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REUNIÓN POST CONGRESO DE LA
SOCIEDAD EUROPEA DE ONCOLOGÍA MÉDICA 2025

Presentaciones más destacadas en cáncer renal

Dr. Álvaro Pinto

Hospital Universitario La Paz, Madrid

DISCLOSURES

Research funding: *Pfizer, BMS*

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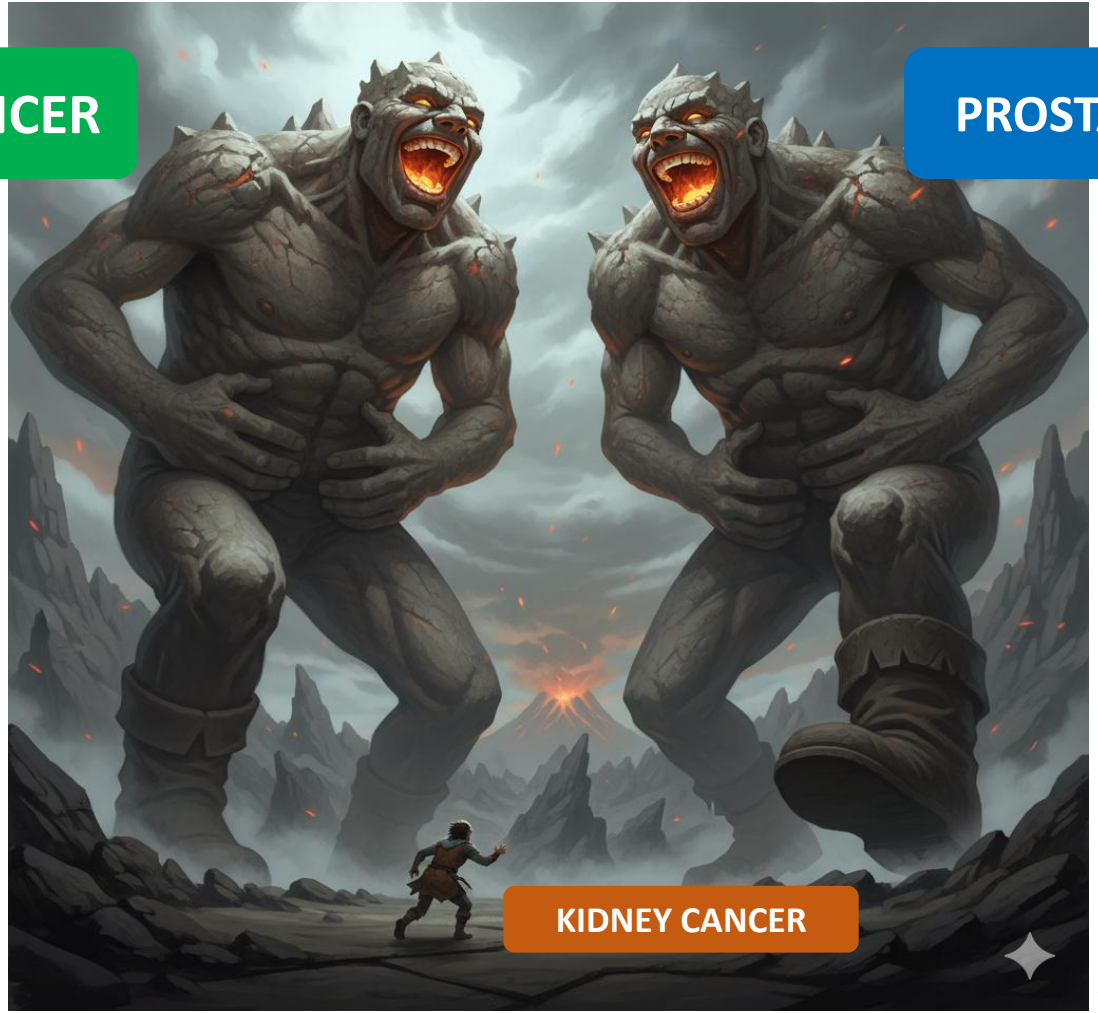
Travel arrangements: *Janssen, Roche, Pfizer, BMS, Ipsen, Bayer*

BLADDER CANCER

PROSTATE CANCER



BERLIN 2025 ESMO congress

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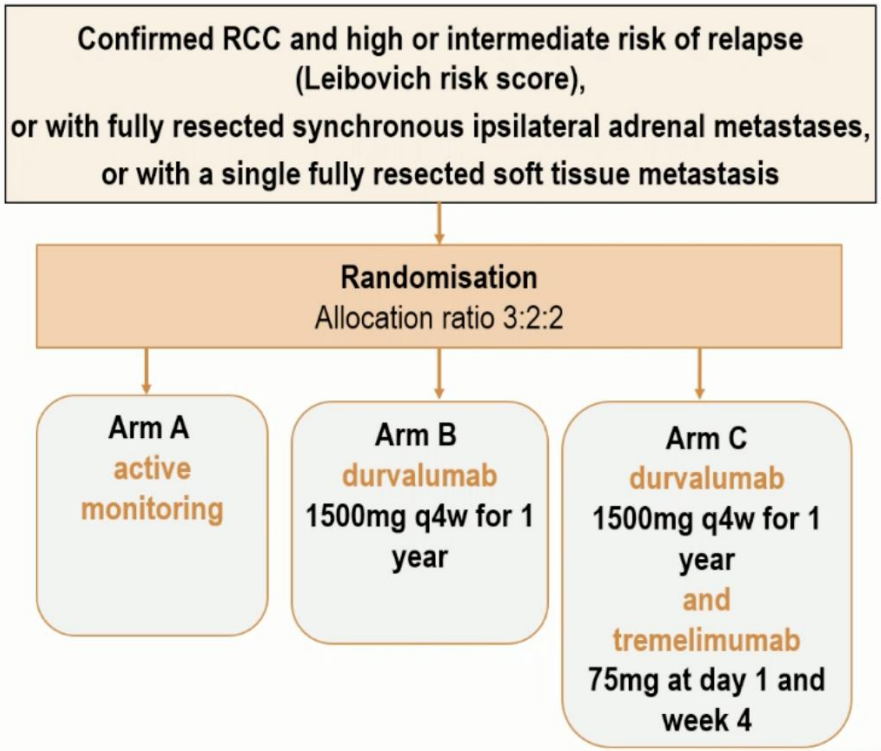
RAMPART Trial Design

- Multi-arm multi-stage (MAMS) platform design
- Original sample size: 1750
- Impacted by COVID-19 and KEYNOTE-564 results
- Modified design blinded to accumulating outcome data
- New target sample size: 750
- Primary outcome: Disease Free Survival (DFS)
- Pre-specified and pre-powered analysis: DFS by risk of relapse at baseline
- Durvalumab and tremelimumab (Arm C) versus active monitoring (Arm A)



Leibovich Score Calculation

Component	Category	Score
Pathological T category	pT1a	0
	pT1b	2
	pT2	3
	pT3a-4	4
Regional lymph node status	pNx or pN0	0
	pN1-pN2	2
Tumour size	<10cm	0
	≥10cm	1
Nuclear grade	1 or 2	0
	3	1
	4	3
Histological tumour necrosis	No	0
	Yes	1

Risk Group	Scores
Low risk	0-2
Intermediate risk	3-5
High risk	6-11

Leibovich BC et al., Prediction of progression after radical nephrectomy for patients with clear cell renal cell carcinoma: a stratification tool for prospective clinical trials. Cancer. 2003 Apr 1;97(7):1663-71.

