2021 ASCO ANNUAL MEETING

ONCO NOUVELLE-AQUITAINE Réseau Régional de Cancérologie

BRIO BORDEAUX | Recherche Intégrée Oncologie

Les « scoops » en oncologie urologique

Dr Marine Gross-Goupil
Oncologie médicale – CHU Bordeaux

Dr Sabrina Falkowski
Oncologie médicale - Clinique Chénieux, Limoges

2021 ASCO ANNUAL MEETING

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Rein

Dr Marine Gross-Goupil
Oncologie médicale – CHU Bordeaux

Keynote-564 : Pembrolizumab vs placébo post néphrectomie

Cancer du Rein à cellules claires
Post néphrectomie
- **M1 réséquée**
- **pT2 grade4 ou sarcomatoide**
- **pT3-pT4, N+, tous grades**

R* (11)

Pembrolizumab 200 mg / 3 semaines IV, 14 cycles

Placébo / 3 semaines IV, 14 cycles

Obj I : SSP (inv / ITT)
Obj II : SG ITT
Et tolérance

Characteristic, n (%)	Pembro N = 496	Placebo N = 498
Age, median (range), yrs	60 (27–81)	60 (25–84)
Male	347 (70.0)	359 (72.1)
ECOG PS		
0	421 (84.9)	426 (85.5)
1	75 (15.1)	72 (14.5)
Disease risk category		
M0 intermediate-high risk	427 (86.1)[a]	433 (86.9)
M0 high risk	40 (8.1)	36 (7.2)
M1 NED	29 (5.8)	29 (5.8)

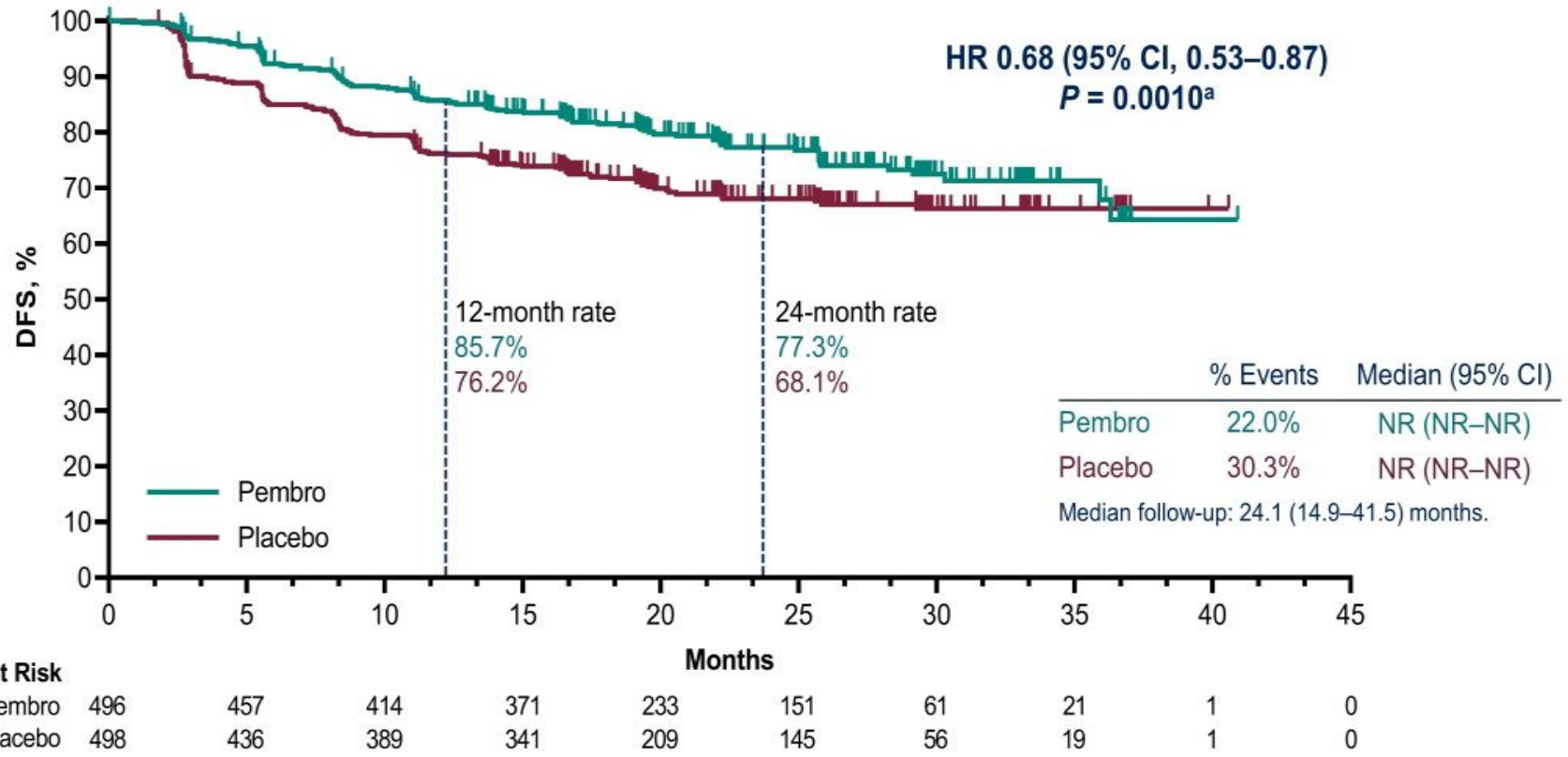
Characteristic, n (%)	Pembro N = 496	Placebo N = 498
PD-L1 status		
CPS <1	124 (25.0)	113 (22.7)
CPS ≥1	365 (73.6)	383 (76.9)
Missing	7 (1.4)	2 (0.4)
Sarcomatoid features		
Present	52 (10.5)	59 (11.8)
Absent	417 (84.1)	415 (83.3)
Unknown	27 (5.4)	24 (4.8)

Intermediate-High Risk		High Risk		M1 NED
pT2 Grade 4 or sarcomatoid N0 M0	pT3 Any grade N0 M0	pT4 Any grade N0 M0	Any pT Any grade N+ M0	NED after resection of oligometastatic sites ≤1 year from nephrectomy

Choueiri T, et al. LBA 4

Keynote-564 : Pembrolizumab vs placébo post néphrectomie

Survie Sans Maladie (Investigateur)



	% Events	Median (95% CI)
Pembro	22.0%	NR (NR–NR)
Placebo	30.3%	NR (NR–NR)

Median follow-up: 24.1 (14.9–41.5) months.

