GONORTE
Grupo Oncológico

REUNIÓN POST CONGRESO DE LA
SOCIEDAD EUROPEA DE ONCOLOGÍA MÉDICA 2024

Presentaciones más destacadas en cáncer renal

Dra. Teresa Alonso

Hospital Universitario Ramón y Cajal, Madrid

DISCLOSURES

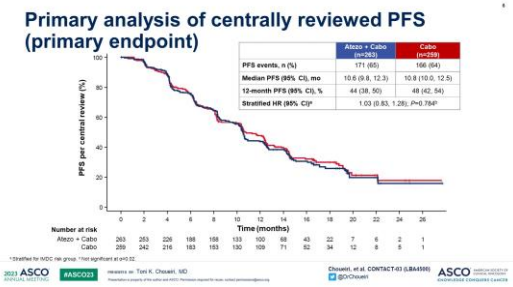
Personal conflicts of interest Scientific consultancy role (speaker and advisory roles) from Lilly, Ipsen, Bayer, Johnson & Johnson, Astellas, Eisai, Advanced Accelerator Applications, MSD, Pfizer.

Research support Research grants from Pfizer, Roche, IPSEN, Johnson & Johnson.

SOME QUESTIONS FROM THE ADVANCED DISEASE MANAGEMENT

IO RECHALLENGE
TKI SEQUENCING
ROLE OF HIF2ALFA INHIBITION

Previous data (PD-L1 inhibition + TKI immediately after PD-1/PD-L1 progression) → **CONTACT 03**



IO RECHALLENGE

TKI SEQUENCING

ROLE OF HIF2ALFA INHIBITION

TiNivo-2: P

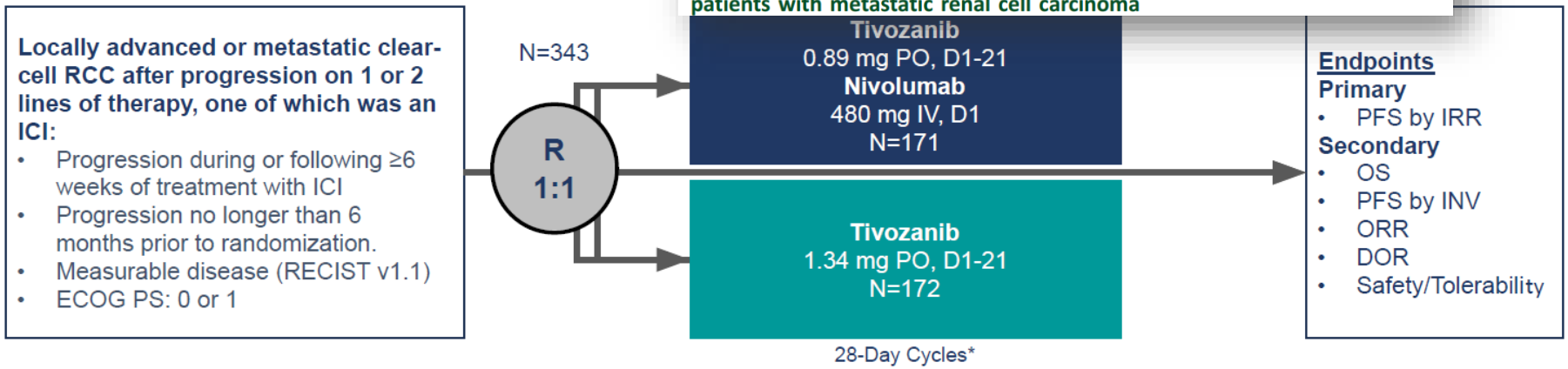
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

Tivozanib 1.5mg/24h + Nivo 480 mg Q4W

ORIGINAL ARTICLE

TiNivo: safety and efficacy of tivozanib-nivolumab combination therapy in patients with metastatic renal cell carcinoma



Stratification Factors
- IMDC risk category
- Prior therapy (ICI as most recent therapy or not)

Key Considerations
- Reduced dose of tivozanib in combination arm was agreed with regulatory authorities due to potential risk of higher rate of grade 3/4 hypertension
- Prior therapy (ICI as most recent therapy or not)
  - Test if ICI break impacts outcome (reset the immune system?)

Motzer TK, et al. ESMO 2024

BASELINE CHARACTERISTICS		CONTACT-03 (2020-2021)	TINIVO-2 (2021 – 2023)
Number of patients		522	343
Experimental arm		Cabozantinib 60 mg/24h + Atezolizumab 1200 mg iv q3w	Tivozanib 0.89 mg/24h 3/1 + nivolumab 480mg
Control arm		Cabozantinib 60 mg/24h	Tivozanib 1.34 mg/24h
Median follow up, months		15.6	11.8
Sarcomatoid pheatures, N (%)		25 (10)	-
IMDC	Favorable, N (%) Intermediate, N (%) Poor, N (%)	49 (19) 172 (65) 41 (16)	30 (18) 114 (67) 27 (16)
Previous treatment	**Adjuvant, N (%)** 1L Metastatic, N (%) 2L Metastatic, N (%)	**1 (<1)** 144 (55) 118 (45)	**25 (15%)** 111 (65%) 60 (35%)
1L treatment		Ipilimumab + nivolumab 80 (31%) Sunitinib 77 (29%); Pazopanib 36 (14%) **Axitinib + pembrolizumab 36 (14%)**	Ipilimumab + nivolumab 63 (39%); Nivolumab 6 (4%) Sunitinib or Pazopanib 11 (6%) **TKI + IO 60 (35%)**
2 L treatment		**Nivolumab 104/119 (87%)**	Cabozantinib/Sunitinib 38/65 (22%); **Nivolumab 11/65 (6%)**
VEGFR-TKI treatment	0L, N(%) 1L, N(%) **2L, N(%)**	93 (35%) 166 (63%) **4 (2%)**	53 (31%) 96 (56%) **22 (13%)** **Most recent therapy Non ICI: 49 (29%)**