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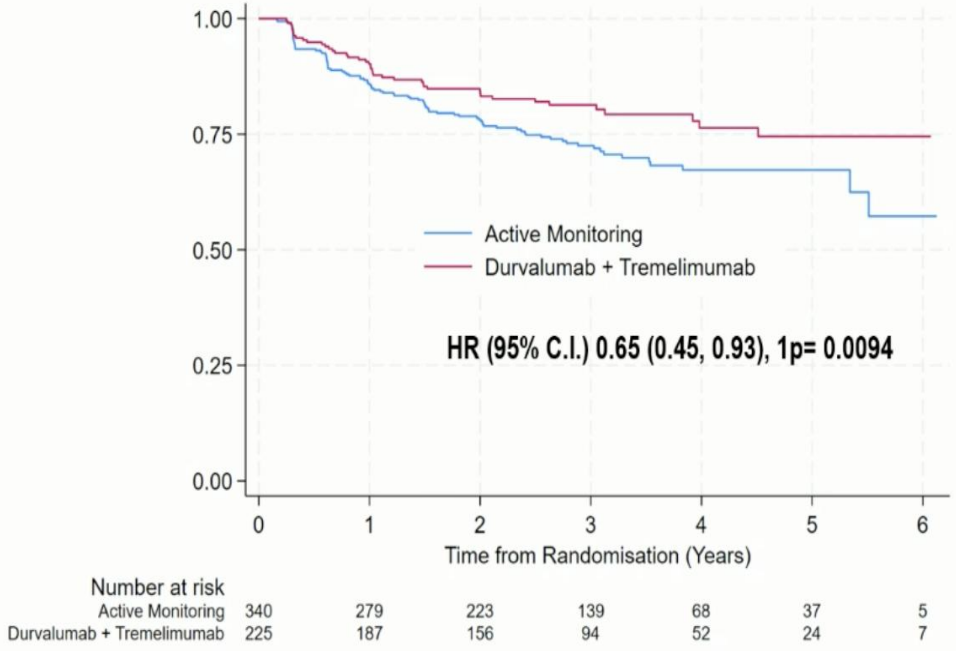
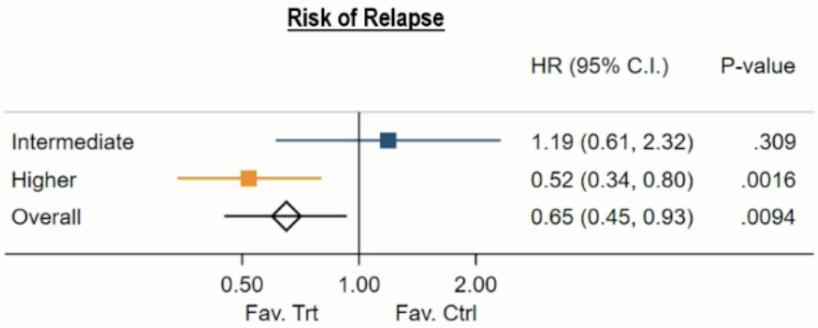
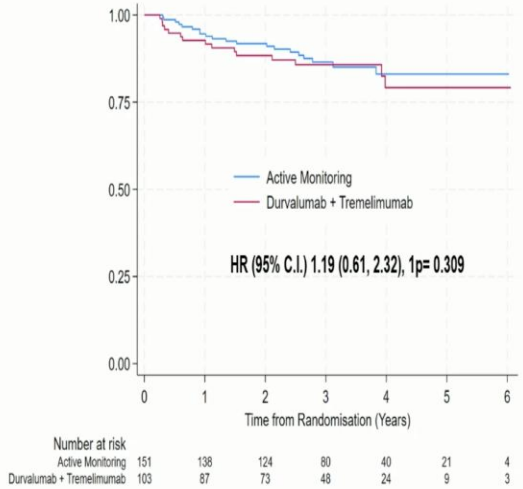
RAMPART Disease Free Survival (DFS) – ITT Population



3-year DFS	
Durvalumab + Tremelimumab (N= 225)	**Active Monitoring (N= 340)**
81%	73%
Median Follow Up: 3 years	



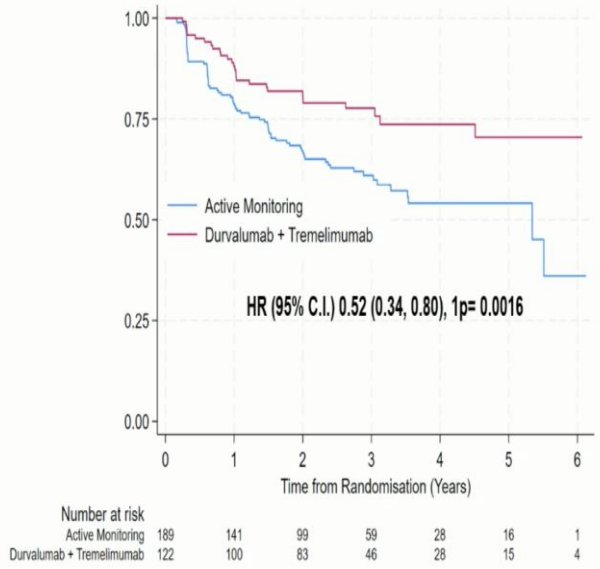
RAMPART DFS in the Intermediate Risk Population - ITT



Pre-specified, pre-powered subgroup analysis

3-year DFS	
Durvalumab + Tremelimumab (N= 103)	Active Monitoring (N= 151)
86%	87%
Median Follow Up: 3.1 years	

RAMPART DFS in the Higher Risk Population – ITT



Pre-specified, pre-powered subgroup analysis

3-year DFS	
Durvalumab + Tremelimumab (N= 122)	Active Monitoring (N= 189)
78%	61%
Median Follow Up: 3 years	

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RAMPART Safety Summary

	Active Monitoring (N= 340)	Durvalumab + Tremelimumab (N= 207)
Any-grade AE, any cause, N(%)	**213 (63%)**	**201 (97%)**
Immune related	2 (<1)	137 (66%)
Durvalumab related	-	185 (89%)
Tremelimumab related	-	164 (79%)
Grade ≥ 3 AE, any cause, N(%)	**28 (8%)**	**83 (40%)**
Immune related	-	63 (30%)
Durvalumab related	-	80 (39%)
Tremelimumab related	-	72 (35%)
Any-grade SAE, any cause, N(%)	**20 (6%)**	**70 (34%)**
Durvalumab related	-	51 (25%)
Tremelimumab related	-	49 (24%)
Deaths	**15 (4%)**	**9 (4%)**
Treatment related	-	2* (<1%)
AE leading to treatment discontinuation, N(%)	**-**	**66 (32%)****
Durvalumab	-	59 (29%)
Tremelimumab	-	30 (14%)

Corticosteroid use:
Steroid use was reported for 36% of participants receiving durvalumab and tremelimumab.