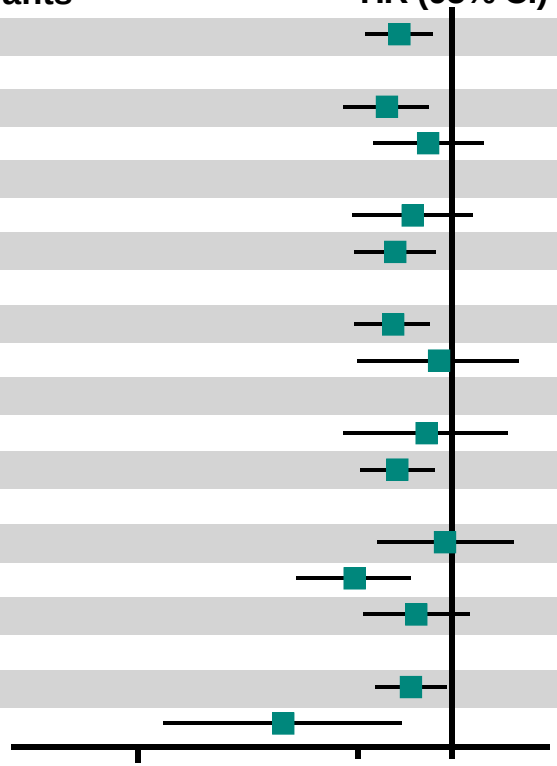
[a]Crossed prespecified p-value boundary for statistical significance of 0.0114.
ITT population included all randomized participants. NR, not reached. Data cutoff date: December 14, 2020.

Choueiri T, et al. LBA 4

Keynote-564 : Pembrolizumab vs placébo post néphrectomie

Survie Sans Maladie (Investigateur)

	Events/Participants	HR (95% CI)
Overall	260/994	0.68 (0.53-0.87)
Age		
<65 yrs	166/664	0.62 (0.45-0.84)
≥65 yrs	94/330	0.84 (0.56-1.26)
Sex		
Female	79/288	0.75 (0.48-1.16)
Male	181/706	0.66 (0.49-0.89)
ECOG PS		
0	215/847	0.65 (0.49-0.85)
1	45/147	0.91 (0.50-1.63)
PD-L1 status		
CPS <1	42/237	0.83 (0.45-1.51)
CPS ≥1	215/748	0.67 (0.51-0.88)
Region		
US	61/231	0.95 (0.58-1.57)
EU	97/375	0.49 (0.32-0.74)
Rest of world	102/388	0.77 (0.52-1.14)
Metastatic staging		
M0	234/936	0.74 (0.57-0.96)
M1 NED	26/58	0.29 (0.12-0.69)



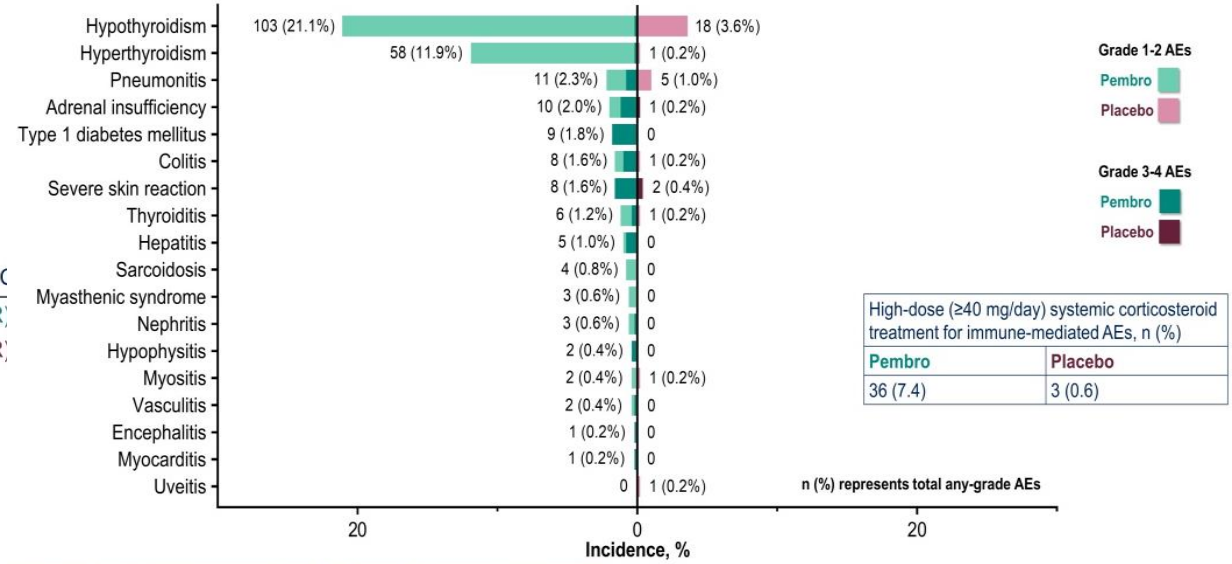
Choueiri T, et al. LBA 4

Keynote-564 : Pembrolizumab vs placébo post néphrectomie

Survie Globale*

* Analyse intermédiaire, non mature

Profil de toxicité évènements Immunoinduits



High-dose (≥40 mg/day) systemic corticosteroid treatment for immune-mediated AEs, n (%)	
Pembro	Placebo
36 (7.4)	3 (0.6)

on a prespecified list of terms included regardless of attribution to study treatment by investigator.
reactions, pembro: any grade in 7 participants (1.4%), grade 3 in 2 participants (0.4%). Infusion reactions, placebo: any grade in 5 participants (1.0%), grade 3-4 in no participants. No deaths due to
-mediated events occurred. As-treated population included all participants who received ≥1 dose of study treatment. Data cutoff date: December 14, 2020.

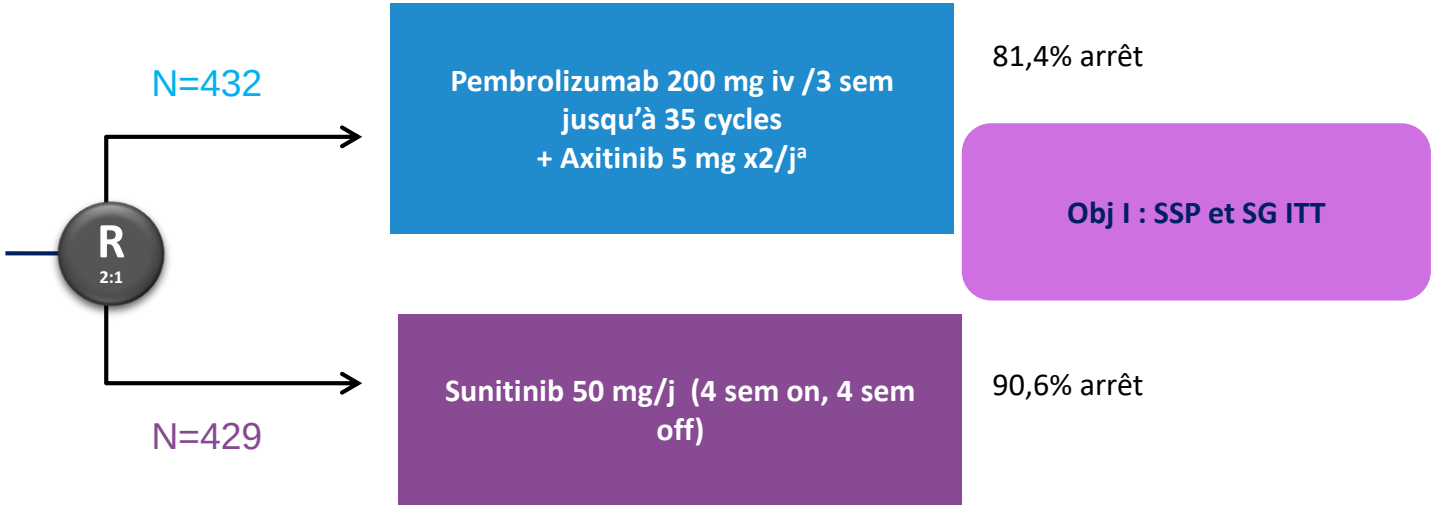
Bénéfice d'1 an de traitement par pembrolizumab post néphrectomie pour les ccRCC à risque de rechute sur la survie sans maladie