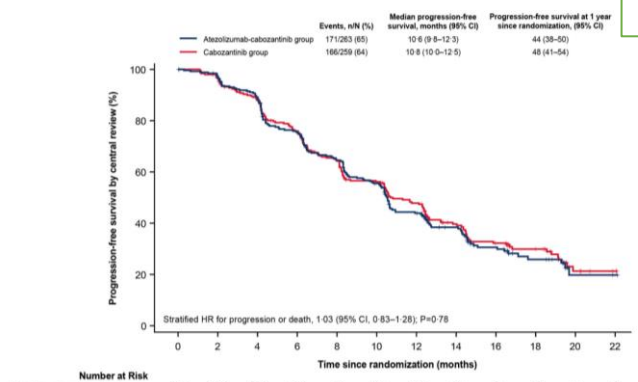
Pal SK, et al. Lancet. 2023 Jul 15;402(10397):185-195; Choueiri TK, et al. ESMO 2024; Choueiri TK, et al. Lancet. 2024; Published Online September 13, 2024.

GONORTE Grupo Oncológico

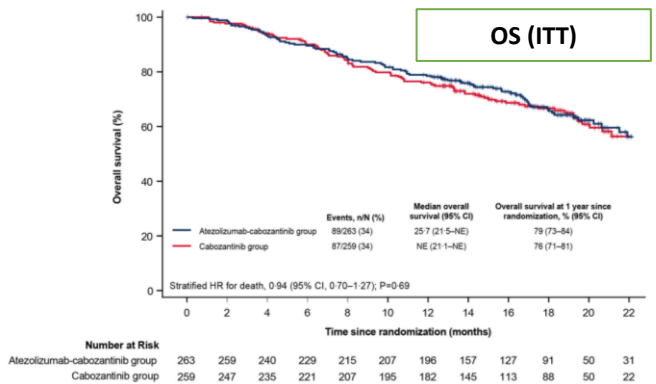
REUNIÓN POST CONGRESO DE LA SOCIEDAD EUROPEA DE ONCOLOGÍA MÉDICA 2024

CONTACT-03

PFS (BICR ITT)

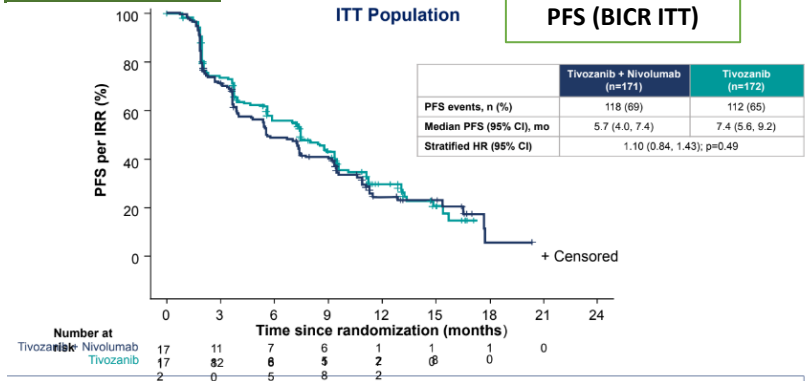


OS (ITT)



TINIVO-2

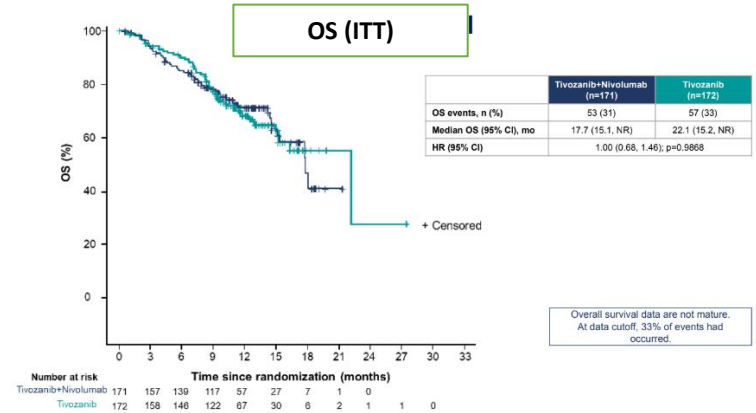
PFS (BICR ITT)



	Tivozanib + Nivolumab (n=171)	Tivozanib (n=172)
PFS events, n (%)	118 (69)	112 (65)
Median PFS (95% CI), mo	5.7 (4.0, 7.4)	7.4 (5.6, 9.2)
Stratified HR (95% CI)	1.10 (0.84, 1.43); p=0.49	

Median follow up was 11.8 months for the tivozanib + nivolumab cohort and 12.5 months for tivozanib monotherapy

OS (ITT)



	Tivozanib+Nivolumab (n=171)	Tivozanib (n=172)
OS events, n (%)	53 (31)	57 (33)
Median OS (95% CI), mo	17.7 (15.1, NR)	22.1 (15.2, NR)
HR (95% CI)	1.00 (0.68, 1.46); p=0.9868	

Overall survival data are not mature. At data cutoff, 33% of events had occurred.

