2022 ASCO ANNUAL MEETING

Les « Scoops » en Oncologie Urologique

Rein et Vessie

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Liens d'intérêts

- Consultant : BMS
- Orateur pour un laboratoire pharmaceutique : BMS
- Prise en charge par un laboratoire pharmaceutique de la participation à un congrès national ou international: Pfizer

1. EVEREST

- EVEREST: Everolimus for renal cancer ensuing surgical therapy—A phase III study

  (SWOG S0931, NCT01120249)

  Ryan C.W et al. ASCO 2022, abstract #LBA4500

Design

Critères de jugement
Principal : SSR
Secondaires : SG, toxicité

Critères d'inclusion:

- Cancer du rein opéré dans les 12 semaines avant randomisation
- Néphrectomie totale ou néphrectomie partielle
- TNM
  - pT1b G3-4
  - pT2-4, tout G
  - N+
- Histologie : cellules claires ou non
- M0
- PS 0-1

Randomisation 1:1

Stratification:
- Groupes à risque (intermédiaire haut versus Très haut)
- cellules claires *versus* non à cellules claires
- PS 0 versus 1

Everolimus per os 10mg/jour pendant 54 semaines

Placebo per os pendant 54 semaines

Groupes à risque

- Modified UCLA Integrated Staging System

Risque Intermédiaire- Haut			Très haut risque		
pT1b	pT2	pT3a	pT3a	pT3b-c, T4	Tous T
Grade 3-4	Tout grade	Grade 1-2	Grade 3-4	Tous grades	Tous grades
N0	N0	N0	N0	N0	N+

- 1545 patients randomisés : entre avril 2011 et septembre 2016
- Everolimus n=755
- Placebo n=744
- Suivi médian 76 mois

Baseline Characteristics

Characteristic	Everolimus (N=755)	Placebo (N=744)
Age, median (yrs)	58.7	58.4
Male	69%	70%
Performance Status		
0	80%	79%
1	20%	21%
Race		
White	91%	90%
Black	5%	4%
Asian	1%	3%
Other/Unknown	3%	3%

Characteristic	Everolimus (N=755)	Placebo (N=744)
Risk Group		
Very High	55%	55%
Intermediate High	45%	45%
Nephrectomy		
Radical	91%	89%
Partial	9%	11%
Histology		
Clear Cell	83%	84%
Non-Clear Cell	17%	16%
Papillary	8%	7%
Chromophobe	7%	6%
Other	2.5%	3.2%

Most Frequent Adverse Events

Adverse Event*	Everolimus (N=740)		Placebo (N=723)	
	All Grades	G3+	All Grades	G3+
Any AE**	96%	46%	81%	11%
Gastrointestinal				
Mucositis oral	64%	14%	19%	0%
Diarrhea	33%	1%	15%	1%
Nausea	24%	0	17%	0
Skin				
Rash maculo-papular	31%	2%	8%	0
Rash acneiform	29%	2%	5%	0
Pruritus	18%	1%	8%	0
Dry skin	17%	1%	8%	0

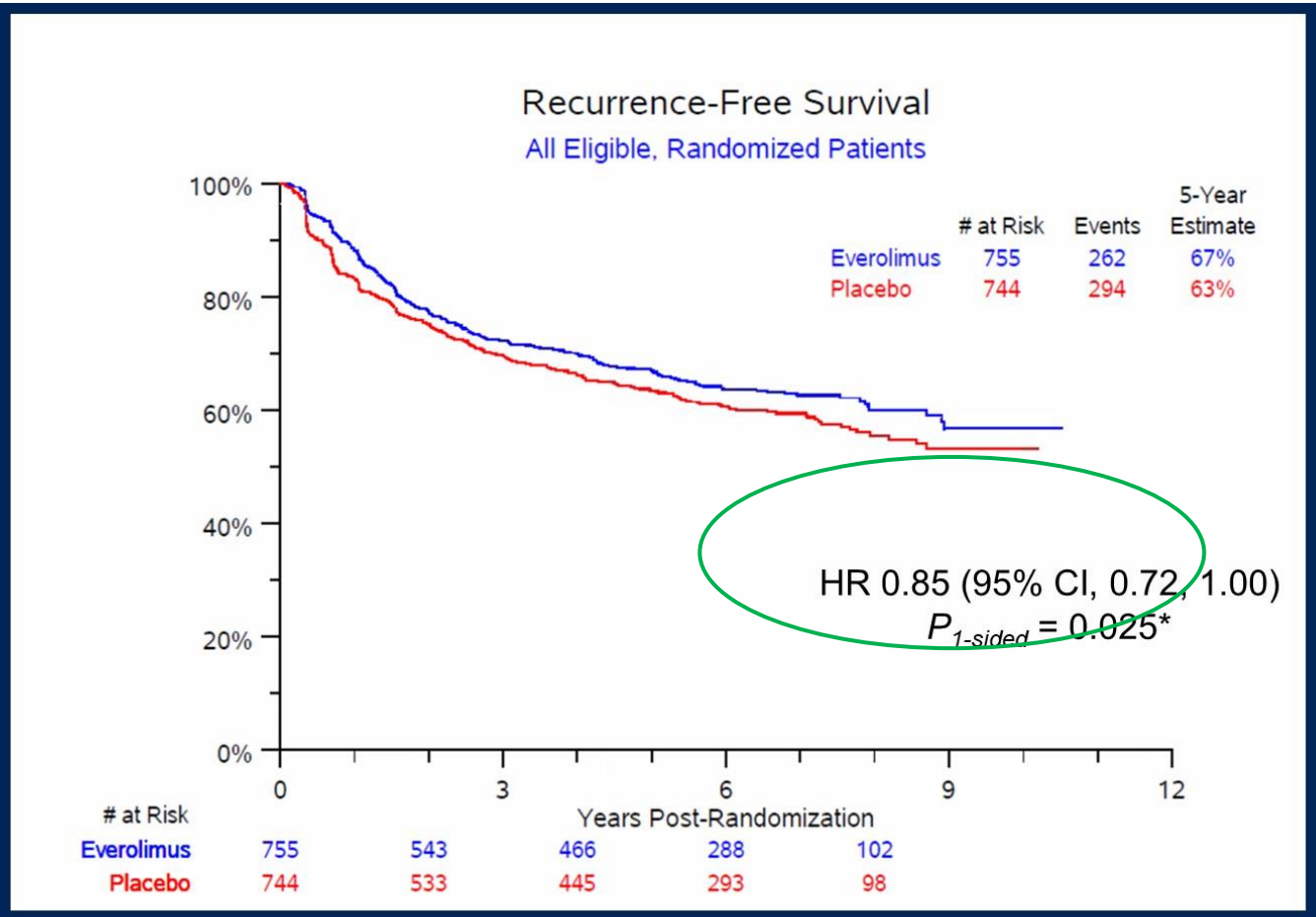
Adverse Event*	Everolimus (N=740)		Placebo (N=723)	
	All Grades	G3+	All Grades	G3+
Nervous System				
Headache	18%	0	11%	0
Vascular				
Hypertension	16%	4%	13%	3%
Nutrition				
Anorexia	16%	1%	5%	0
Respiratory				
Dyspnea	15%	1%	6%	0
Pneumonitis	13%	1%	0	0
General Disorders				
Fatigue	56%	4%	41%	1%
Edema limbs	15%	0	5%	0