Choueiri T, et al. LBA 4

Keynote – 426 : actualisation à 42 mois

Principaux critères d'inclusion:
- RCC à cellules claires avancé ou métastatique
- 1ère ligne
- Karnofsky performance status ≥70
- Maladie mesurable (RECIST v1.1)

Stratification:
- Score IMDC (favorable vs intermédiaire vs défav.)

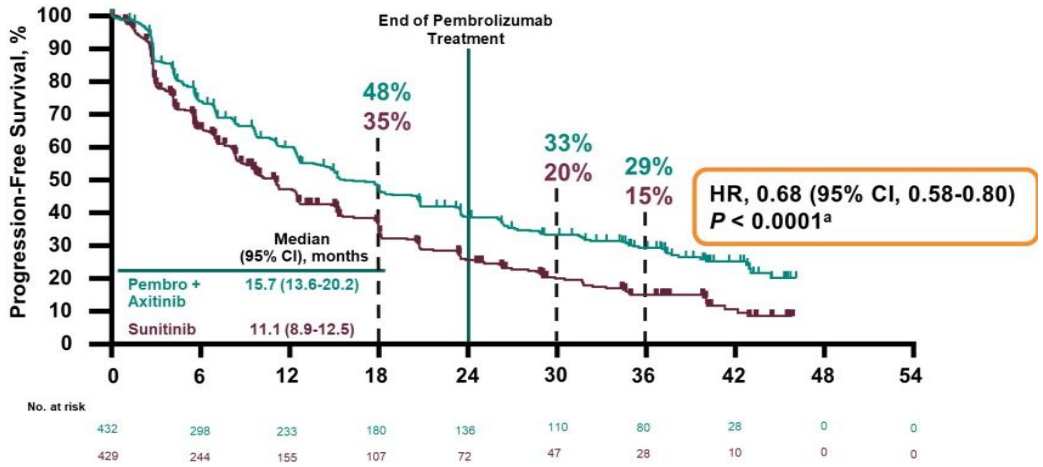


	P+A	Su
Received any subsequent therapy	**n = 349** 204 (58.4)	**n = 385** 281 (73.0)
By type of treatment	**n = 204**	**n = 281**
Any PD-1/PD-L1 inhibitor	44 (21.6)	209 (74.4)
Any VEGF/VEGFR inhibitor	180 (88.2)	193 (68.7)
Other[a]	66 (32.4)	64 (22.8)

Rini B et al. Abstr 4500

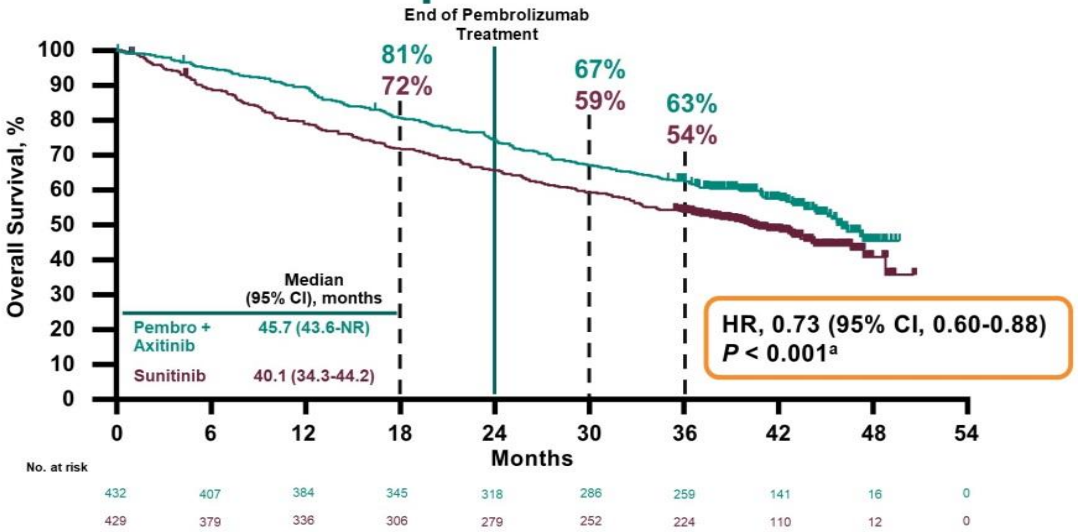
Keynote – 426

PFS in the ITT Population

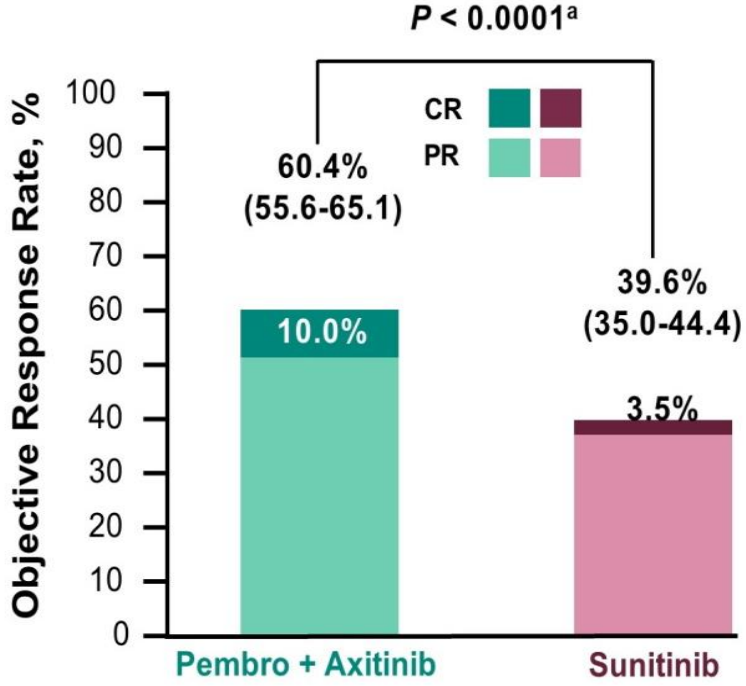


aBecause superiority of pembrolizumab + axitinib was shown at the first interim analysis, no alpha was allocated to PFS; only nominal *P* values are reported. Data cutoff: January 11, 2021.