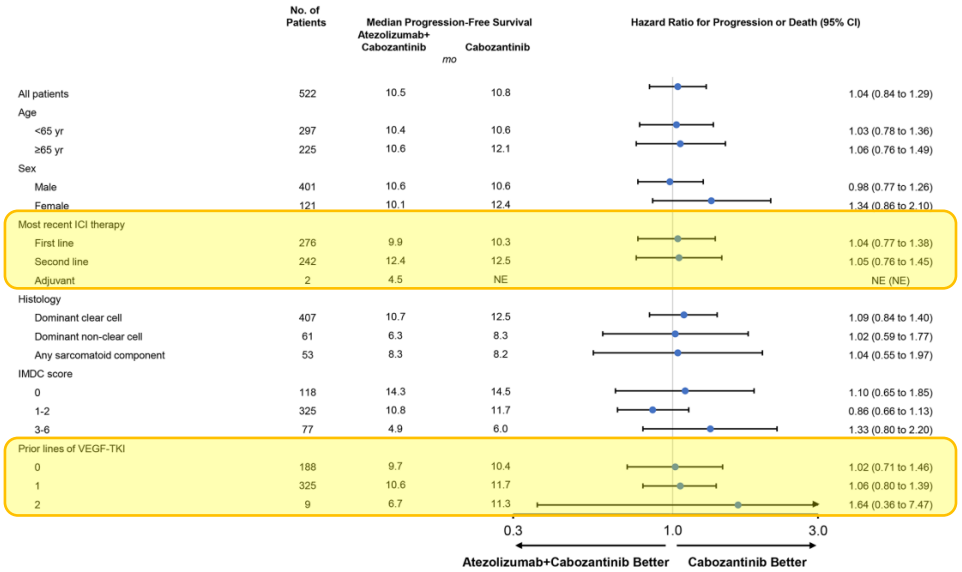
Motzer TK, et al. ESMO 2024; Pal SK, et al. Lancet. 2023 Jul 15;402(10397):185-195.

GONORTE Grupo Oncológico

REUNIÓN POST CONGRESO DE LA SOCIEDAD EUROPEA DE ONCOLOGÍA MÉDICA 2024

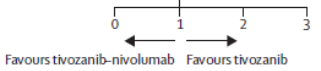
CONTACT-03

PFS subgroup analysis



TINIVO-2

	Tivozanib–nivolumab event/N	Tivozanib event/N	Tivozanib–nivolumab median progression-free survival, months (95% CI)	Tivozanib median progression-free survival, months (95% CI)	Hazard ratio for progression or death (95% CI)
Age (years)					
<65	68/89	65/97	4·8 (3·4–7·3)	7·4 (5·5–9·2)	1·25 (0·89–1·76)
≥65	50/82	47/75	9·2 (5·5–9·6)	7·6 (5·2–10·0)	0·92 (0·61–1·37)
Sex					
Male	86/125	88/134	5·6 (3·9–7·5)	7·4 (5·5–9·2)	1·01 (0·75–1·36)
Female	32/46	24/38	6·7 (3·7–10·9)	7·4 (5·6–12·9)	1·27 (0·75–2·16)
ECOG					
0	52/76	53/85	7·3 (4·0–9·4)	8·8 (7·2–11·1)	1·15 (0·78–1·69)
1	66/94	59/87	5·5 (3·7–9·0)	6·0 (3·7–8·6)	0·95 (0·67–1·36)
IMDC risk category					
Favourable	18/30	15/31	9·3 (4·0–11·4)	11·2 (9·3–13·1)	1·37 (0·69–2·73)
Intermediate	78/114	75/115	5·7 (4·0–9·4)	7·4 (4·5–8·4)	0·99 (0·72–1·36)
Poor	22/27	22/26	3·7 (2·7–7·4)	5·7 (2·3–9·2)	1·35 (0·73–2·50)
Previous nephrectomy status					
Complete	45/70	59/85	9·0 (5·5–9·6)	9·3 (5·5–11·1)	0·99 (0·65–1·49)
Partial	21/32	15/22	4·8 (2·2–10·9)	7·5 (2·1–15·2)	1·17 (0·60–2·27)
Other	4/6	11/14	5·8 (1·9–NE)	5·2 (1·5–9·2)	0·60 (0·19–1·97)
Previous systemic anticancer therapies (line of therapy)					
Second line	71/111	64/105	7·3 (5·4–9·3)	9·2 (7·4–10·0)	1·15 (0·82–1·62)
Third line	47/60	48/67	4·8 (3·2–7·5)	5·5 (2·9–7·4)	0·97 (0·65–1·45)
Use of immune checkpoint inhibitor in most recent line					
Yes	78/122	75/122	7·4 (5·6–9·6)	9·2 (7·4–10·0)	1·10 (0·80–1·52)
No	40/49	37/50	3·7 (2·7–5·4)	3·7 (1·9–7·2)	0·95 (0·61–1·50)
Use of VEGFR TKI in most recent line*					
Yes	37/45	37/50	3·4 (2·2–4·8)	3·7 (1·9–7·2)	0·96 (0·61–1·52)
No	37/66	36/65	9·6 (7·5–11·2)	9·3 (7·4–14·7)	0·95 (0·60–1·51)
Previous use of VEGFR TKI (any previous line)					
0 VEGFR TKI	29/53	28/53	9·6 (7·4–15·3)	9·4 (7·4–15·5)	1·03 (0·61–1·74)
1 VEGFR TKI	69/96	70/101	5·4 (3·7–6·7)	7·4 (5·5–8·8)	1·04 (0·74–1·45)
2 VEGFR TKI	20/22	14/18	3·1 (2·1–4·0)	3·8 (1·9–7·2)	1·33 (0·67–2·65)



