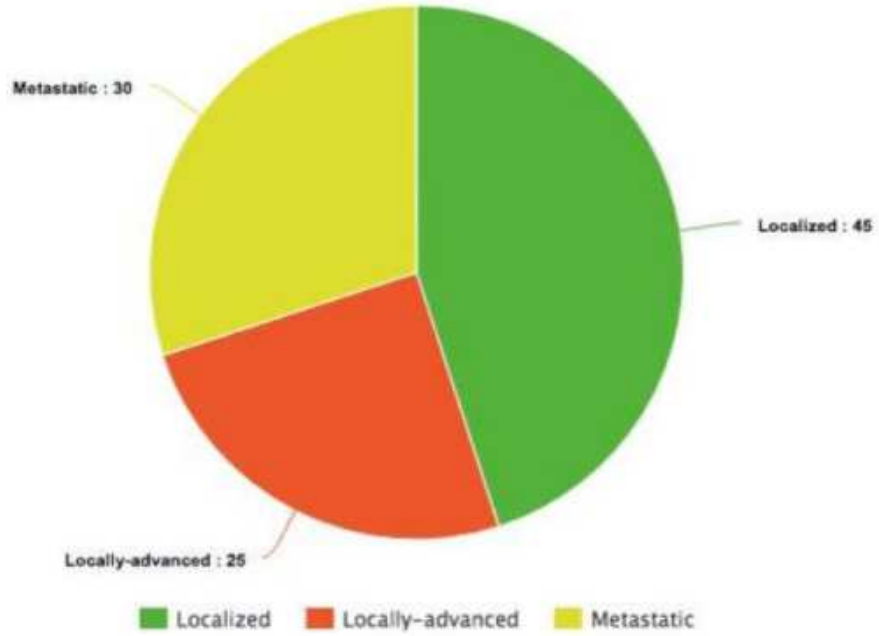
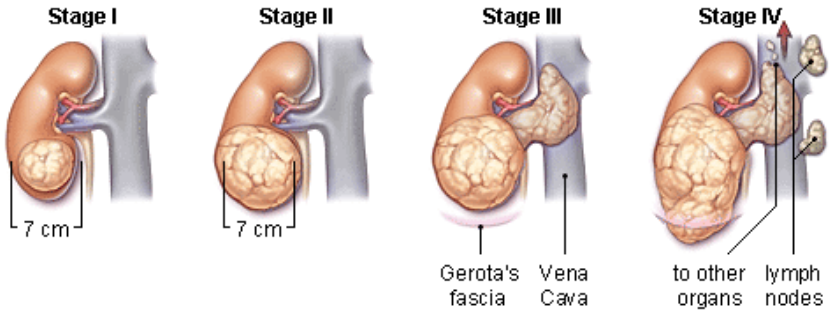
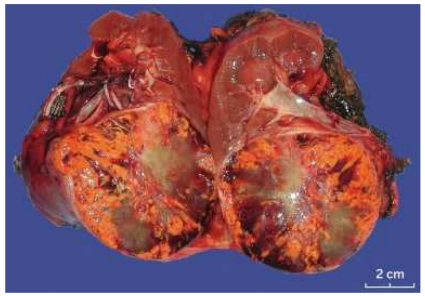


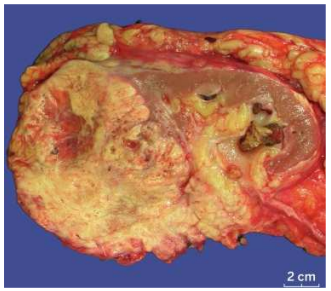
1. National Cancer Institute. SEER cancer statistics fact sheet: cancer of the kidney and renal pelvis. Accessed 2009;
2. Flanigan RC et al. Curr Treat Options Oncol 2003;4:385–90.