OS in the ITT Population



aBecause superiority of pembrolizumab + axitinib was shown at the first interim analysis, no alpha was allocated to OS; only nominal *P* values are reported. Data cutoff: January 11, 2021.



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Keynote – 426 : actualisation à 42 mois

Parameter	ITT		Favorable Risk		Intermediate/Poor Risk	
	Pembro + Axitinib n = 432	Sunitinib n = 429	Pembro + Axitinib n = 138	Sunitinib n = 131	Pembro + Axitinib n = 294	Sunitinib n = 298
OS, HR (95% CI)	0.73 (0.60-0.88)		1.17 (0.76-1.80)		0.64 (0.52-0.80)	
42-month rate, %	57.5	48.5	72.3	73.0	50.6	37.6
PFS, HR (95% CI)	0.68 (0.58-0.80)		0.76 (0.56-1.03)		0.67 (0.55-0.81)	
Median, months	15.7	11.1	20.7	17.8	13.8	8.2
ORR, %	**60.4**	**39.6**	**68.8**	**50.4**	**56.5**	**34.9**
CR, %	10.0	3.5	11.6	6.1	9.2	2.3
PR, %	50.5	36.1	57.2	44.3	47.3	32.6

Rini B et al. Abstr 4500

CLEAR : Données de qualité de vie

Principaux critères d'inclusion:
RCC à cellules claires avancé ou métastatique
1ère ligne
Karnofsky performance status ≥70
Maladie mesurable (RECIST v1.1)

- Phase III, mFup :27 mois

R 1:1::1

N=355 → **Pembrolizumab 200 mg iv/3sem + Lenvatinib 20 mg / jour Pos**

N=357 → **Lenvatinib 18 mg/j + everolimus 5 mg /j**

N=357 → **Sunitinib 50 mg/j (4 sem on, 2 sem off)**

Obj I : SSP (centralisée)

Obj II : SG, taux de réponses tolérance

Study period	Pre-randomization	Randomization (21-day cycles)				
	Baseline	Treatment period				
Day	-3 to -1	Cycle 1 Day 1	Cycle 2 Day 1	Cycle 3 Day 1	Cycle 4 Day 1 to Last Cycle Day 1	Off-treatment
HRQoL	X		X	X	X	X

FKSI-DRS	EORTC QLQ-C30	EQ-5D-3L
• 9 symptoms deemed important for advanced kidney cancer	• 9 multiple-item scales (5 functional scales, 3 symptom scales, 1 GHS/QoL scale) • 6 single-item symptom scales	• Descriptive system of 5 items • A visual analog scale (VAS)
• Total score ranges from 0 to 36 • Higher scores represent better HRQoL	• Scores for all scales range from 0 to 100 • For the GHS/QoL and functional scales, a higher score corresponds to better HRQoL • For symptom scales, a higher score represents worse symptoms	• Index scores range from 0 (health state equivalent to death) to 1 (perfect health) • Higher VAS scores (0 to 100) represent better current health

Motzer RJ et al. Abstr 4502; Motzer RJ et al; Abstr 269, GUASCO2021

CLEAR : Données de qualité de vie

Mean EORTC QLQ-C30 Physical Functioning Score: LEN + PEMBRO vs SUN

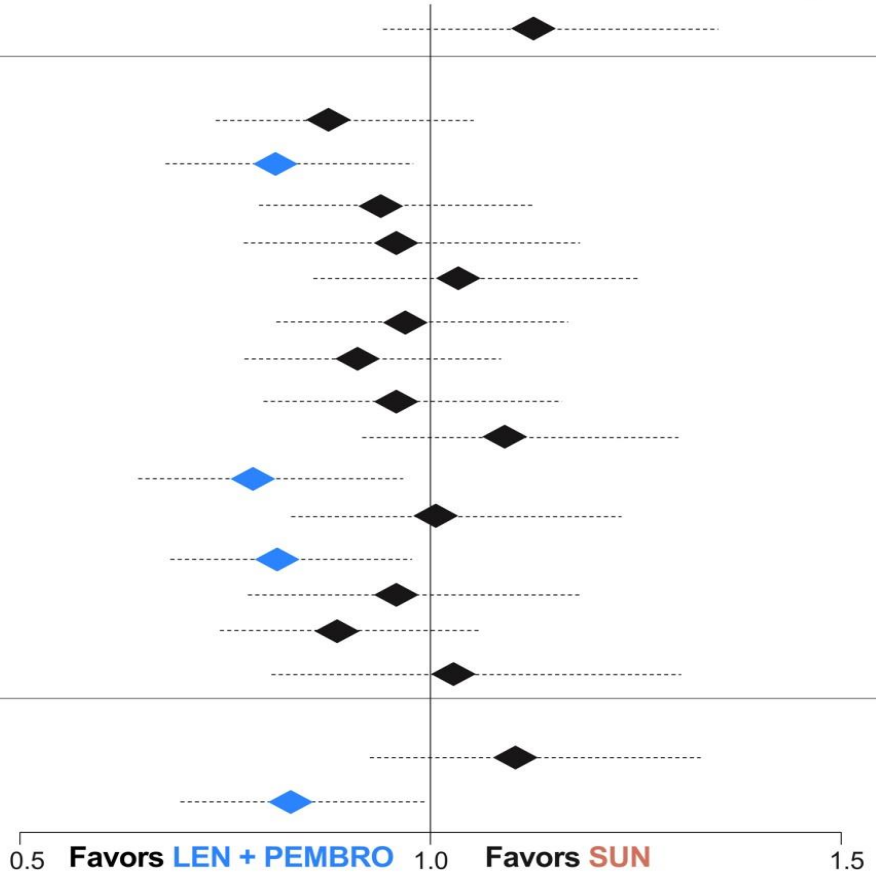
Scores for this scale range from 0 to 100. Mean follow-up time for HRQoL during treatment was 46 weeks (cycle 15).
C, cycle.