Motzer TK, et al. ESMO 2024

CONTACT-03

RECIST 1.1 per central review[a]

	Atezo + Cabo (n=259)	Cabo (n=254)
Confirmed objective response, n, (%) [95% CI]	105 (40.5) [34.5, 46.8]	104 (40.9) [34.8, 47.3]
Complete response, n (%)	0	2 (0.8)
Partial response, n (%)	105 (40.5)	102 (40.2)
Stable disease, n (%)	131 (50.6)	121 (47.6)
Progressive disease, n (%)	11 (4.2)	13 (5.1)
Not evaluable or missing, n (%)	12 (4.6)	16 (6.3)
Ongoing response at data cutoff, n/N (%)[b]	53/105 (50.5)	55/104 (52.9)
Median duration of response (range), mo	12.7 (2.1+ to 22.9+)	14.8 (2.3+ to 25.6+)

TINIVO-2

	Tivozanib + Nivolumab (n=171)	Tivozanib (n=172)
ORR, n (%), [95% CI]	33 (19.3) [13.7, 26.0]	34 (19.8) [14.1, 26.5]
CR, n (%)	1 (0.6)	1 (0.6)
PR, n (%)	32 (18.7)	33 (19.2)
SD, n (%)	74 (43.3)	81 (47.1)
PD, n (%)	49 (28.7)	43 (25.0)
NE, n (%)	15 (8.8)	14 (8.1)
mDOR, mo (95% CI)	15.77 (5.65-NR)	9.66 (3.71-NR)

Motzer TK, et al. ESMO 2024

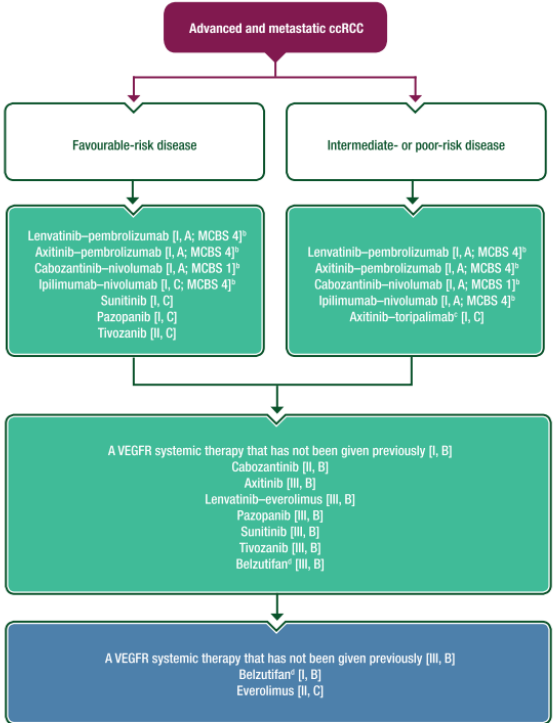
	CONTACT-03	TINIVO-2
	Cabozantinib 60 mg/24	**Tivozanib 1.34 mg/24h**
Grade 3-4 Aes	47.3%	35%
TR discontinuation	4%	19%
AE interruption or reduction	87.1%	76%
Diarrhea	70.7%	36%
Nausea	35.9%	28%
Asthenia	29.3%	21%
Fatigue	23.8%	40%
Anemia	18.8%	9%
Hypertension	34%	50%

Motzer TK, et al. ESMO 2024

IO RECHALLENGE

TKI SEQUENCING

ROLE OF HIF2ALFA



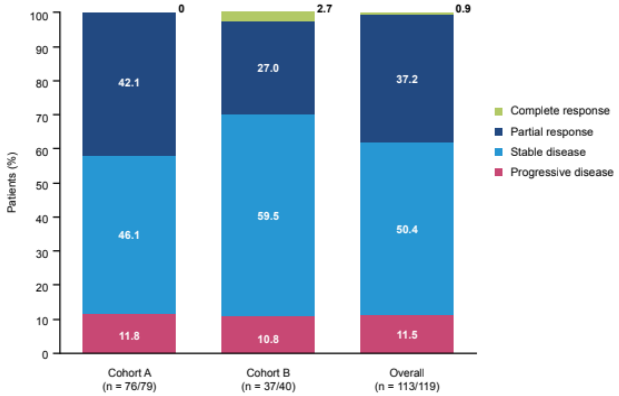
Powles T, et al. Ann Oncol. 2024;35(8):692-706