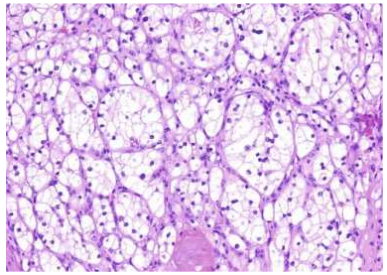
Leibovich Risk Score

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





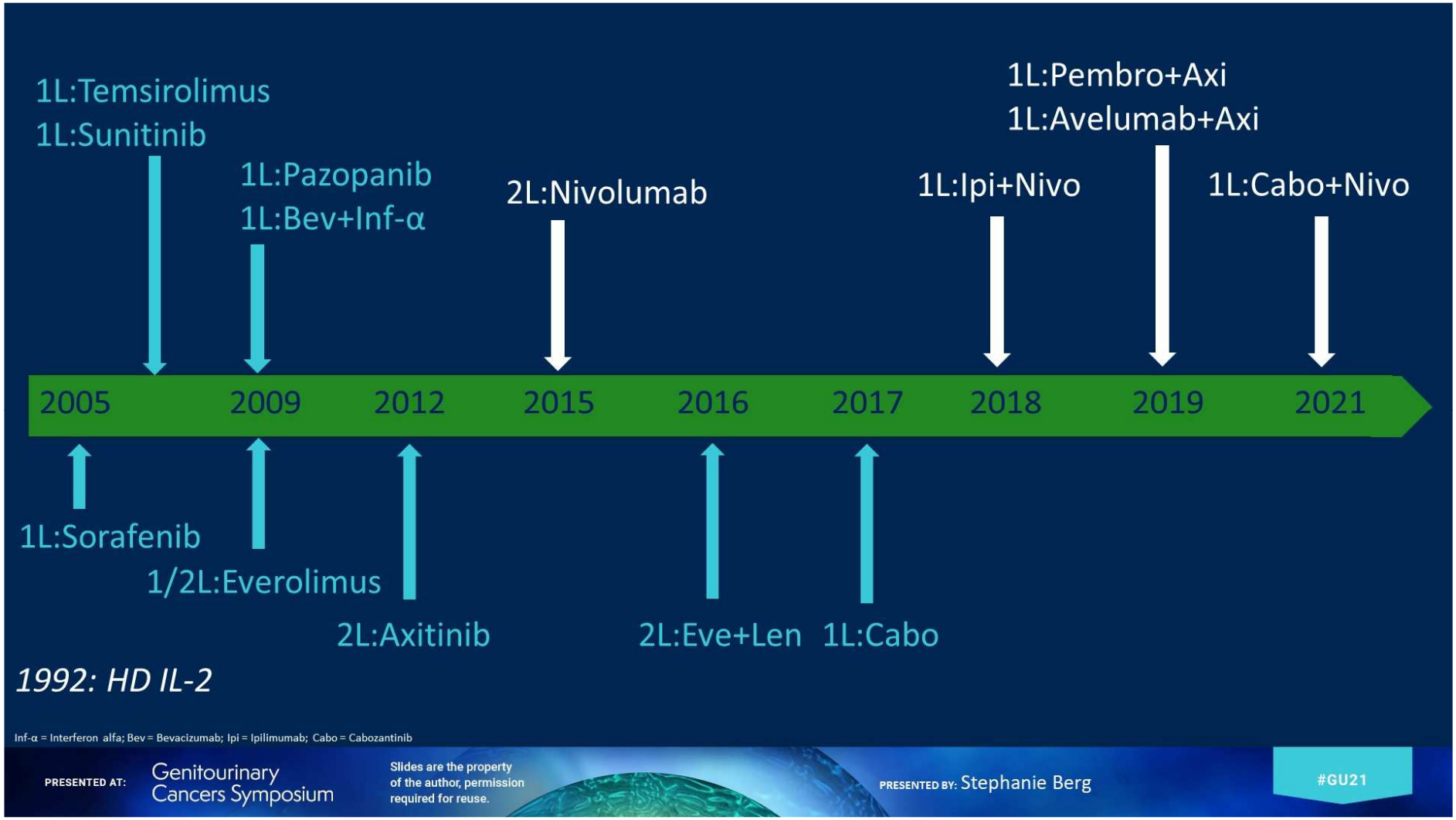




UCLA Integrated Staging System (UISS)

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
	III	>1	0
High	III	>1	≥1
	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