Motzer RJ et al. Abstr 4502

CLEAR : Données de qualité de vie

Time to First Deterioration[a]: LEN + PEMBRO vs SUN

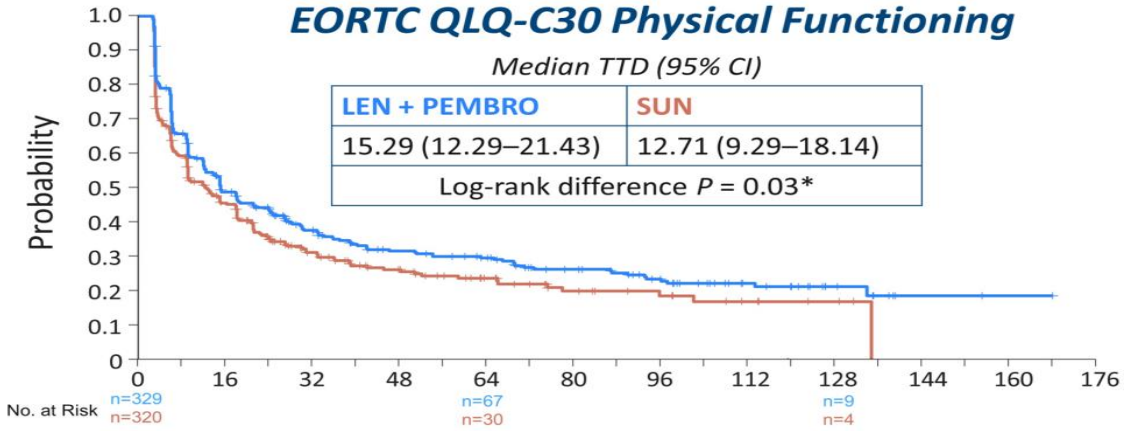
Scale	# Pts with Events L + P/S	Hazard Ratio (95% CI)
FKSI-DRS total score	265 / 218	1.13 (0.94–1.35)
EORTC QLQ-C30		
GHS/QoL	255 / 242	0.88 (0.74–1.05)
Physical functioning*	236 / 228	0.81 (0.68–0.98)
Role functioning	254 / 245	0.94 (0.79–1.13)
Emotional functioning	189 / 158	0.96 (0.77–1.18)
Cognitive functioning	232 / 199	1.04 (0.86–1.25)
Social functioning	247 / 224	0.97 (0.81–1.17)
Fatigue	279 / 265	0.92 (0.77–1.09)
Nausea and vomiting	241 / 203	0.96 (0.80–1.16)
Pain	271 / 240	1.09 (0.92–1.30)
Dyspnea*	190 / 189	0.79 (0.64–0.97)
Insomnia	217 / 184	1.01 (0.83–1.23)
Appetite loss*	251 / 233	0.82 (0.68–0.98)
Constipation	192 / 166	0.96 (0.78–1.18)
Diarrhea	266 / 232	0.89 (0.74–1.06)
Financial difficulties	158 / 118	1.03 (0.81–1.31)
EQ-5D-3L		
Index	260 / 222	1.11 (0.93–1.33)
EQ-VAS*	246 / 246	0.83 (0.70–0.99)

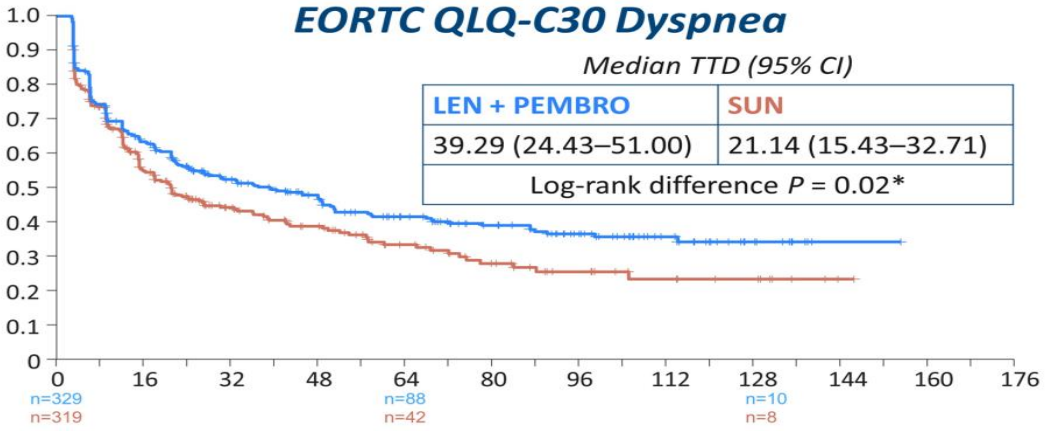


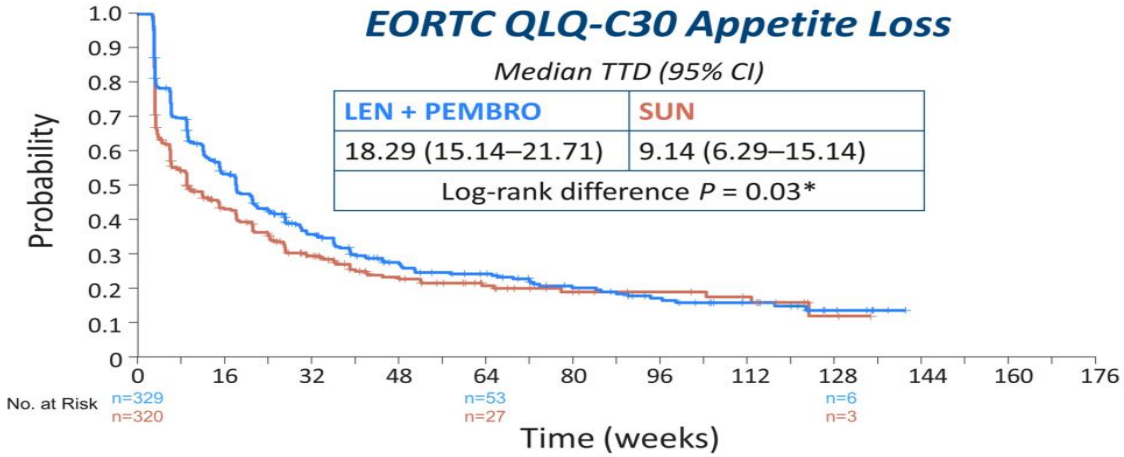
[a]The number of weeks between randomization and the first deterioration event. Thresholds used to determine deterioration: FKSI-DRS: decrease of ≥3 points; EORTC QLQ-C30 functional and GHS/QoL score: decrease of ≥10 points; EORTC QLQ-C30 symptom scores: increase of ≥10 points; EQ-5D-3L Index: decrease of ≥0.08 points, VAS: decrease of ≥7 points. *Statistically significant differences for the hazard of time to first deterioration.