* ≥10% incidence, any grade, treatment related

No grade 5 AEs

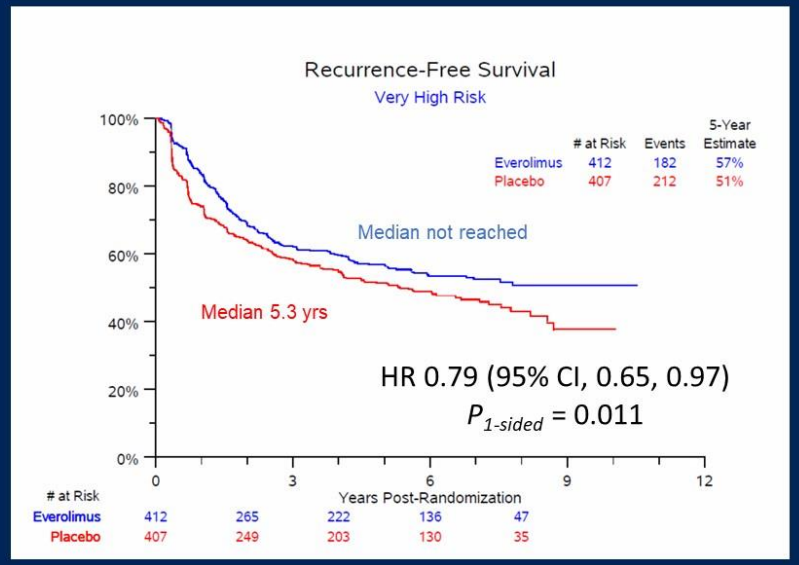
** Including lab abnormalities, worst grade for each patient

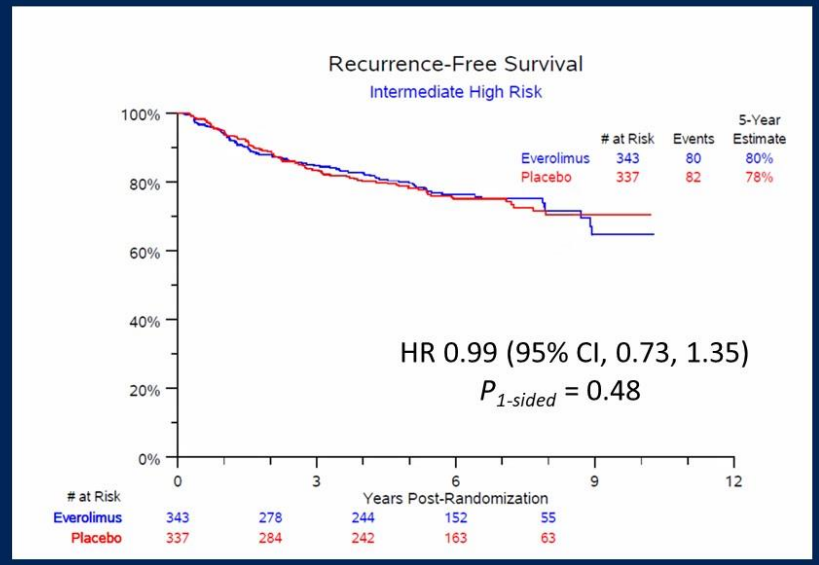
	EVEROLIMUS (n=755)	PLACEBO (n= 744)
Durée de traitement (médiane, mois)	9,3	12,6
Réduction de dose	37%	7%
Arrêt de traitement (autres motifs que progression ou décès)	47%	17%