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

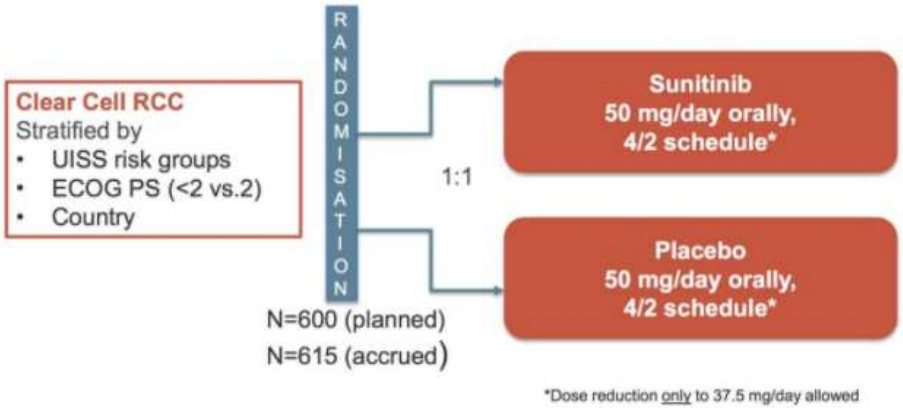
Study	N	Intervention	Primary Endpoint(s)	Outcome
Clark et al 2003[23]	69	IL-2 vs observation	DFS	Closed early; interim analysis non-significant (P=0.73)
Messing et al 2003[24]	283	IFN-α vs observation	OS	Non-significant (P=0.09)
Pizzocaro et al 2001[25]	247	IFN-α2b vs observation	OS, EFS	Non-significant (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)
Atzpodien et al 2005[27]	203	IL-2 + IFN-α2a + 5-FU vs observation	RFS	Non-significant (P=0.24)
Aitchison et al 2014[28]	309	IL-2 + IFN-α2a + 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)

Tacconi E et al OncoTargets and Therapy 2020

ETUDES DE PHASE III DE TKI EN ADJUVANT

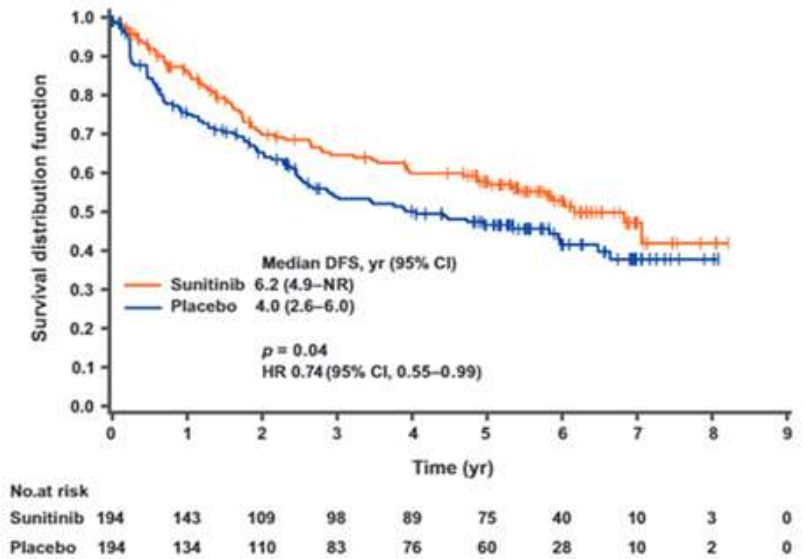
Trial	Arms	Years	N	Primary Endpoint	Clear Cell Only	Eligibility	Hazard Ratio Confidence Interval
ASSURE (Haas, Lancet, 2016)	Sunitinib vs. Sorafenib vs. Placebo*	1	1943	DFS	No	pT1bG3-4N0, pT2-4GxN0, TxGxN+	Sunitinib – 1.02 (97.5% CI 0.85-1.23) Sorafenib – 0.97 (97.5% CI 0.80-1.17)
STRAC (Ravaud, NEJM, 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