** 6 myocarditis SAEs in 4 patients, 2 resulting in death*
***One or both treatments leading to toxicity discontinuation*

James Larkin

Conclusion

- Adjuvant therapy with durvalumab and tremelimumab following RCC resection improved DFS
- Good evidence that effect is largely driven by the effect in the higher risk population
- Safety findings consistent with the known profiles of durvalumab and tremelimumab
- No difference in overall health and quality of life (OHQL) at month 15
- Results of durvalumab vs active monitoring comparison expected in 2026

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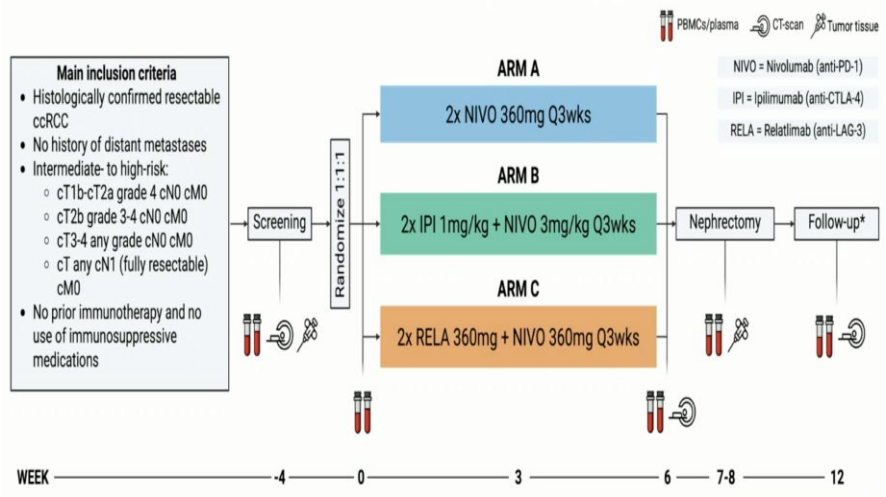


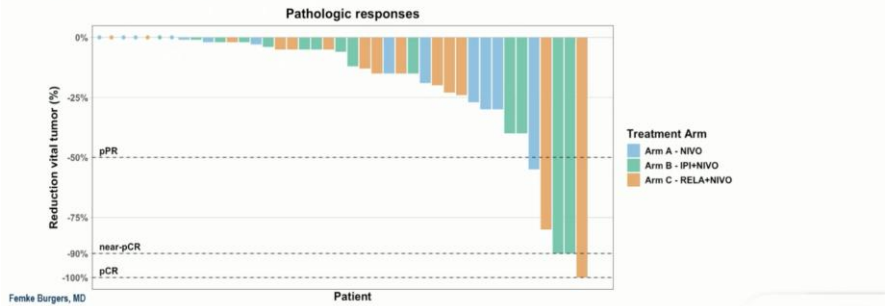
Pathologic responses

The primary endpoint of at least 2 pathologic responses (first stage) was met for:

- **Arm B - IPI+NIVO**: 2 near-pCR (14.3%)
- **Arm C - RELA+NIVO**: 1 pPR and 1 pCR (14.3%)

Primary endpoint not met for arm A – NIVO: 1 pPR (7.1%)

pCR = pathologic complete response
near-pCR = near-complete pathologic response
pPR = partial pathologic response



Femke Burgers, MD

Conclusion

- (Ultra)short neoadjuvant ICI for six weeks resulted in remarkable pathologic responses in a limited number of patients with intermediate- to high-risk ccRCC.
  - In Stage 1, the primary endpoint of ≥2 pathologic responses was met in the IPI+NIVO (2 near-pCR) and RELA+NIVO (1 pPR and 1 pCR) treatment arms.
- Neoadjuvant ICI showed acceptable safety profiles, with minimal impact on surgical timing.
- Preliminary survival results suggest favorable EFS and RFS, especially in the IPI+NIVO arm and in patients with a pathologic response.

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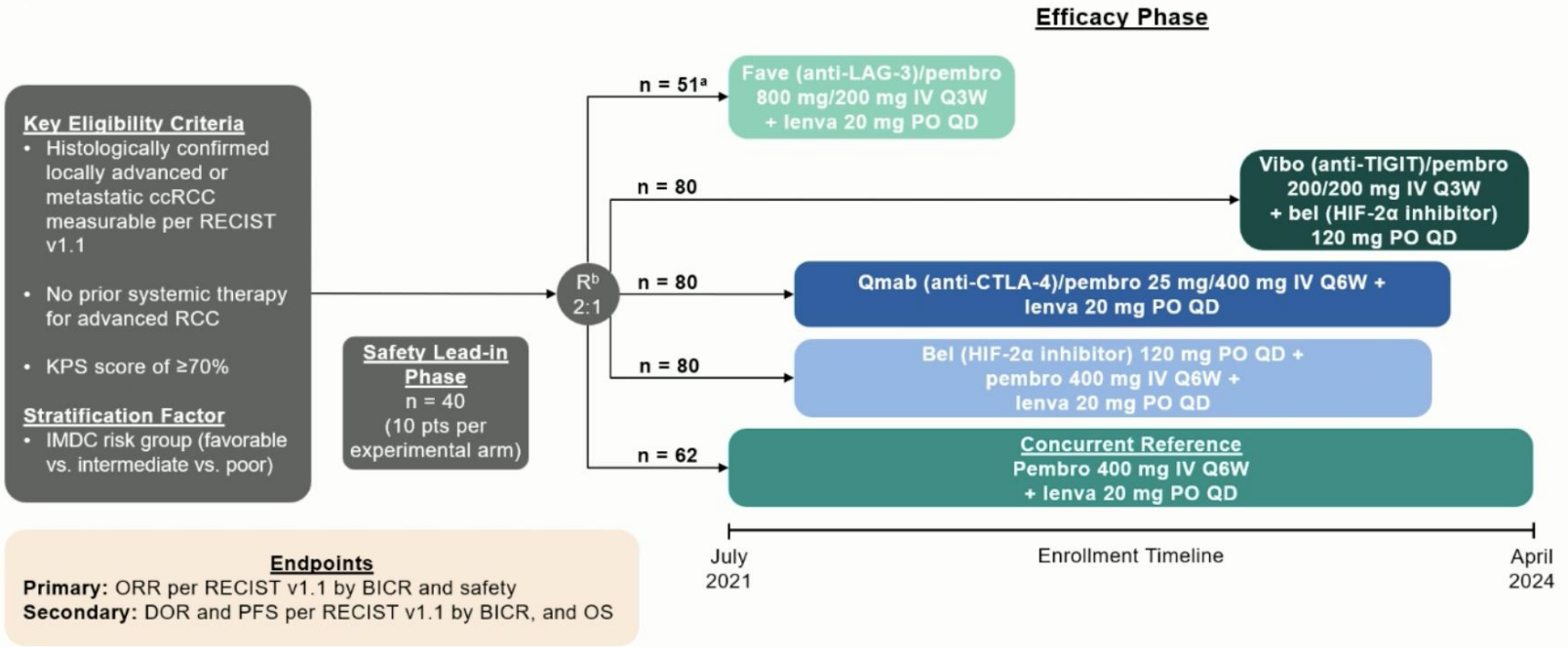
KEYMAKER-U03 Substudy 03A (NCT04626479)