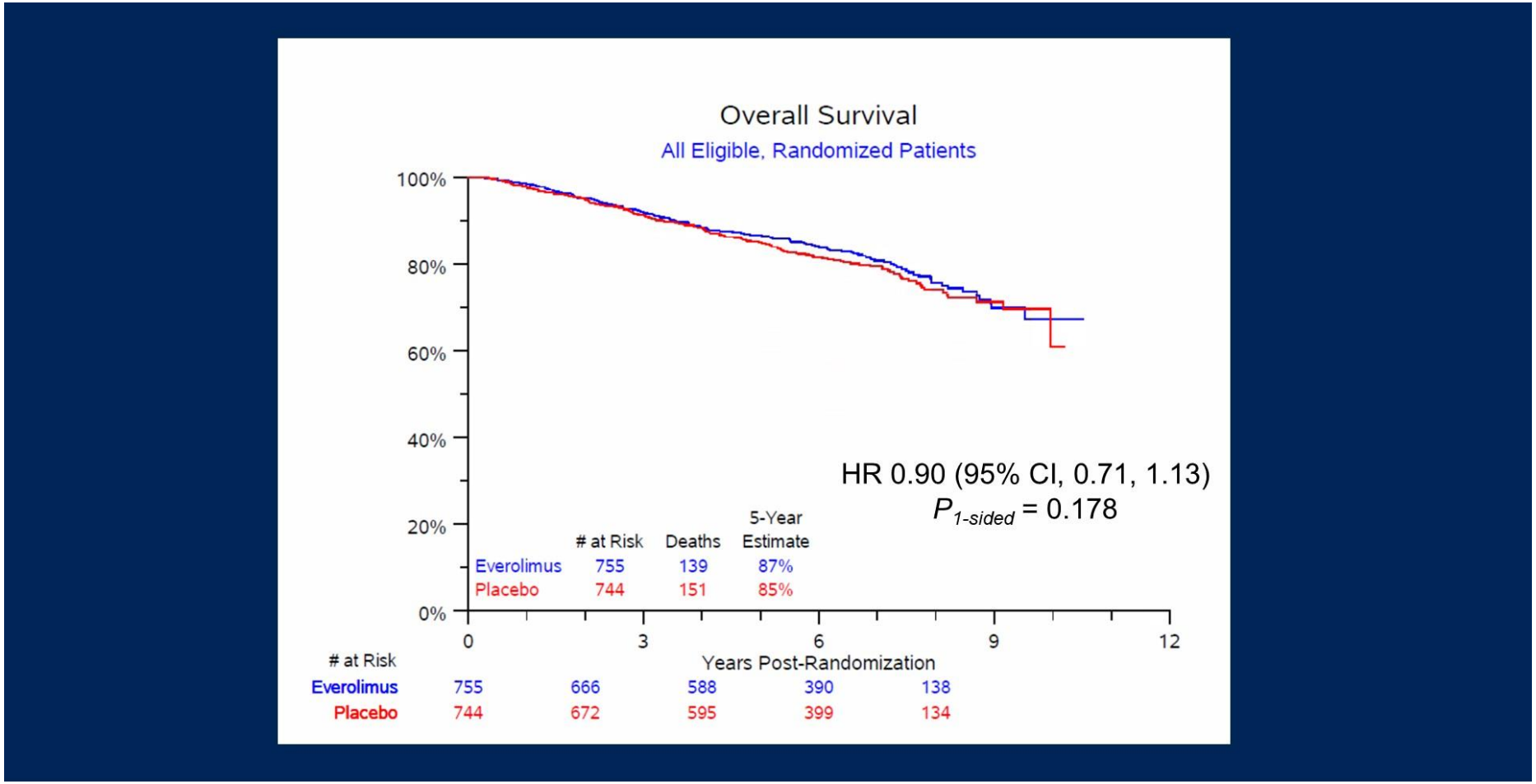


*did not cross prespecified p-value boundary for statistical significance of 0.022

RFS Treatment Effect by Risk Group






Overall Survival
All Eligible, Randomized Patients
100%
80%
60%
40%
20%
0%
HR 0.90 (95% CI, 0.71, 1.13)
$P_{1\text{-sided}}$ = 0.178
at Risk
Deaths
5-Year Estimate
Everolimus 755 139 87%
Placebo 744 151 85%
0
3
6
9
12
Years Post-Randomization
at Risk
Everolimus 755 666 588 390 138
Placebo 744 672 595 399 134

2. CheckMate 9ER

- Association between depth of response and clinical outcomes: exploratory analysis in patients with previously untreated advanced renal cell carcinoma in CheckMate 9ER

  Suarez C et al. ASCO 2022, abstract #4501

Design

Critères de jugement
Principal : SSP (relecture centralisée)
Secondaires : SG, ORR, toxicité

N= 651

Critères d'inclusion:

- Cancer du rein LA ou métastatique
- Cellules claires
- Tous groupes IMDC

Randomisation 1:1

Stratification:
- IMDC
- Expression PD-L1
- Région d'inclusion

N= 323

NIVOLUMAB 240 mg IV J1=J15 + CABOZANTINIB PO 40mg/j

N= 328

SUNITINIB 50 mg/j, 4 semaines/6

Sous-groupes DepOR

Sous-groupe DepOR	Définition
CR	Réponse complète
PR1	Réponse partielle avec meilleure réponse ≥ 80%
PR2	Réponse partielle avec meilleure réponse ≥ 60% < 80%
PR3	Réponse partielle avec meilleure réponse <60%
SD	Stabilité
PD	Progression

Analyses:

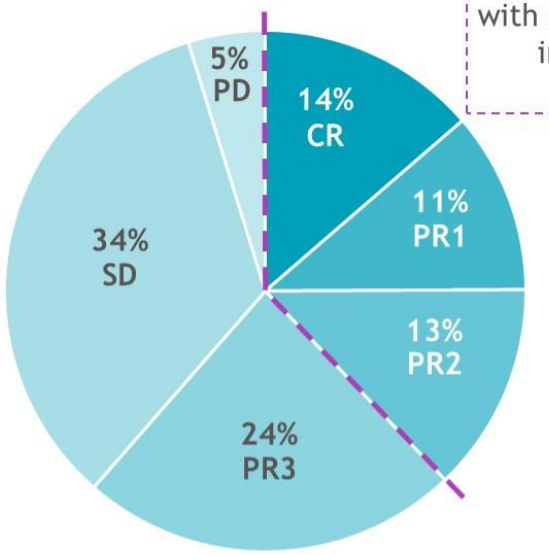
- SSP et SG à 6 mois après randomisation
- Temps nécessaire pour atteindre la réponse objective et durée de cette réponse
- EI dans les 30 jours après analyses

Distribution of DepOR subgroups by treatment arm[a]

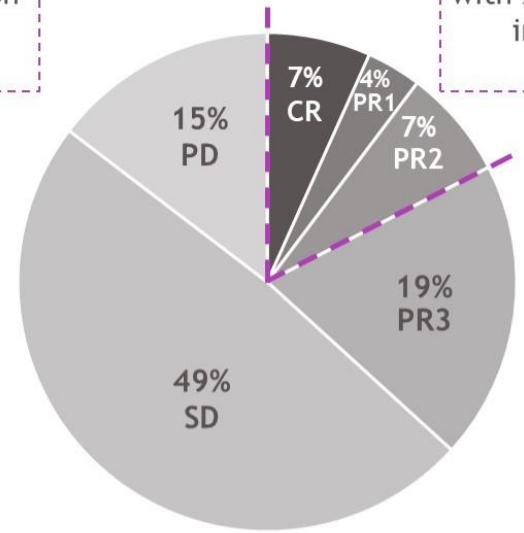
Patients alive at 6 months with ≥ 60% best reduction in target lesions[b]: 38%[c]

Patients alive at 6 months with ≥ 60% best reduction in target lesions[b]: 17%[c]

NIVO+CABO N = 293



SUN N = 253



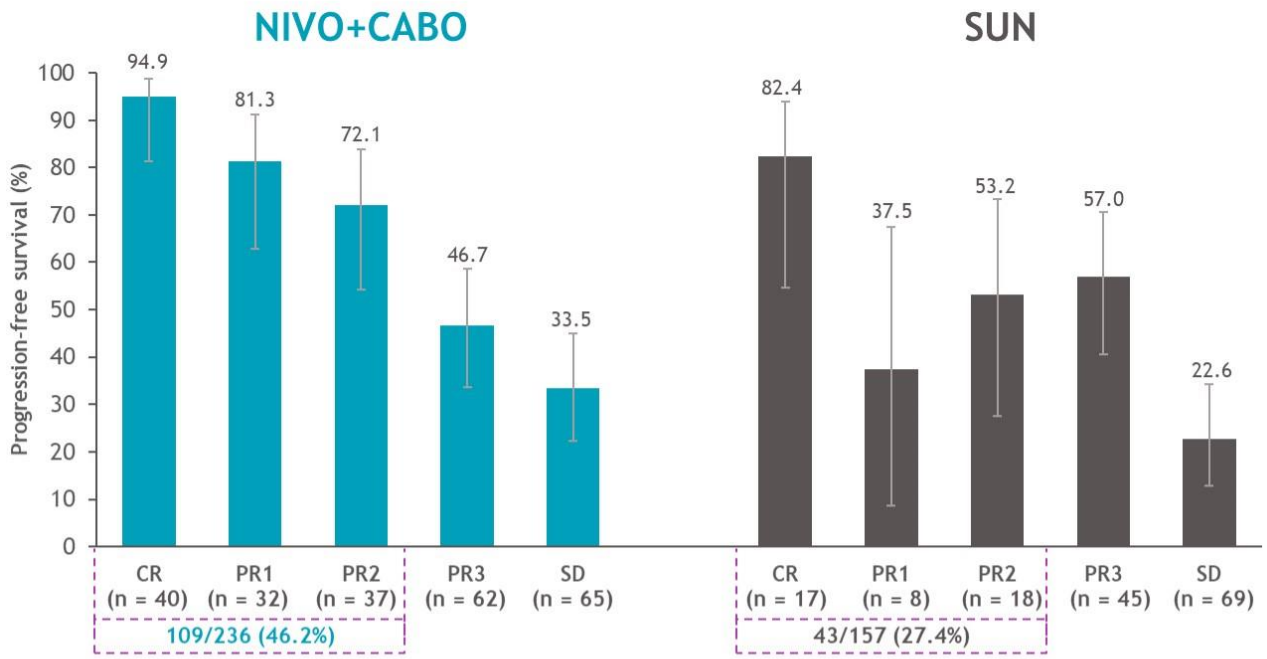
- Among patients alive at the 6-month landmark, greater proportions receiving NIVO+CABO had CR, PR1, or PR2 versus SUN
- A lower proportion of patients receiving NIVO+CABO had PD versus SUN