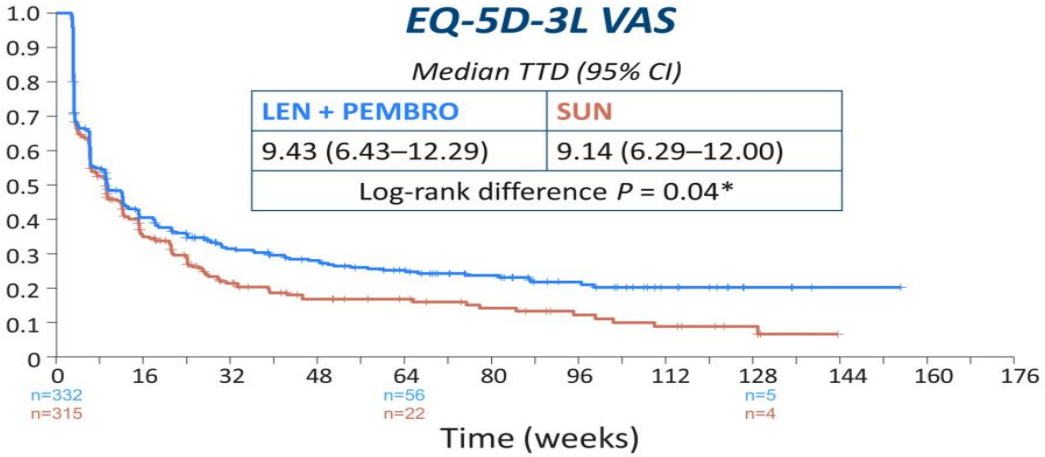
Motzer RJ et al. Abstr 4502

Time to First Deterioration[a]: LEN + PEMBRO vs SUN









[a]The number of weeks between randomization and the first deterioration event. *Statistically significant log-rank difference of distribution of time to first deterioration for LEN + PEMBRO vs SUN ($P < 0.05$). TTD, time to first deterioration.

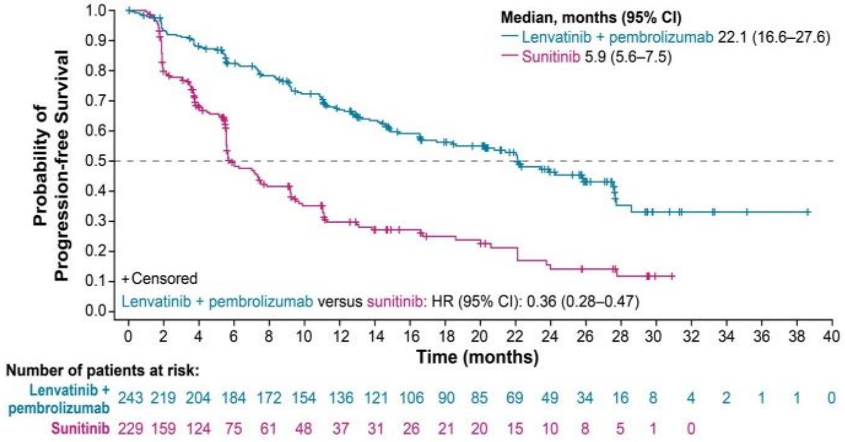
Motzer RJ et al. Abstr 4502

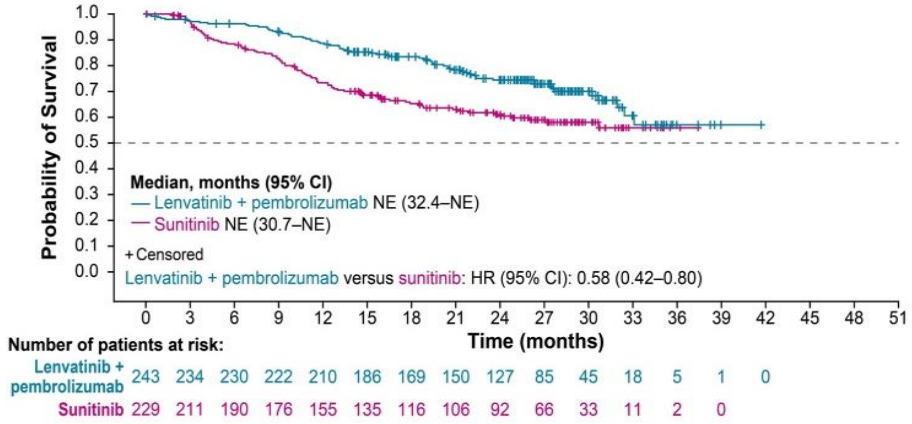
CLEAR : analyse efficacité selon groupe IMDC