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Summary of Key Efficacy Data

	Fave (anti-LAG-3)/ pembro + lenva n = 51	Vibo (anti-TIGIT)/ pembro + bel (HIF-2α inhibitor) n = 80	Qmab (anti-CTLA-4)/ pembro + lenva n = 80	Bel (HIF-2α inhibitor) + pembro + lenva n = 80	Reference: Pembro + lenva n = 62
Median follow-up (range), mo	39.2 (28.8–44.6)	16.4 (11.8–23.4)	22.1 (13.5–40.6)	23.4 (14.1–41.0)	21.2 (11.9–44.4)
ORR, % (95% CI)	63 (48–76)	42 (32–54)	71 (60–81)	78 (67–86)	81 (69–90)
CR, % (95% CI)	10 (3–21)	5 (1–12)	6 (2–14)	12 (6–22)	6 (2–16)
Median DOR, mo (range)	26.3 (1.4+–34.4+)	14.0 (2.7+–18.2+)	25.0 (2.4–37.1+)	33.4 (2.6–37.6+)	25.6 (1.4+–41.2+)
Median PFS, mo (95% CI)	26.0 (8.2–31.8)	15.2 (12.4–NR)	18.0 (11.6–34.3)	31.8 (26.3–NR)	26.3 (15.3–39.8)
PFS HR (95% CI)	1.26 (0.65–2.42)	1.42 (0.75–2.67)	0.96 (0.57–1.61)	0.45 (0.25–0.83)	-
PFS 24-mo rate, % (95% CI)	53 (38–67)	NR (NR–NR)	46 (33–58)	67 (53–78)	53 (37–67)
OS 24-mo rate, % (95% CI)	76 (62–86)	NR (NR–NR)	73 (60–83)	86 (73–92)	77 (60–87)

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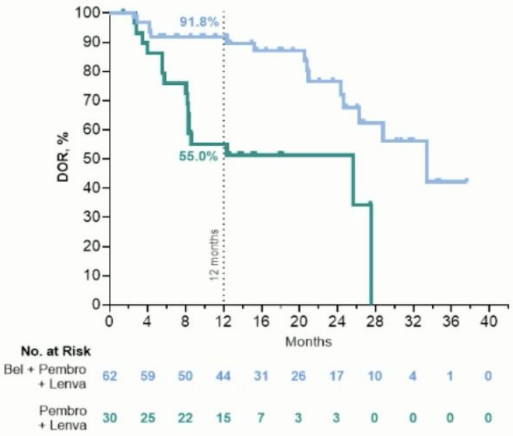
HIF-2α Combination (Belzutifan + Pembrolizumab + Lenvatinib), Efficacy Population

DOR

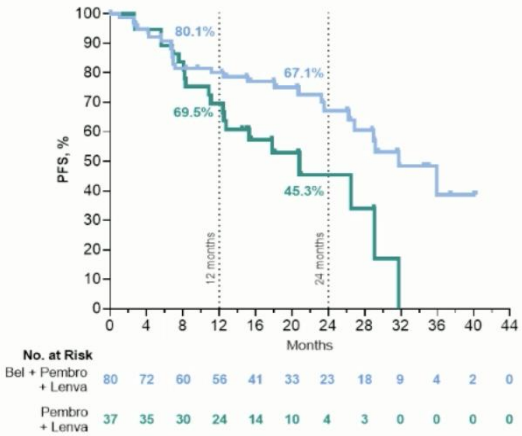
	Median TTR (range), mo	Median DOR (range), mo
Bel + Pembro + Lenva (n = 62)	2.8 (2.6–12.6)	33.4 (2.6–37.6+)
Pembro + Lenva (n = 30)	2.8 (0.9–23.5)	25.6 (1.4+–27.6)



No. at Risk											
Bel + Pembro + Lenva	62	59	50	44	31	26	17	10	4	1	0
Pembro + Lenva	30	25	22	15	7	3	3	0	0	0	0

PFS

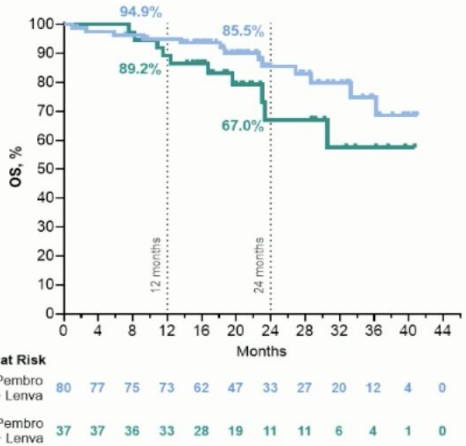
	Events, n (%)	Median PFS (95% CI), mo	HR (95% CI)
Bel + Pembro + Lenva (n = 80)	27 (33.8)	31.8 (26.3–NR)	0.45 (0.25–0.83)
Pembro + Lenva (n = 37)	20 (54.1)	20.8 (12.4–29.0)	



No. at Risk											
Bel + Pembro + Lenva	80	72	60	56	41	33	23	18	9	4	2	0
Pembro + Lenva	37	35	30	24	14	10	4	3	0	0	0	0