[a]Based on all randomized patients with baseline and available postbaseline best overall response who were alive at the 6-month landmark. [b]Deep responses were considered to be CR or PR with a high degree of tumor shrinkage (ie, ≥ 60%).[1] [c]Percent may not match values in the pie chart due to rounding.

1. Braun DA, et al *Nat Rev Clin Oncol* 2021;18:199-214.

Suarez et al. ASCO 2022

12-month PFS rates by DepOR subgroups[a,b]



- Deeper responses led to improved 12-month PFS rates

Bars represent 95% confidence intervals.
[a]Based on all randomized patients with baseline and available postbaseline best overall response who were alive and progression-free at the 6-month landmark. [b]12-month PFS rates are presented due to low patient numbers at later time points.

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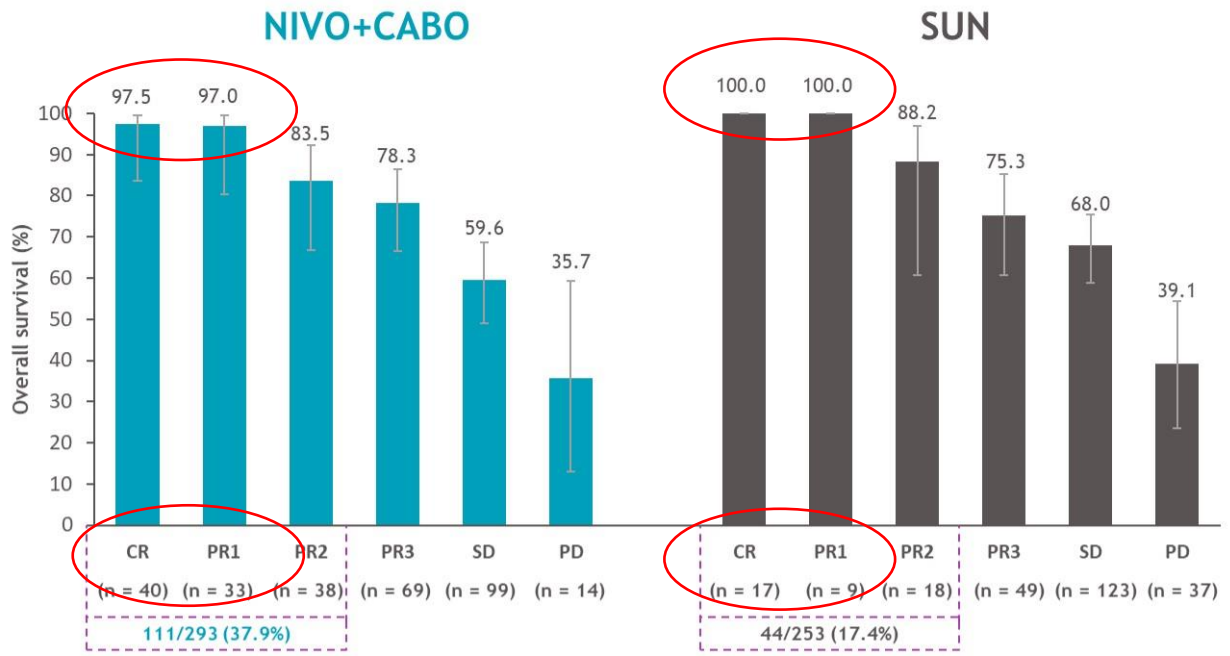
18-month OS rates by DepOR subgroups[a]



- Increasingly deeper responses led to better OS outcomes

Bars represent 95% confidence intervals.
[a]Based on all randomized patients with baseline and available postbaseline best overall response who were alive at the 6-month landmark.