Progression-free Survival

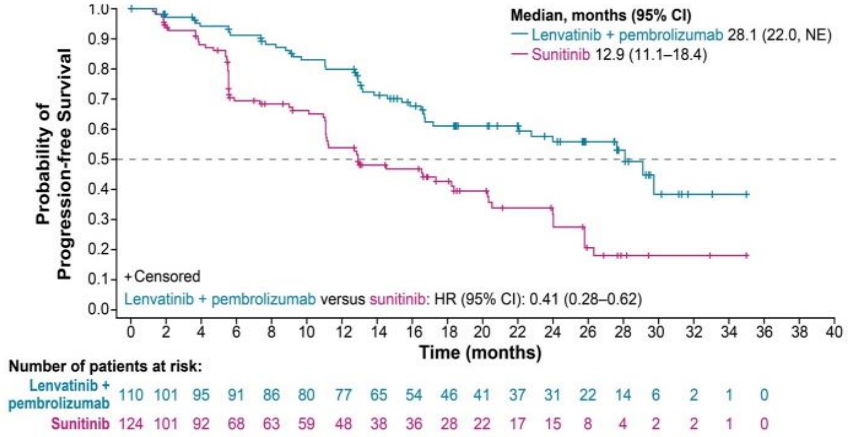
Overall Survival

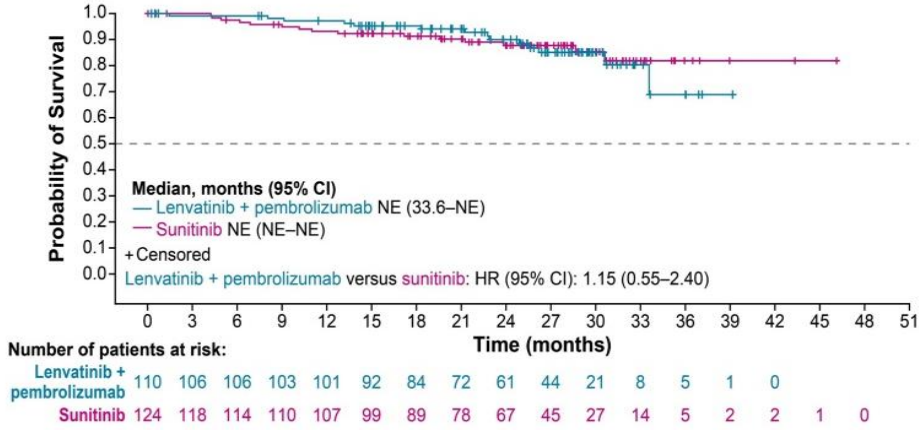
IMDC-Intermediate/ Poor Risk Subgroup





IMDC-Favorable Risk Subgroup





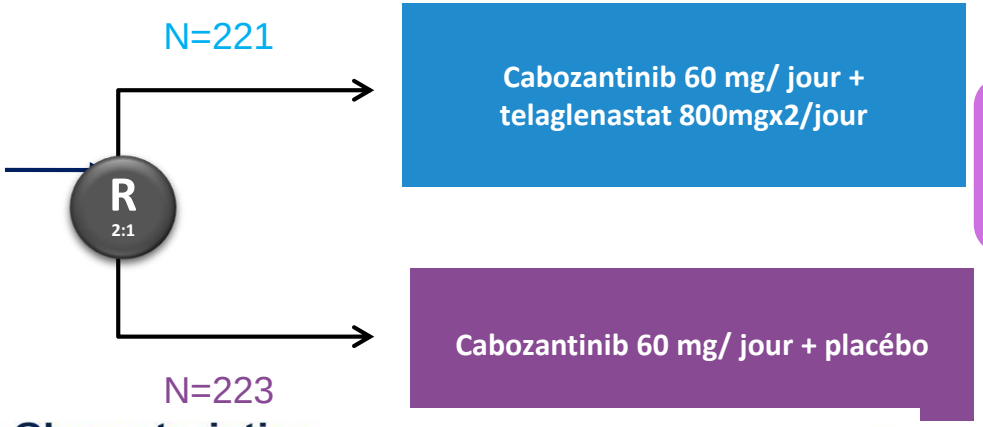
Tumors assessed by Independent Review Committee per RECIST v1.1.

V. Grünwald, et al, Abstr 4560

CANTATA : cabozantinib + telaglenastat ou placébo

Phase II randomisée

Principaux critères d'inclusion:
- **RCC à cellules claires avancé ou métastatique**
- **Karnofsky performance status ≥70**
- **1 ou 2 ligne incluant TKI antiangiogénique ou Nivo+ipi**



Obj I : SSP (IRC)
Obj II : SG, SSP (Inv)

Demographics and Patient Characteristics

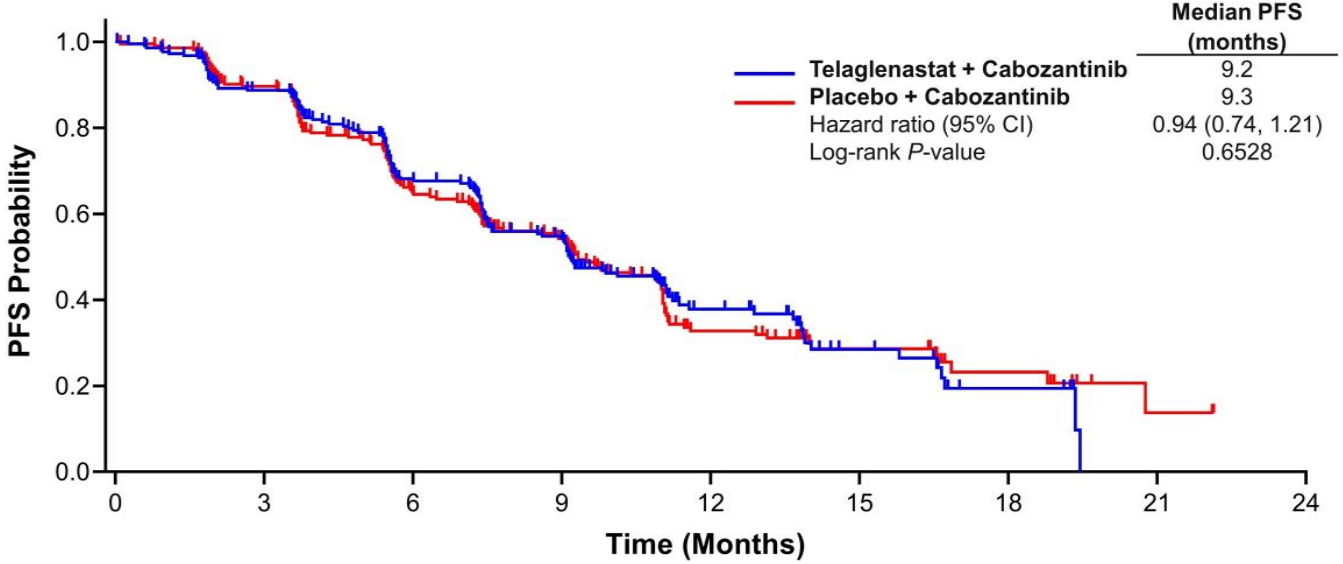
6

		Tela + Cabo (n=221)	Pbo + Cabo (n=223)
Median age, years (range)		61 (21–81)	62 (29–83)
Male, n (%)		174 (79)	155 (70)
Race, n (%)	White	174 (79)	176 (79)
	Black or African American	3 (1)	6 (3)
	Asian	2 (1)	6 (3)
	Other or not reported	42 (19)	35 (16)
Karnofsky performance status, n (%)	100	64 (29)	66 (30)
	90	86 (39)	80 (36)
	80	61 (28)	61 (27)
	70	10 (5)	15 (7)
	60	0 (0)	1 (<1)
IMDC prognostic risk group, n (%)*	Favorable	37 (17)	37 (17)
	Intermediate	149 (67)	152 (68)
	Poor	35 (16)	34 (15)
Prior lines of therapy, n (%)	1	125 (57)	127 (57)
	2	96 (43)	93 (42)
	3	0	3 (1)
Prior anti-angiogenic therapy, n (%)	0	47 (21)	46 (21)
	1	163 (74)	159 (71)
	2	11 (5)	18 (8)
Prior ICI therapy, n (%)*		137 (62)	139 (62)
Prior nivolumab + ipilimumab		63 (29)	65 (29)

Cabo, cabozantinib; ICI, immune checkpoint inhibitor; IMDC, International Metastatic RCC Database Consortium; Pbo, placebo; Tela, telaglenastat
*Stratification factors