OS

	Events, n (%)	Median OS (95% CI), mo
Bel + Pembro + Lenva (n = 80)	13 (16.3)	NR (36.2–NR)
Pembro + Lenva (n = 37)	10 (27.0)	NR (23.3–NR)



No. at Risk											
Bel + Pembro + Lenva	80	77	75	73	62	47	33	27	20	12	4	0
Pembro + Lenva	37	37	36	33	28	19	11	11	6	4	1	0

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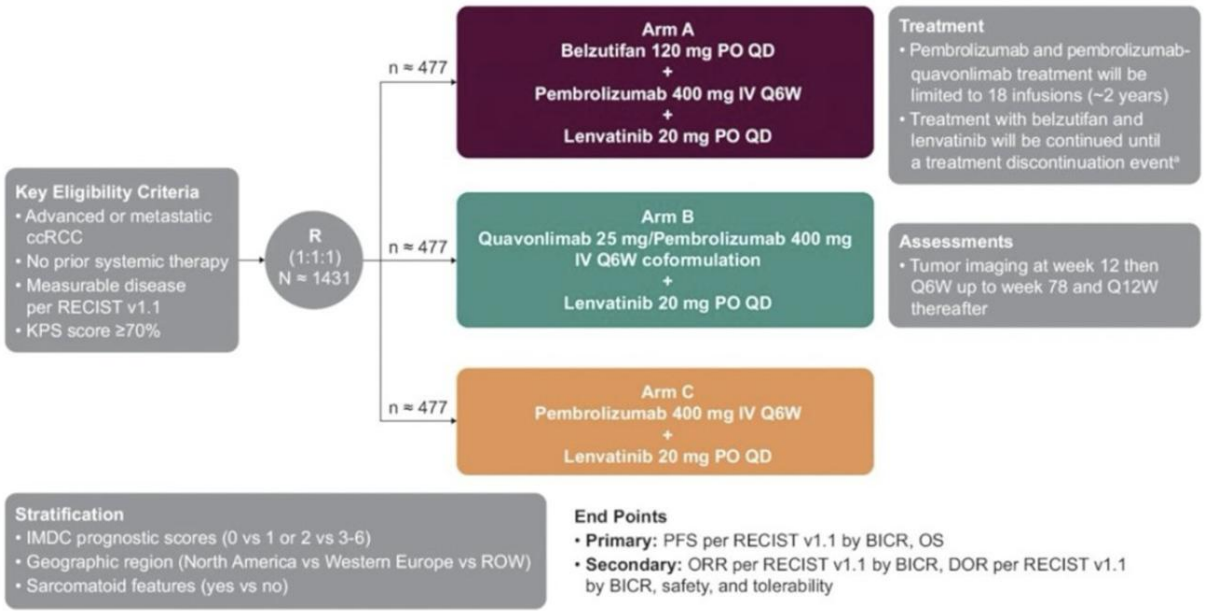
Litespark-012 – Belzutifan Combination in Frontline



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Summary and Conclusions

- Observed efficacy and safety of pembro + lenva were confirmatory of prior observations for this combination
- Bel + pembro + lenva and qmab/pembro + lenva had similar ORR compared with pembro + lenva as first-line therapy in pts with previously untreated advanced ccRCC
  - Responses were potentially less favorable with fave/pembro + lenva and vibo/pembro + bel compared with pembro + lenva
- Bel + pembro + lenva, but not the other investigative arms, may have been associated with a higher proportion of CRs, prolonged DOR, and prolonged PFS compared with pembro + lenva
  - Duration of follow-up was insufficient to detect long-term contributions to OS
- Safety findings for all investigative regimens were generally consistent with the safety profiles of the individual drugs
- Bel + pembro + lenva and qmab/pembro + lenva are currently being explored in the fully enrolled, randomized phase 3 LITESPARK-012 study

OPtimal Treatment by Invoking biologic Clusters in Renal Cell Carcinoma (OPTIC RCC)

Key Eligibility Criteria

- ECOG 0 or 1
- Metastatic clear cell RCC without prior systemic therapy in any setting
- Available tumor tissue for RNA-sequencing/cluster prediction