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3. CLEAR

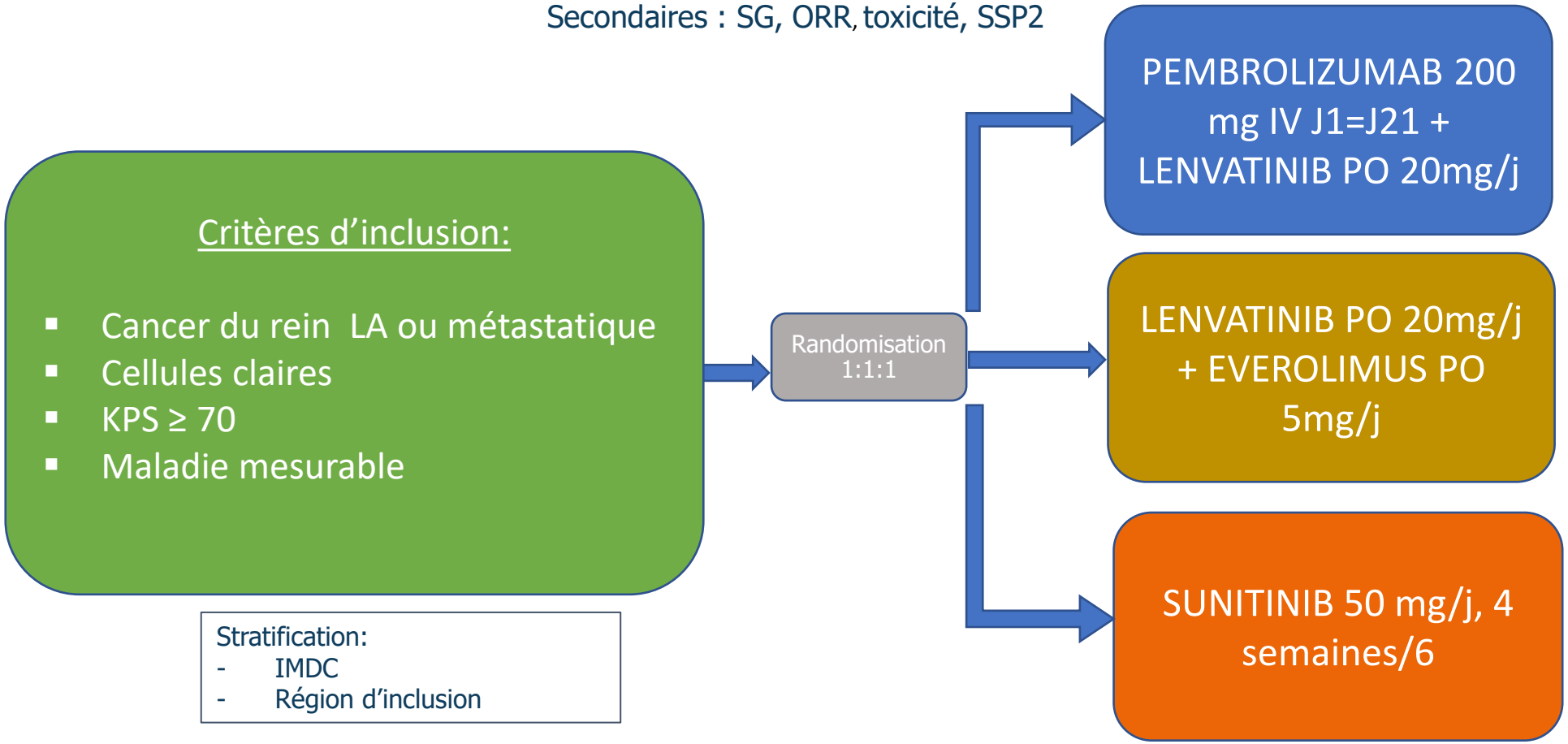
- Impact of subsequent therapies in patients with advanced renal cell carcinoma receiving lenvatinib plus pembrolizumab or sunitinib in the CLEAR study

  Voss MH. et al. ASCO 2022, abstract #4514

- PFS2 (SSP2): temps à partir de la randomisation jusqu'à la progression avec le traitement de 2ème ligne, ou décès
- Analyse pré-spécifiée dans la population ITT

Design

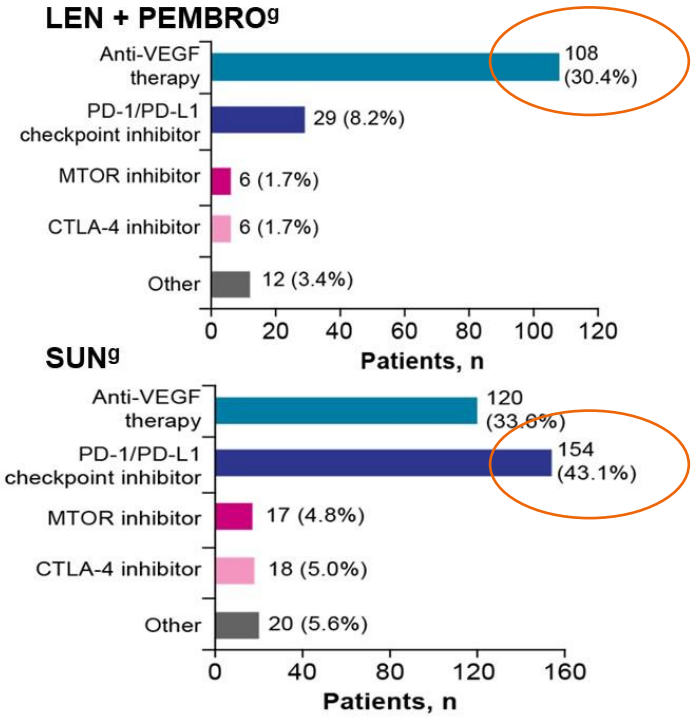
Critères de jugement
Principal : SSP (relecture centralisée)
Secondaires : SG, ORR, toxicité, SSP2



Stratification:
- IMDC
- Région d'inclusion

Results: Subsequent anticancer treatment during survival follow-up

Parameter[a]	LEN + PEMBRO (n = 355)	SUN (n = 357)
Pts who initiated first-line study treatment, n (%)	352 (99.2)	340 (95.2)
Pts who discontinued first-line study treatment, n (%)	210 (59.2)	273 (76.5)
Pts who received any subsequent systemic anticancer treatment[b,c], n (%)	117 (33.0)	206 (57.7)[d]
Time from randomization to initiation of first subsequent systemic anticancer treatment		
Median (range), months[e]	12.68 (1.45–37.36)	6.62 (0.39–28.52)
Duration of first subsequent systemic anticancer treatment		
Median (range), months[f]	5.16 (0.10–30.23)	6.82 (0.03–30.72)