GONORTE Grupo Oncológico

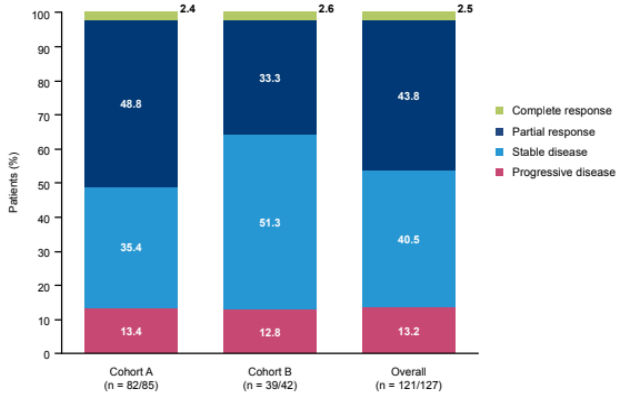
CABOPOINT

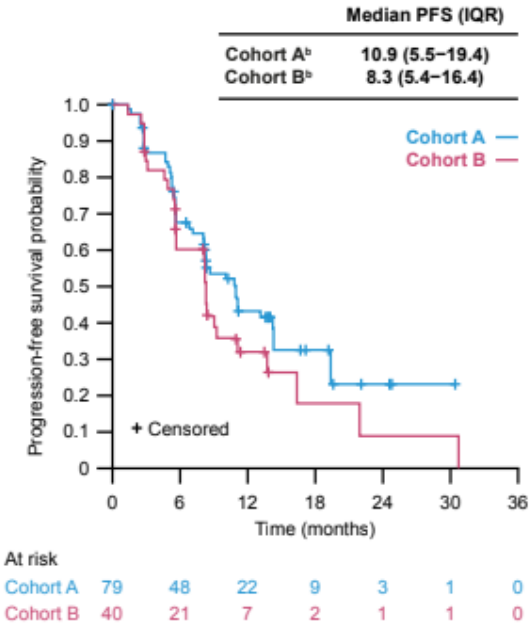
REUNIÓN POST CONGRESO DE LA SOCIEDAD EUROPEA DE ONCOLOGÍA MÉDICA 2024

	Cohort A	Cohort B	Overall	
	79	40	119	Patients, n
$p < 0.0001$[b]	**32 (40.5) 29.6–52.1**	**11 (27.5) 14.6–43.9**	**43 (36.1) 27.5–45.4**	**ORR, n (%) 95% CI**
	67 (84.8) 75.0–91.9	33 (82.5) 67.2–92.7	100 (84.0) 76.2–90.1	DCR, n (%) 95% CI



	Cohort A	Cohort B	Overall	
	85	42	127	Patients, n
	42 (49.4) 38.4–60.5	**14 (33.3) 19.6–49.5**	**56 (44.1) 35.3–53.2**	**ORR, n (%) 95% CI**
	71 (83.5) 73.9–90.7	34 (81.0) 65.9–91.4	105 (82.7) 75.0–88.8	DCR, n (%) 95% CI





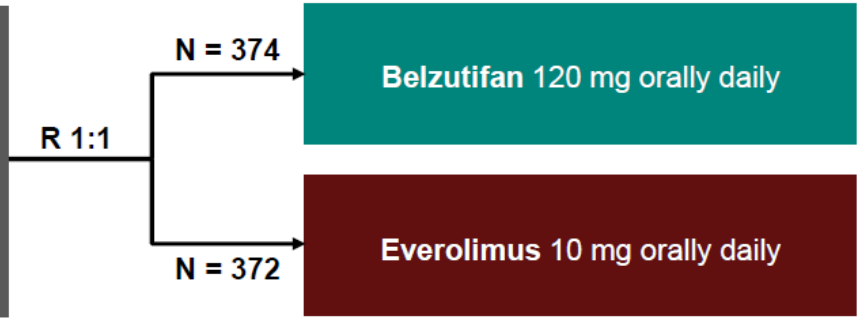
Albiges L, et al. ESMO 2024

IO RECHALLENGE
TKI SEQUENCING
ROLE OF HIF2ALFA INHIBITION

LITESPARK-005

Key Eligibility Criteria

- Unresectable, locally advanced or metastatic clear cell RCC
- Disease progression after 1-3 prior systemic regimens, including ≥1 anti–PD-(L)1 mAb and ≥1 VEGFR-TKI
- Karnofsky Performance Status score ≥70%



Stratification Factors

- IMDC prognostic score[a]: 0 vs 1-2 vs 3-6
- Prior VEGFR-targeted therapies: 1 vs 2-3

Dual Primary Endpoints:

- PFS per RECIST 1.1 by BICR
- OS
- The study was considered positive if either of the dual primary endpoints was met

Key Secondary Endpoint:

- ORR per RECIST 1.1 by BICR

Other Secondary Endpoints Include:

- DOR per RECIST 1.1 by BICR
- Safety

Rini B, et al. ESMO 2024

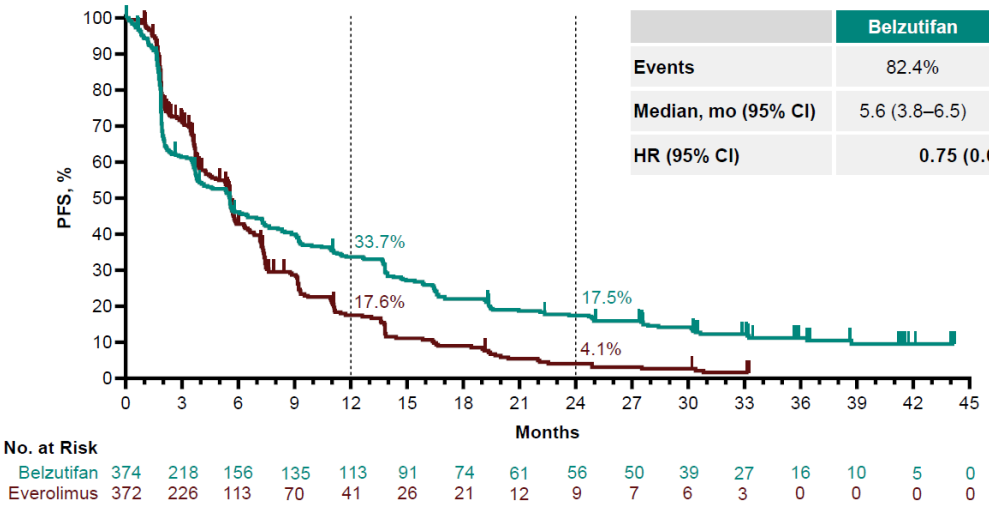
LITESPARK-005

Characteristic	ITT		Ongoing Treatment
	Belzutifan (N = 374)	Everolimus (N = 372)	Belzutifan (n = 54)
Age, median (range), yrs	62 (22–90)	63 (33–87)	64 (44–79)
Male, %	79.4	76.3	81.5
KPS score[a], %			
90/100	63.6	64.5	81.5
70/80	36.1	35.2	18.5
IMDC risk categories, %			
Favorable	21.7	22.6	31.5
Intermediate	66.3	65.1	59.3
Poor	12.0	12.4	9.3
Sarcomatoid features present, %	11.2	8.3	11.1
Prior nephrectomy, %	69.8	69.6	83.3
No. prior VEGFR-TKIs, %			
1	49.7	51.1	46.3
2-3	50.3	48.9	53.7
No. prior lines of therapy[b], %			
1	12.0	14.0	16.7
2	42.2	44.6	44.4
3	45.2	40.3	38.9

Rini B, et al. ESMO 2024

LITESPARK-005

Primary Endpoint: PFS per RECIST 1.1 by BICR

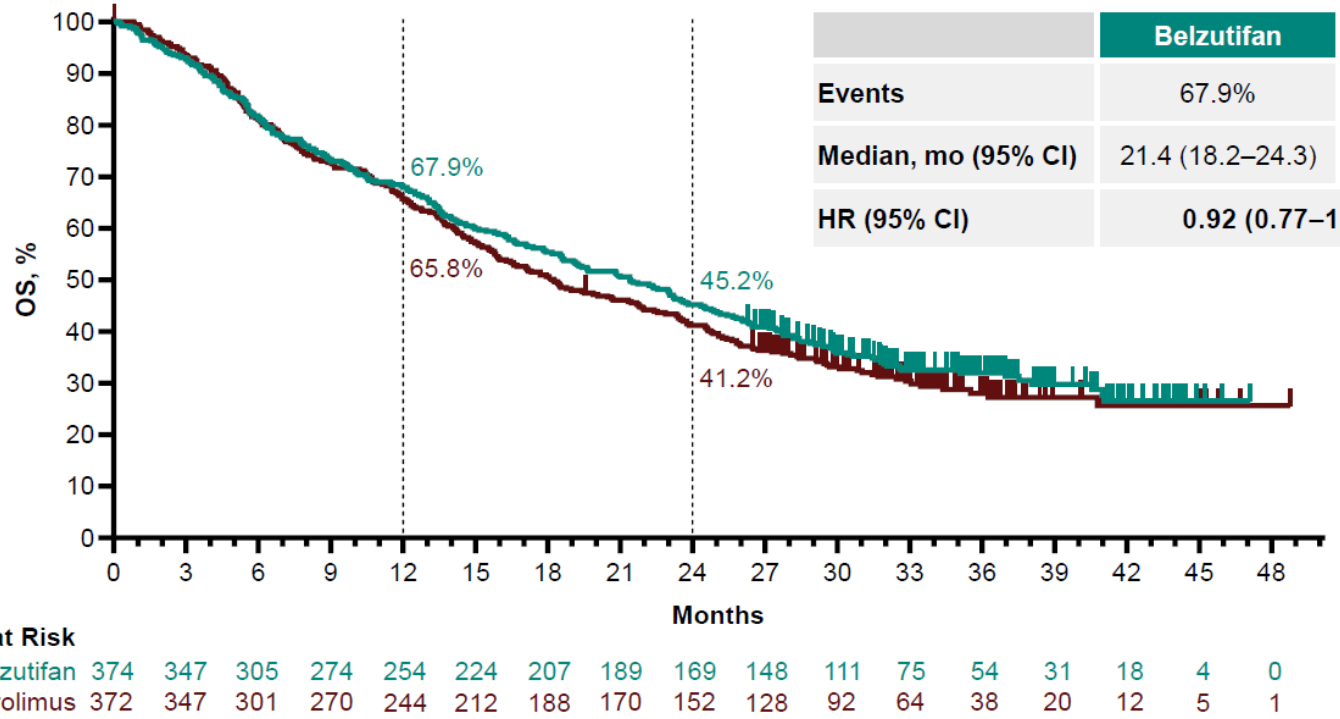


	Belzutifan	Everolimus
Events	82.4%	75.0%
Median, mo (95% CI)	5.6 (3.8–6.5)	5.6 (4.8–5.8)
HR (95% CI)	0.75 (0.63–0.88)	