Rini | Haake | Beckermann | Reddy

Simon's Minimax Two-Stage Design

Clusters 1/2 → **Nivolumab/Cabozantinib (N=26)**

- H_0: ORR ≤ 55%
- H_A: ORR > 75%

Stage I (N=12) ≥7/12 responders → **Stage II (N=14)** ≥18/26

Clusters 4/5 → **Ipilimumab/Nivolumab (N=28)**

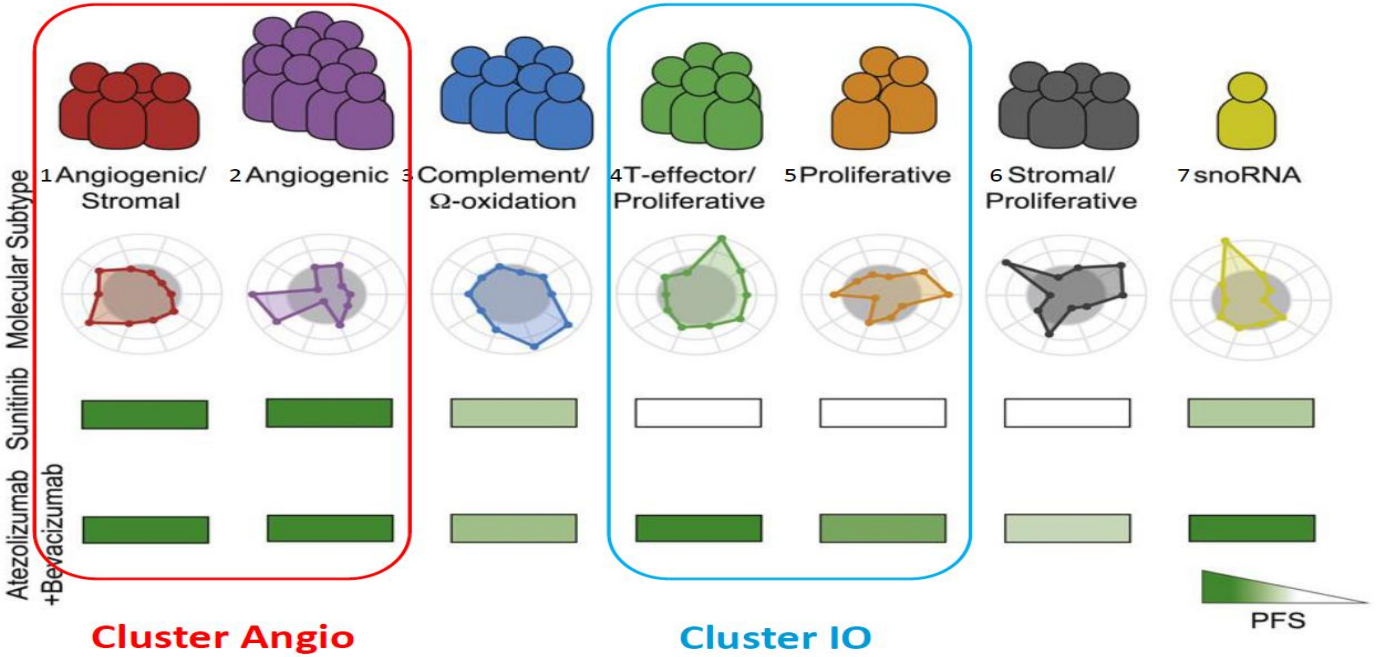
- H_0: ORR ≤ 40%
- H_A: ORR > 60%

Stage I (N=16) ≥7/16 responders → **Stage II (N=12)** ≥15/28

Clusters 3/6/7 → **Excluded from trial**

- Primary Endpoint: Objective response rate (ORR)
- Secondary Endpoints: Progression free survival (PFS), depth of response >80% at 6 months, immune-related adverse events

IMmotion 151 RNAseq-Defined Clusters



CONSORT diagram & cluster distribution

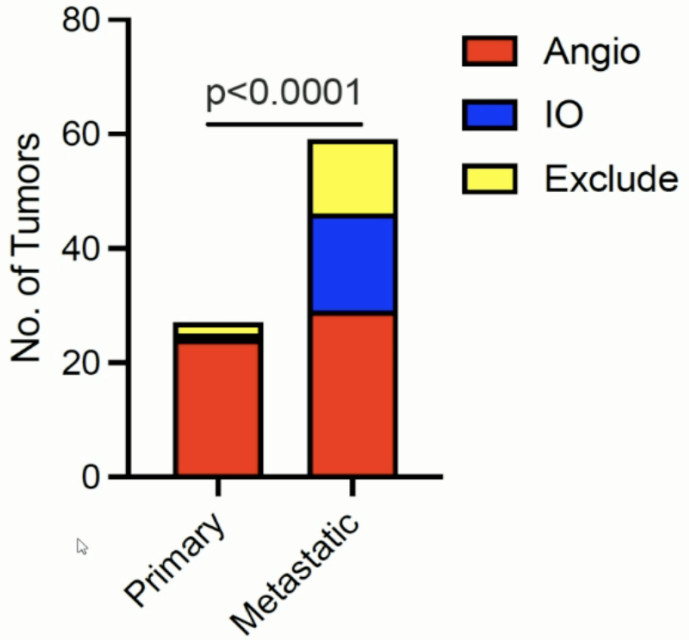
101: signed screening consent

12: Cluster IO (ipi/nivo)
14: Cluster exclude (excluded from study)
7: Cluster assigned, observed off therapy
3: Pending RNAseq results

23: Failed QC
5: Met exclusion criteria

1: Died during screening
6: Withdrew consent
2: Insurance denied

27: Cluster angio (cabo/nivo)



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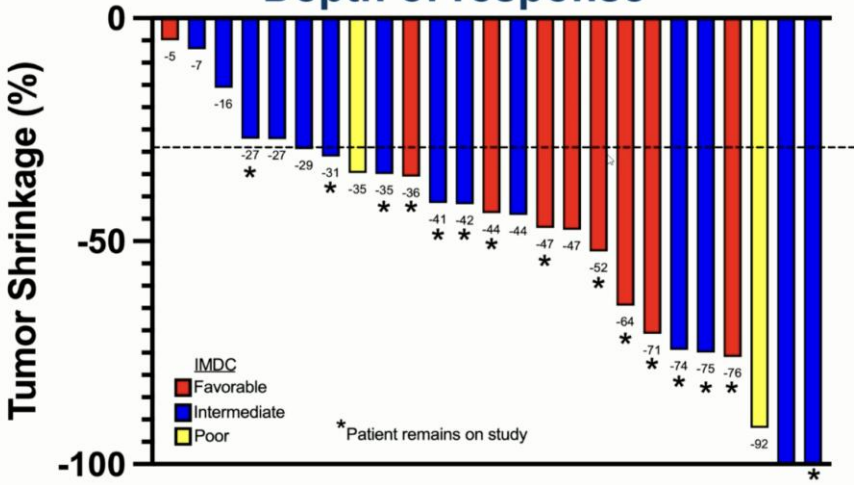
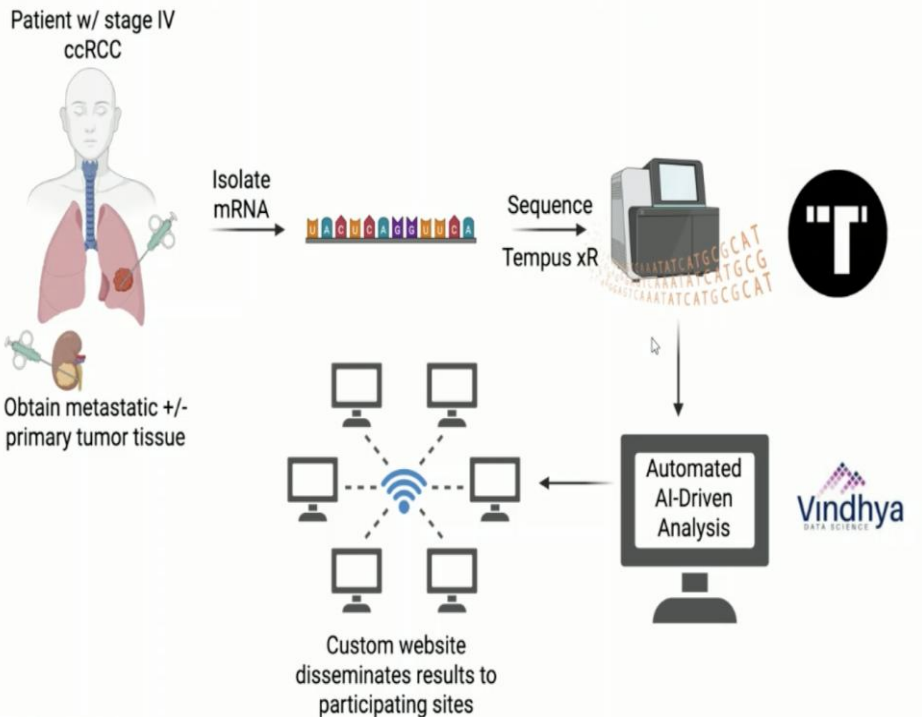
Objective Response

	Cluster 1/2 (n=25)*
Objective response – no. (%)	19 (76)
Best overall response – no. (%)	
Complete response	2 (8)
Partial response	17 (68)
Stable disease	6 (24)
Progressive disease	0 (0)
Patients with tumor burden reduction – no. (%)	25 (100)
% tumor shrinkage – median (range)	42 (5-100)

* 2 patients recently enrolled without a post-baseline scan to date
- Median follow-up: 11.1 months (range 0.9 – 31.5); 17 of 27 patients remain on study

Depth of response





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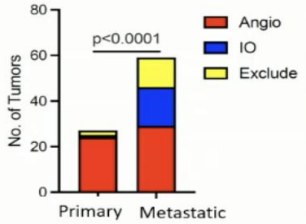
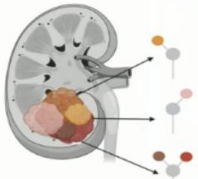
Inevitably there are some limitations at this stage

The proportion of tumours deemed 'angiogenic' differed between samples from renal primary & metastases.