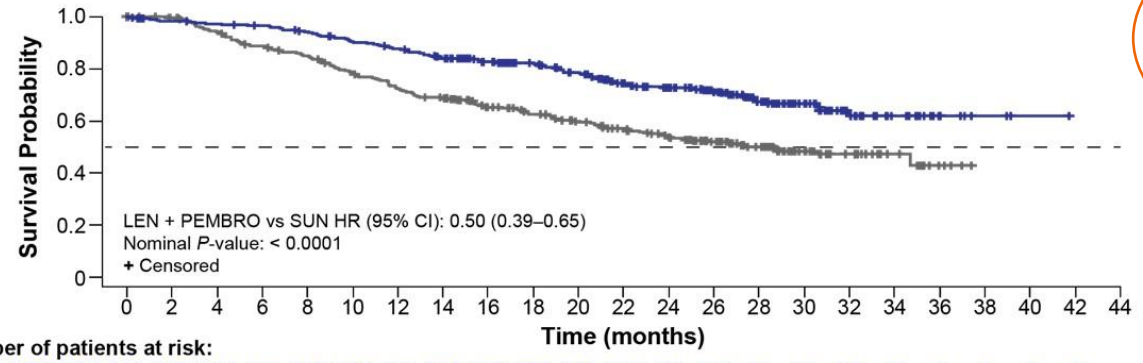
CABOZATINIB 14,9%

NIVOLUMAB 39,8%

Note: Patients may have received > 1 medication within a medication type. Percentages are based on all randomly assigned patients regardless of the treatment actually received.

[a]Percentages are based on the total number of patients in the Full Analysis Set (all randomized patients regardless of the treatment actually received) within the relevant treatment group; [b]monotherapy or in combination; [c]medications were coded using World Health Organization Drug Dictionary Version WHODDMAR20B3G; [d]includes 3 patients who did not receive study treatment; [e]includes patients with available start date of first subsequent systemic anticancer medication; [f]includes patients with available start and end dates of first subsequent systemic anticancer medication; [g]the most common subsequent systemic anticancer medication in patients randomly assigned to receive LEN + PEMBRO was cabozantinib (14.9%); the most common subsequent systemic anticancer medication in patients randomized to receive SUN was nivolumab (39.8%).

Results: PFS2[a] in LEN + PEMBRO Versus SUN Arms



Number of patients at risk:

LEN + PEMBRO	355	345	340	336	326	311	300	284	253	237	214	186	170	139	96	58	29	17	8	3	1	0
SUN	357	340	318	298	284	261	239	225	191	176	156	141	127	102	74	42	25	12	4	0		

Parameter	LEN + PEMBRO (n = 355)	SUN (n = 357)
PFS2 median, months (95% CI)	Not reached (NE–NE)	28.7 (23.0–NE)
HR (95% CI)	0.50 (0.39–0.65)	
Nominal *P*-value	< 0.0001	
PFS2 rate, % (95% CI)		
At 12 months	87.6 (83.6–90.6)	72.5 (67.3–76.9)
At 24 months	72.7 (67.3–77.4)	54.2 (48.4–59.6)

- Among all patients, **PFS2 was longer in the LEN + PEMBRO arm versus in the SUN arm** (median: not reached vs 28.7 mos; HR, 0.50; 95% CI 0.39–0.65; nominal *P* < 0.0001)
- **PFS2 rates at 12 and 24 months were also higher in the LEN + PEMBRO arm** versus the SUN arm.
- **OS benefit with LEN + PEMBRO versus SUN treatment** observed in the primary analysis (HR, 0.66; 95% CI, 0.49–0.88) (Motzer 2021, NEJM) was even more pronounced after accounting for subsequent therapy **(HR, 0.54; bootstrap 95% CI, 0.39–0.72)**.

[a]Defined as the time from randomization to disease progression on next-line of treatment or death from any cause (whichever occurred first).

4. COSMIC-021

- Cabozantinib in combination with atezolizumab in urothelial carcinoma: Results from Cohorts 3, 4, 5 of the COSMIC-021 study
- Phase 1b

  Pal SK. et al. ASCO 2022, abstract #4504

Design – Phase 1b

Critères d'inclusion:

- Cancer urothélial LA ou métastatique
- PS 0-1
- Cohorte 3 : traitement naïf (sauf néoAdj/Adj > 12 mois) et cisplatine-inéligible
- Cohorte 4: traitement naïf et cisplatine–éligible
- Cohorte 5 : 1 ligne d'immunothérapie, ≤ 2 lignes
- N = 30 par cohorte