Tannir NM et al. Abstr 4501

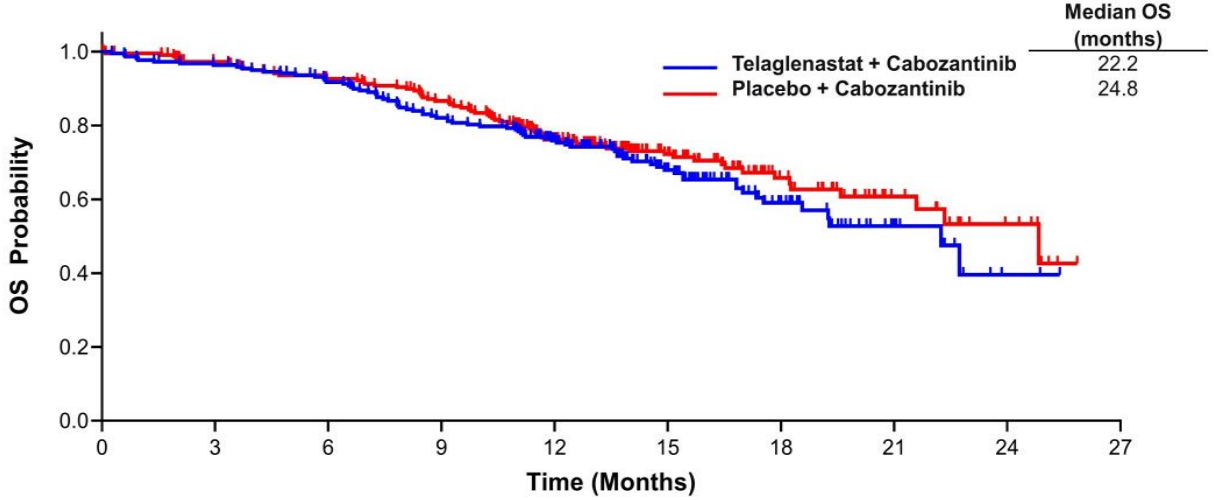
Survie Sans Progression (IRC)



Number at risk

Telaglenastat + Cabozantinib:	221	185	131	97	37	15	6	0	0
Placebo + Cabozantinib:	223	184	117	90	40			2	0

Survie Globale



Number at risk

Telaglenastat + Cabozantinib:	221	212	199	178	144	83	38	12	2	0
Placebo + Cabozantinib:	223	211	201	187	144	89	44	19	8	0

Tannir NM et al. Abstr 4501

2021 ASCO ANNUAL MEETING

CLEAR : analyse efficacité selon groupe IMDC

Parameter	IMDC-Intermediate / Poor Risk		IMDC-Favorable Risk		Patients with target kidney lesions	
	LEN + PEMBRO (n = 243)	SUN (n = 229)	LEN + PEMBRO (n = 110)	SUN (n = 124)	LEN + PEMBRO (n = 78)	SUN (n = 74)
Best overall response, n (%)						
CR	34 (14.0)	9 (3.9)	23 (20.9)	6 (4.8)	2 (2.6)	1 (1.4)
PR	142 (58.4)	57 (24.9)	52 (47.3)	57 (46.0)	54 (69.2)	19 (25.7)
SD	40 (16.5)	93 (40.6)	28 (25.5)	41 (33.1)	13 (16.7)	31 (41.9)
PD	15 (6.2)	42 (18.3)	3 (2.7)	8 (6.5)	4 (5.1)	14 (18.9)
Unknown / not evaluable	12 (4.9)	28 (12.2)	4 (3.6)	12 (9.7)	5 (6.4)	9 (12.2)
Objective response rate (CR + PR), n (%)	176 (72.4)	66 (28.8)	75 (68.2)	63 (50.8)	56 (71.8)	20 (27.0)
(95% CI)	(66.8–78.0)	(23.0–34.7)	(59.5–76.9)	(42.0–59.6)	(61.8–81.8)	(16.9–37.1)
Difference (%) (95% CI)	43.6 (35.5–51.7)		17.4 (5.0–29.8)		44.8 (30.6–59.0)	
Odds Ratio (95% CI)	6.60 (4.39–9.90)		2.00 (1.17–3.42)		10.55 (4.54–24.52)	
Duration of objective response, median, months (95% CI)	25.8 (20.3–27.2)	12.9 (8.0–18.4)	26.3 (25.5–NE)	14.7 (9.3–19.0)	20.3 (14.7–25.8)	24.0 (3.7–NE)

V. Grünwald, et al, Abstr 4560

Carcinomes non à cellules claires : Nivolumab + cabozantinib

Phase II (NCT03635892) monocentrique

Cancer du Rein non à cellules claires
Avancés ou métastatiques
0 à 1 ligne antérieure

→

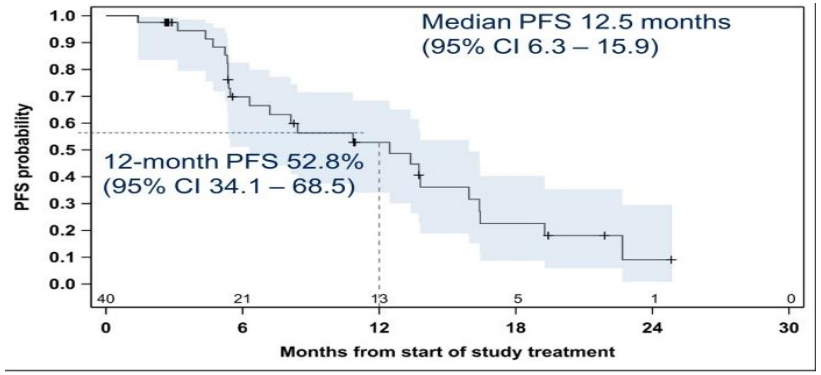
NIVO 240 mg IV / 2 sem (ou 480 mg / 4 sem) + Cabo 40 mg/jour 7/7 PO

Obj I : ORR
Obj II :
SSP RECIST, SSP iRECIST
SG
tolérance

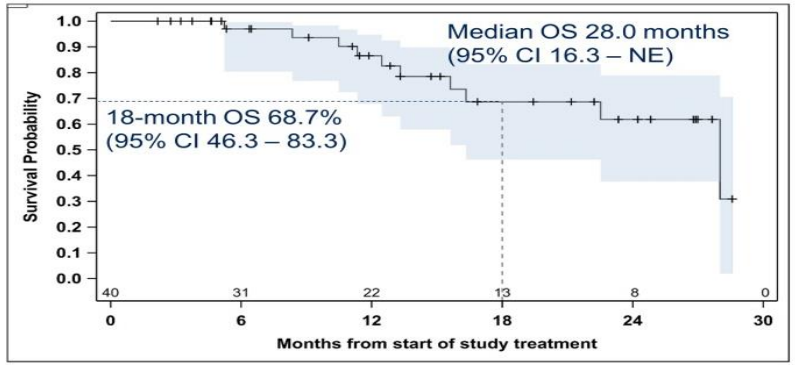
- Relecture anapath centralisée ;
- Cohorte 1 : papillaires, non classés, avec translocation (N=20+20) ; Cohorte 2 : chromophobes (N=7)

	Cohorte 1	Cohorte 2
RO (%)	47%	0%
Maladie stable (%)	50%	71%
Progression	3%	14%
Durée médiane de réponse (mois)	13,6 mois (9,7-19,8)	-

SSP (cohorte 1)



SG (cohorte 1)



→ NIVO-CABO : Piste thérapeutique pour les carcinomes papillaires, et à translocation, avec bénéfice clinique de 97%
Pas de place pour les chromophobes

Lee CH et al. Abstr 4509