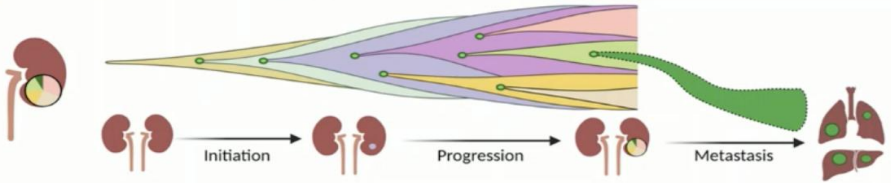
Likely due to 'spatial & temporal heterogeneity' - 'evolution' of genetic changes



At any moment biopsies from different regions of the same tumour can show differing genetic alterations



Also, over time, tumours develop different genetic alterations



1. Gerlinger et al, Intratumor heterogeneity NEJM 2012;366:883-92. 2. Turajlic et al. Deterministic evolution…Cell 2018;173:595-610.

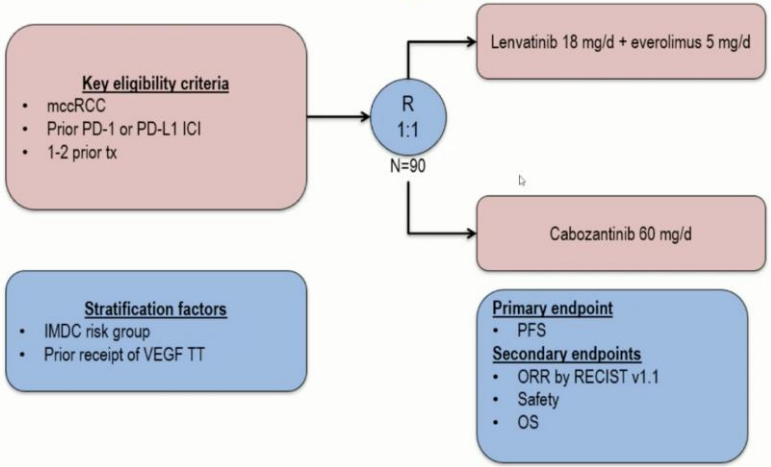
Images courtesy of Zayd Tippu and Daqi Deng

- A biopsy from an archived renal primary is unlikely to represent the dominant driving biology / genetics at the time a patient develops progression
- Taking biopsies from metastatic sites is challenging **but is probably required for this strategy to yield its full potential.**

Conclusions

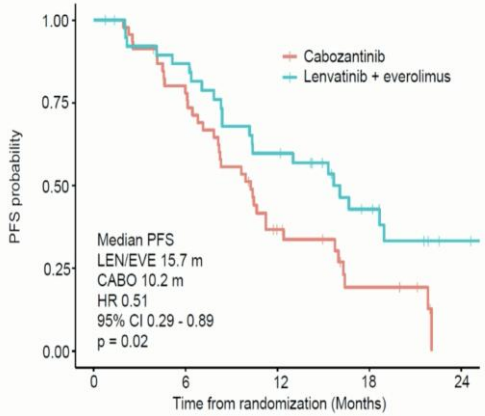
- Prospective investigation of tissue-based RNAseq biomarkers to guide therapy is operationally feasible in a front-line metastatic ccRCC population
- Primary and metastatic tumors can exhibit different gene expression signatures, requiring metastatic tumor biopsies for a biomarker-driven study
- Selection of patients exhibiting an angiogenic gene expression signature enriches for clinical outcome to cabozantinib + nivolumab
  - A high objective response rate, reduction of tumor burden in all patients and lack of primary progressive disease was observed
- Time-to-event endpoints such as PFS and duration of response will require additional follow-up

Phase II LenCabo study design



Primary analysis of PFS

- 25/40 (62.5%) who received len/eve and 35/46 (76.1%) who received cabo experienced PD



LenCabo Reflections. *Will this trial change my practice?*

- I already know Len+Eve is an active regimen but its registration study was PhII - less used
- Cabozantinib is widely used and is a (the?) standard of care. I will continue to use it

- This is **a positive phase II trial** noting OS data are not mature
- It demonstrates the efficacy of Len+Eve for IO CPI pre-treated patients with **improved PFS & ORR compared with Cabo although with higher toxicity**
- Is it 'positive enough'? Perhaps depends on you and your patient

- **We can consider using Len+Eve particularly in patients for whom the priority is response & for whom the higher toxicity rate is acceptable**

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2594MO: Association of circulating kidney injury molecule-1 (KIM-1) levels with clinical outcomes in advanced renal cell carcinoma (aRCC): Retrospective analysis of COSMIC-313

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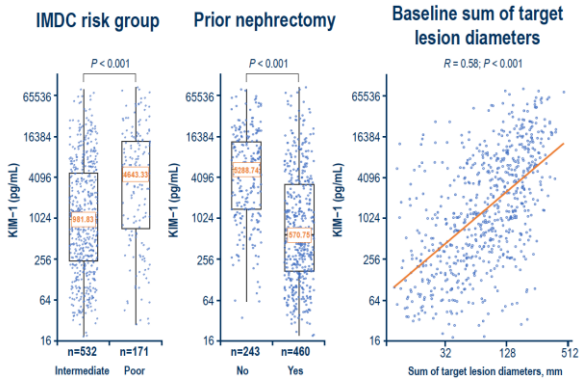
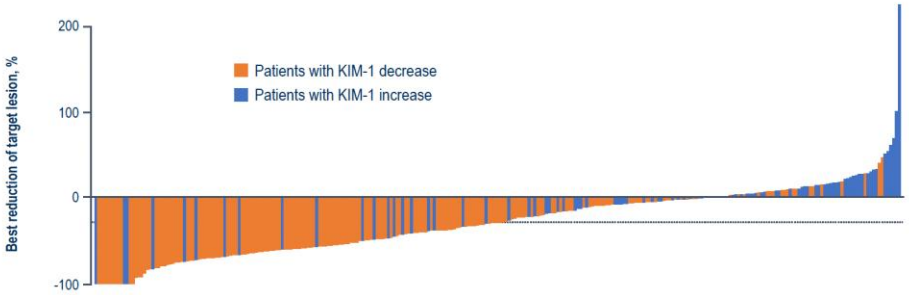
Relationship Between Baseline KIM-1 Levels and Clinical Variables