Cabozantinib PO 40 mg/j

+

ATEZOLIZUMAB IV 1200 mg J1=J21

Critères de jugement

Principal : ORR

Secondaires : toxicité

Exploratoires : Durée de réponse, SSP, SG

Cohorte 2 : post-traitement par sels de platine. ASCO 2020

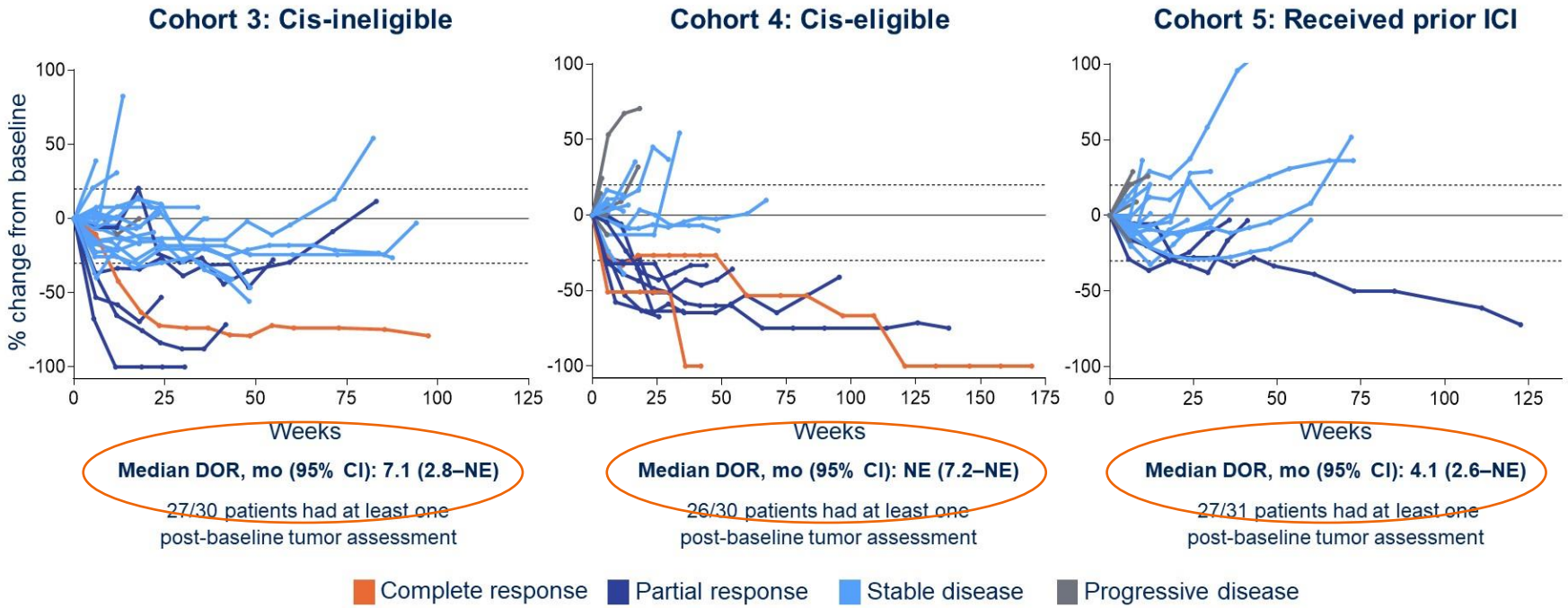
Tumor Response per Investigator by RECIST v1.1

	Cohort 3 Cis-ineligible (N=30)	Cohort 4 Cis-eligible (N=30)	Cohort 5 Received prior ICI (N=31)
ORR, % (95% CI)	**20 (8–39)**	**30 (15–49)**	**10 (2–26)**
Best overall response, n (%)			
Complete response	1 (3)	2 (7)	0
Partial response	5 (17)	7 (23)	3 (10)
Stable disease	18 (60)	10 (33)	16 (52)
Progressive disease	3 (10)	7 (23)	8 (26)
Missing / not evaluable	3 (10)	4 (13)	4 (13)
Disease control rate, % (95% CI)	**80 (61–92)**	**63 (44–80)**	**61 (42–78)**

Objective response rate = complete response + partial response.
Disease control rate = complete response + partial response + stable disease.

CI, confidence interval

Change in Sum of Target Lesions Over Time



NE, not estimable

Treatment-Related Adverse Events Occurring in ≥20%

	Cohort 3 Cis-ineligible (N=30)		Cohort 4 Cis-eligible (N=30)		Cohort 5 Received prior ICI (N=31)	
	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4
Any TRAE, n (%)	29 (97)	19 (63)	28 (93)	13 (43)	28 (90)	14 (45)
Diarrhea	13 (43)	0	10 (33)	1 (3)	11 (35)	0
AST increased	11 (37)	0	6 (20)	2 (7)	6 (19)	0
Decreased appetite	10 (33)	0	8 (27)	2 (7)	12 (39)	1 (3)
ALT increased	9 (30)	0	5 (17)	3 (10)	5 (16)	1 (3)
Fatigue	8 (27)	1 (3)	8 (27)	1 (3)	15 (48)	2 (6)
Nausea	8 (27)	0	5 (17)	0	8 (26)	0
PPE	6 (20)	0	6 (20)	0	3 (10)	0
Amylase increased	6 (20)	2 (7)	2 (7)	0	2 (6)	2 (6)
Stomatitis	4 (13)	0	6 (20)	0	5 (16)	1 (3)

There were no grade 5 TRAEs

ALT, alanine aminotransferase; AST, aspartate aminotransferase; PPE, palmar-plantar erythrodysesthesia

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ONCO NOUVELLE-AQUITAINE Réseau Régional de Cancérologie

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Merci de votre attention !