	Belzutifan (N = 374)	Everolimus (N = 372)
ORR, % (95% CI)	**22.7% (18.6–27.3)**	**3.5% (1.9–5.9)**
Estimated difference in % (95% CI)	**19.2 (14.8–24.1)**	
Confirmed best objective response, %		
CR	3.5%	0
PR	19.3%	3.5%
SD	38.2%	65.9%
PD	34.0%	21.5%
Not evaluable[a]	1.3%	2.4%
No assessment[b]	3.7%	6.7%

Rini B, et al. ESMO 2024

Primary Endpoint: OS



	Belzutifan	Everolimus
Events	67.9%	69.6%
Median, mo (95% CI)	21.4 (18.2–24.3)	18.2 (15.8–21.8)
HR (95% CI)	**0.92 (0.77–1.10); *P*=0.18**	

Rini B, et al. ESMO 2024

	CONTACT-03	TINIVO-2	LITESPARK-005
	Cabozantinib 60 mg/24	Tivozanib 1.34 mg/24h	Belzutifan 120 mg/24h
Grade 3-4 Aes	47.3%	35%	39.5%
TR discontinuation	4%	19%	5.9%
AE interruption or reduction	87.1%	76%	57.5%
Diarrhea	70.7%	36%	11.8%
Nausea	35.9%	28%	18%
Asthenia	29.3%	21%	14.5%
Fatigue	23.8%	40%	31.5%
Anemia	18.8%	9%	82.5%
Hypertension	34%	50%	-

LITESPARK-005

ADR	Incidence, n (%)	Time to onset, median (range), mo
Anemia	310 (83.3)	1.0 (0.03–27.4)
Hypoxia	53 (14.2)	1.0 (0.03–21.1)
Dizziness	50 (13.4)	2.3 (0.03–34.2)
Dyspnea	57 (15.3)	1.9 (0.03–25.8)
Fatigue	120 (32.3)	1.5 (0.03–29.9)
Nausea	69 (18.5)	1.4 (0.03–24.0)
Weight increased	22 (5.9)	3.3 (0.5–15.0)

ADR	Incidence, n (%)	Duration, median (range), mo
Anemia	310 (83.3)	4.6 (0.1+–47.1+)
Hypoxia	53 (14.2)	0.5 (0.03–31.9+)
Dizziness	50 (13.4)	1.1 (0.03–35.2)
Dyspnea	57 (15.3)	3.3 (0.03–39.5+)
Fatigue	120 (32.3)	NR (0.1–43.9+)
Nausea	69 (18.5)	1.2 (0.03–38.6)
Weight increased	22 (5.9)	16.6 (0.6–40.0+)

Rini B, et al. ESMO 2024

VARIANT HISTOLOGIES OF RCC

SUNNIFORECAST

Key Inclusion Criteria (KIC)

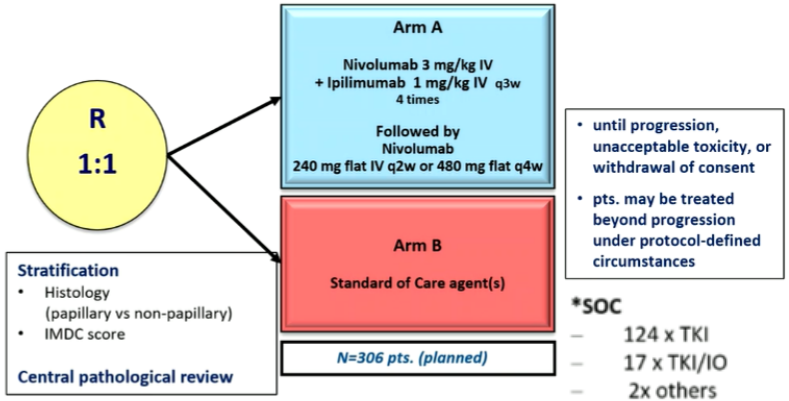
- Metastatic or locally advanced nccRCC (>50% ncc component):

  nccRCC subtypes: papillary, chromophobe, collecting duct carcinoma (CDC), renal medullary carcinoma (RMC), unclassified, etc., or sarcomatoid*
- No prior systemic therapy for RCC
- Tumor material available
- Measurable disease as per RECIST v1.1
- Karnofski performance status ≥ 70%
- No active CNS metastases

*sarcomatoid is defined for lesions with at least 20% sarcomatoid component

Follow-up (median, range):
22.3 mos (0.5 – 70.2)