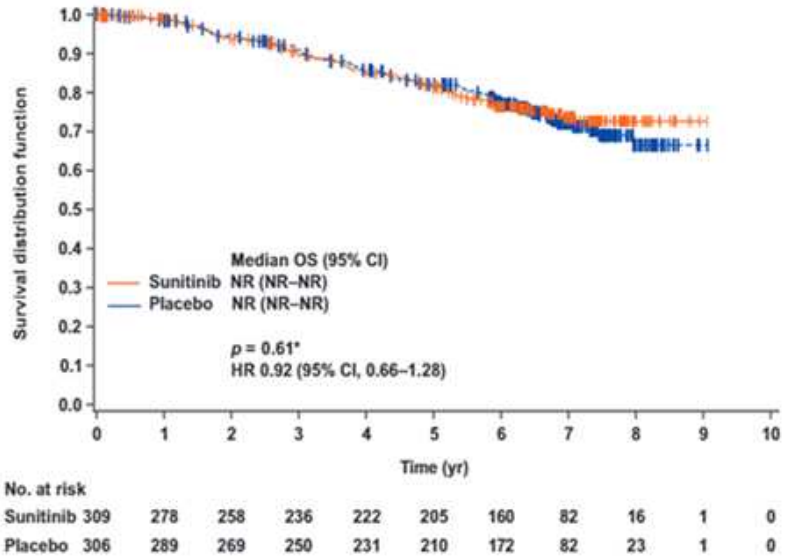


Ravaud A, S-TRAC, NEJM, 2016

Disease-Free Survival



Overall Survival

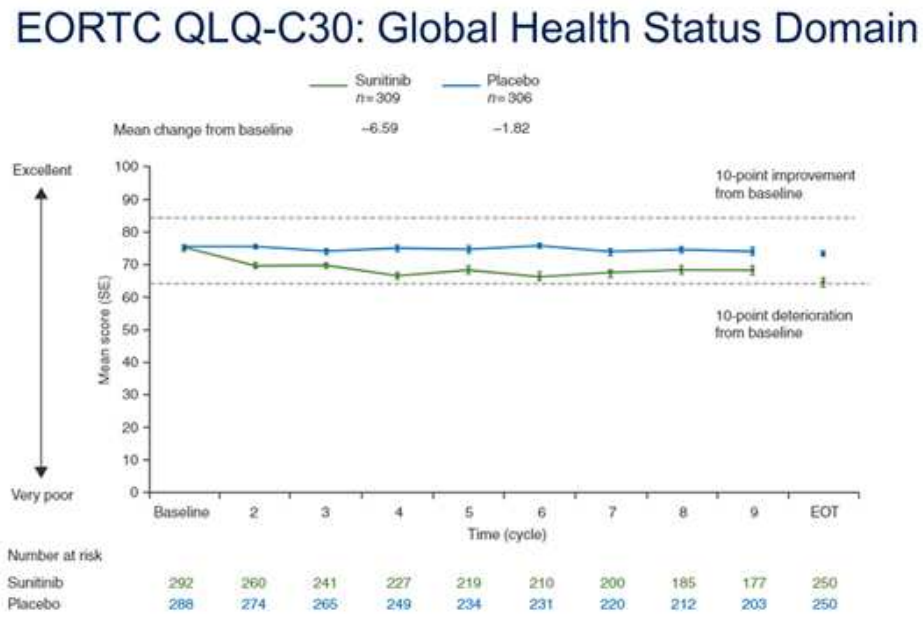


Median follow-up 6.6 years in the sunitinib arm and 6.7 years in the placebo arm

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%



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.

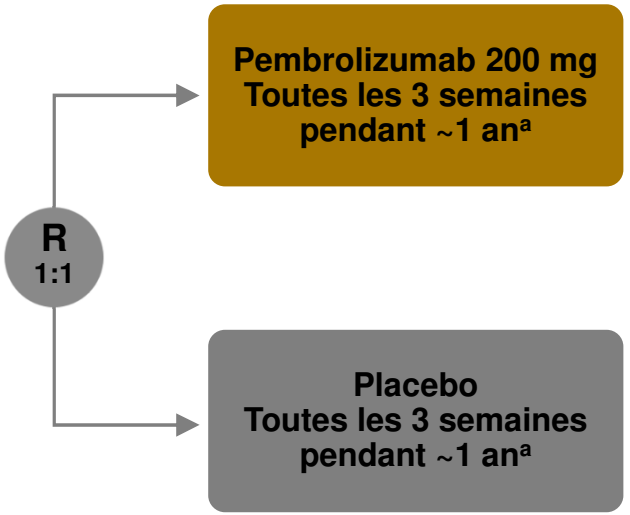
KEYNOTE-564 Schéma de l'étude

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 PS0 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 vs1
  - US vs non-US