- Baseline KIM-1 levels were balanced between treatment arms

	N+I	C+N+I
Mean (±SD) concentration, pg/mL	6333.1 (±12851)	6324.4 (±11741)

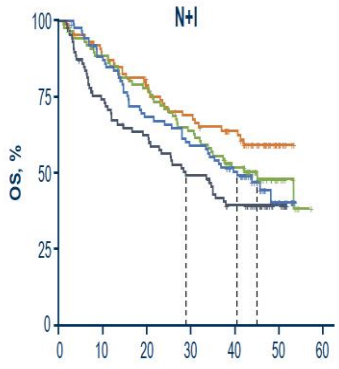
- Patients with poor-risk disease per IMDC, without prior nephrectomy, and with a larger sum of the longest diameters of target lesions had significantly higher baseline KIM-1 levels





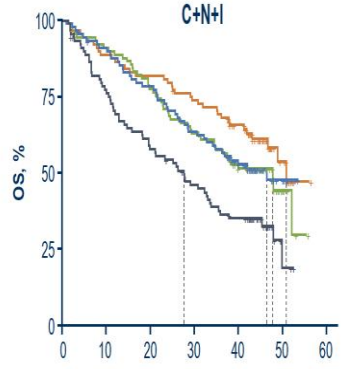
Higher Baseline KIM-1 Levels Were Associated With Worse OS

Kaplan-Meier OS analyses stratified by quartiles of baseline circulating KIM-1



Number at risk:

Q1 : 19–280 pg/mL	87	75	64	55	43	8	0
Q2: 282–1189 pg/mL	87	76	67	54	39	10	0
Q3: 1199–6212 pg/mL	87	75	58	50	39	6	0
Q4: 6393–85,909 pg/mL	86	63	52	41	30	7	0



Number at risk:

Q1 : 18–266 pg/mL	89	78	72	64	49	11	0
Q2: 268–1247 pg/mL	89	81	69	56	38	6	0
Q3: 1279–6743 pg/mL	89	79	68	55	38	10	0
Q4: 6815–77,057 pg/mL	89	66	50	38	27	2	0

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Relevance of the CPS score and tumor nephrectomy in the SUNNIFORECAST trial comparing ipilimumab/nivolumab versus standard of care in non-clear cell renal cell cancer

Reunión post Congreso de la Sociedad Europea de Oncología Médica 2025

Response by PDL1-CPS status

Explorative analysis

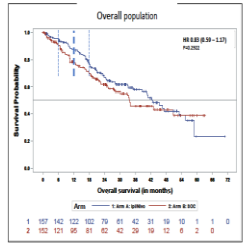
	Overall N (%)		Arm A IPI/NIvo N (%)		Arm B SOC N (%)	
PDL1-CPS	CPS<1	CPS≥1	CPS<1	CPS≥1	CPS<1	CPS≥1
CR	6 (6.0%)	5 (4.0%)	6 (11.1%)	4 (6.6%)	0 (0.0%)	1 (1.6%)
PR	15 (15.0%)	34 (27.4%)	6 (11.1%)	23 (37.7%)	9 (19.6%)	11 (17.5%)
ORR	**21 (21.0%)**	**39 (31.4%)**	**12 (22.2%)**	**27 (43.3%)**	**9 (19.6%)**	**12 (19.1%)**
SD	51 (51.0%)	56 (45.2%)	20 (37.0%)	20 (32.8%)	31 (67.4%)	36 (57.1%)
PD	28 (28.0%)	29 (23.4%)	22 (40.7%)	14 (23.0%)	6 (13.0%)	15 (23.8%)

Comparison ORR vs SD+PD - CPS<1 vs CPS≥1:
Ipi/Novo: p=0.0113 (X^2-Test)
SOC: p=0.685 (X^2-Test)

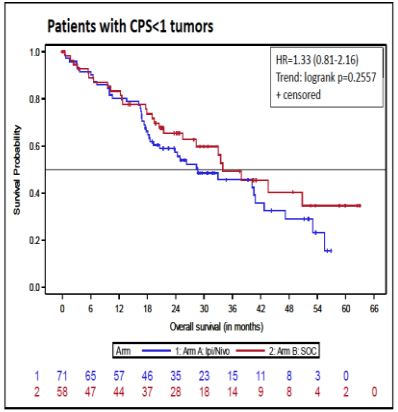
Results

Overall survival by PDL1-CPS status

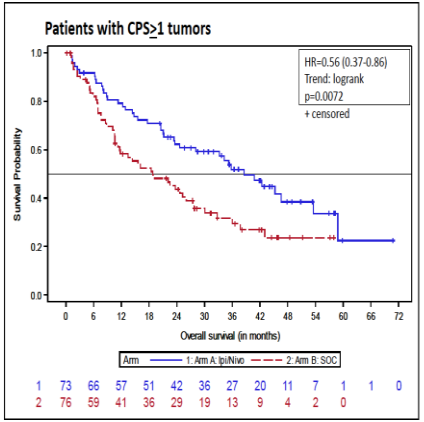
Explorative analysis



Median follow-up: 24.3 mos (0.5 -70.2)



CPS<1: Median OS I/N 28.66 mos (18.55-40.86) vs SOC 33.95 mos (25.52-*)



CPS>1: Median OS I/N 38.55 mos (23.57-53.55) vs SOC 18.81 mos (11.27-27.44)

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MENSAJES FINALES

RAMPART	• Estudio positivo en adyuvancia con inmunoterapia • Alta toxicidad, no impacto demostrado en SG • ¿Rendimiento en tumores no célula clara? • ¿Brazo de Durvalumab en monoterapia?
KEYMAKER	• Resultados que podrían llevar a incorporar Belzutifan a 1ª línea • No parece aumentar ORR, pero sí la supervivencia • ¿Descartamos otras dianas en cáncer renal (LAG3, TIGIT)? • El triplete con anti-CTLA4 tampoco parece muy prometedor…
OPTIC-RCC	• Conceptualmente precioso, pero poco factible • Enriquecimiento de poblaciones respondedoras • ¿Tenemos suficiente evidencia para que los clusters decidan el tto? • No olvidar la gran heterogeneidad del tumor renal

Muchas gracias por su atención

Dr. Álvaro Pinto

Hospital Universitario La Paz, Madrid