Objectif principal :
- SSM par l'investigateur

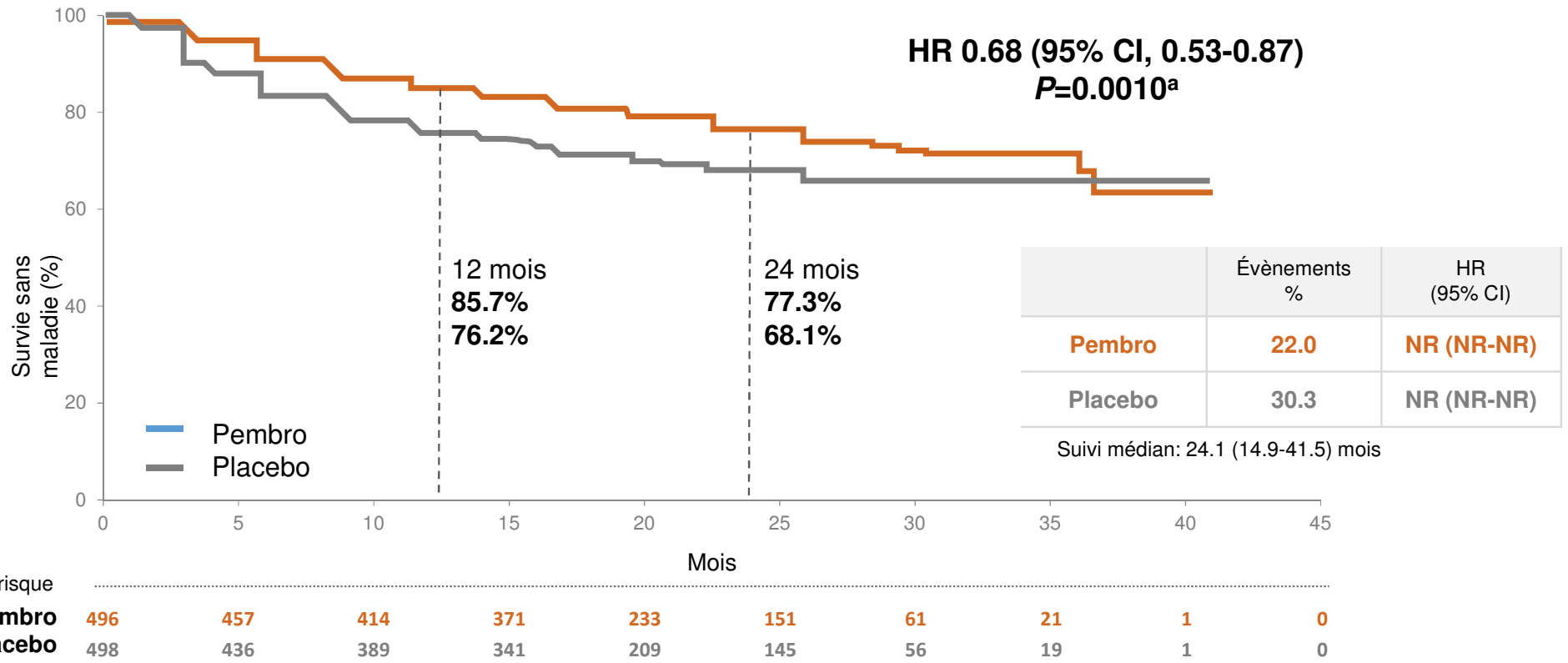
Objectif secondaire clé :
- SG

Autres objectifs secondaires :
- Tolérance

SSM : survie sans maladie. NED : no evidence of disease
[a] ≤17 cycles de traitement, equivalent à ~1 an

T.K. Choueri, et al., ASCO® 2021, Abs #LBA5

Survie sans maladie (intention de traiter)



	Évènements %	HR (95% CI)
Pembro	22.0	NR (NR-NR)
Placebo	30.3	NR (NR-NR)

Suivi médian: 24.1 (14.9-41.5) mois

[a] *Valeur préspécifiée pour significativité statistique 0.0114*

T.K. Choueri, et al., ASCO® 2021, Abs #LBA5

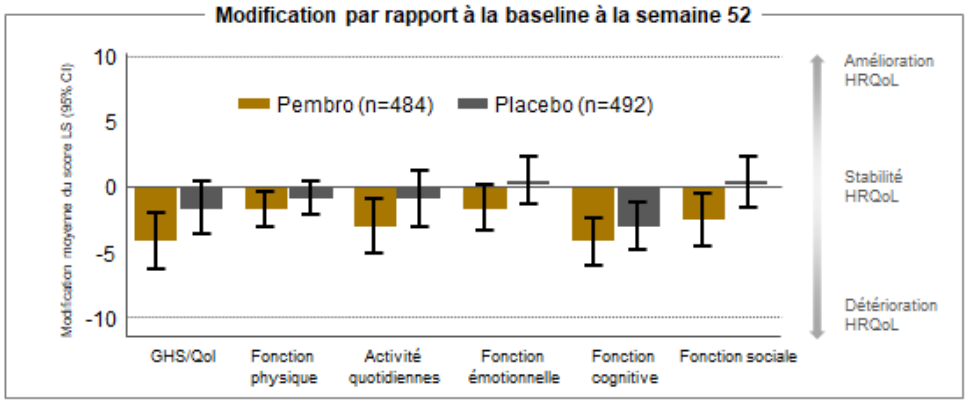
Résumé de la tolérance selon le groupe de traitement

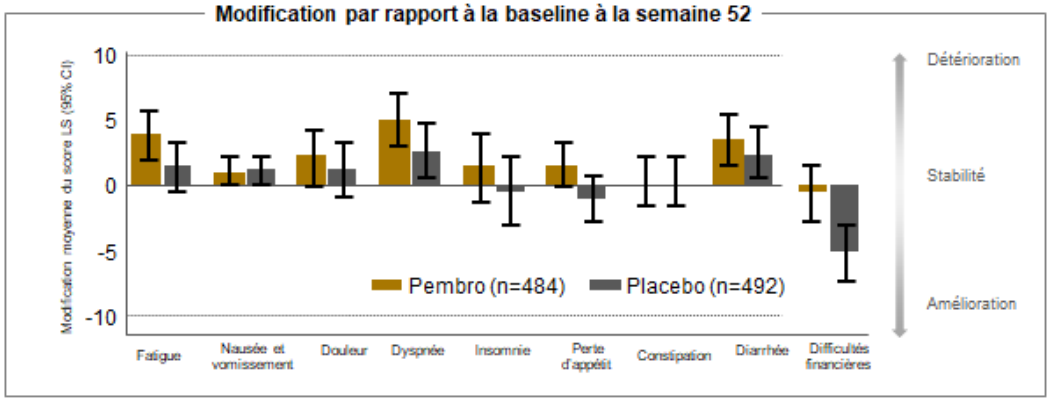
Participants avec 1EI, n (%)	Pembro N = 488	Placebo N = 496
EIs de toutes causes	**470 (96.3)**	**452 (91.1)**
Grade 3-5	158 (32.4)	88 (17.7)
Responsable d'un arrêt de traitement	101 (20.7)	10 (2.0)
Responsable du décès	2 (0.4)	1 (0.2)
EIs graves de toutes causes	**100 (20.5)**	**56 (11.3)**
Responsable d'un arrêt de traitement	49 (10.0)	5 (1.0)
EIs 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

•EIs graves sont les EIs mettant en jeu le pronostic vital, nécessitant une hospitalisation, responsable du décès ou d'un handicap persistant, ou jugé grave par l'investigateur.
La durée médiane de traitement était de 11.1 (0.0-14.3) mois avec le pembro et 11.1 (0.0-15.4) mois avec le placebo.

T.K. Choueri, et al., ESMO® 2021, Abs #653MO

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

Choueiri et al abs ESMO 2021


Bénéfices
Risques