Principal Investigator and Coordinator:
Prof. Dr. L. Bergmann, Med. Klin. II, Goethe University, Frankfurt, Germany



Primary Endpoint: OS rate at 12 months

Key Secondary Endpoints: OS, OS-rate at 6 and 18 months; PFS, ORR, TTP, Safety, QoL

Exploratory Endpoints: predictive biomarkers (e.g.PD-L1 expression)

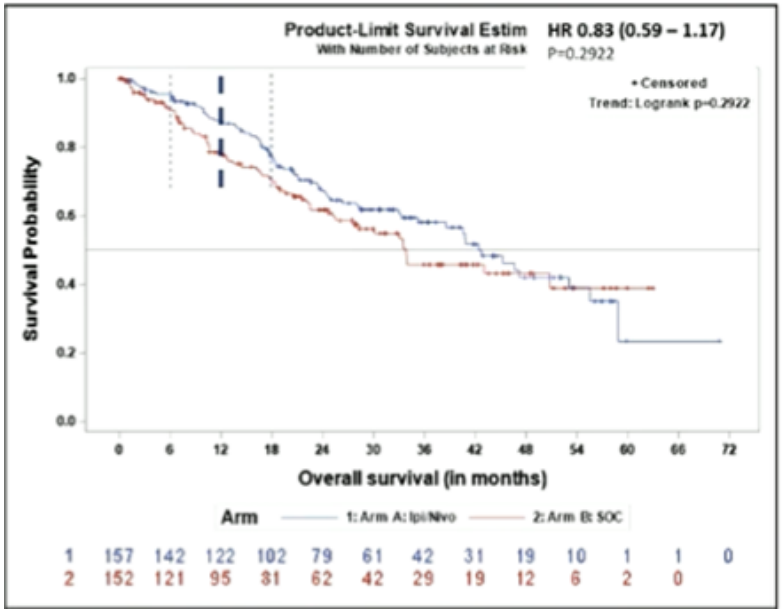
Subtypes of nccRCC (central pathological review)	Total N=309
Papillary RCC	178 (57.6 %)
Chromophobe RCC	60 (19.4 %)
Renal medullary carcinoma	3 (1.0 %)
Translocation RCC (TFE, TEFEB)	17 (5.5%)
Tubulocystic RCC	3 (1.0 %)
Mucinous tubular and spindle cell carcinoma	1 (0.3 %)
Sarcomatoid	14 (4.5 %)
Ductus Bellini carcinoma	3 (1.0%)
Others	21 (6.7 %)

Ahrens M, et al. J Clin Oncol. 2021; 39 (15s): TPS459; Bergmann L, et al. ESMO 2024;

GONORTE
Grupo Oncológico

SUNNIFORECAST

REUNIÓN POST CONGRESO DE LA SOCIEDAD EUROPEA DE ONCOLOGÍA MÉDICA 2024



mOS = 42.38 vs 33.85m
mPFS = 5.2 vs 5.65m

Histology	Treatment	CR	PR	ORR	SD	PD
all nccRCC (N=247*)	Nivo/Ipi	10 (8.0%)	31 (24.8%)	41 (32.8%)	41 (32.8%)	43 (34.4%)
	SOC	2 (1.6%)	22 (18.0%)	124 (19.6%)	75 (61.5%)	23 (18.9%)
				p=0.001		
papillary (N=148)	Nivo/Ipi	7 (9.7%)	14 (19.4%)	21 (29.2%)	27 (37.5%)	24 (33.3%)
	SOC	2 (2.6%)	14 (18.4%)	16 (21.0%)	46 (60.5%)	14 (18.4%)
non-papillary (N=97)	Nivo/Ipi	3 (5.7%)	17 (32.1%)	20 (37.7%)	14 (18.4%)	19 (27.1%)
	SOC	0 (0.0%)	8 (18.2%)	8 (18.2%)	27 (61.4%)	9 (20.5%)
chromophobe (N=54)	Nivo/Ipi	0 (0.0%)	7 (25.9%)	7 (25.9%)	12 (44.4%)	8(29.6%)
	SOC	0 (0.0%)	3 (11.1%)	3 (11.1%)	21 (77.8%)	4 (14.8%)

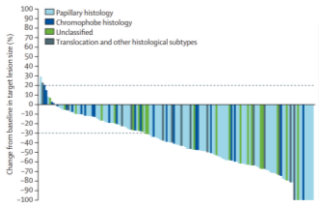
	Nivolpi	SoC
Alive and requiring second-line (n and %)	100 out of 157 63,7%	85 out of 152 56%
Most common 2nd-line tx	Cabo 50%	Nivo 38.9%
Second most common 2nd-line tx	Sunitinib 26%	Cabozantinib 40%

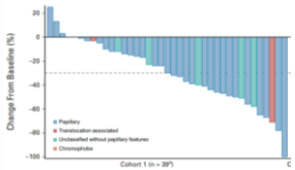
Ahrens M, et al. J Clin Oncol. 2021; 39 (15s): TPS459; Bergmann L, et al. ESMO 2024;

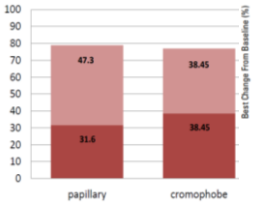
GONORTE
Grupo Oncológico

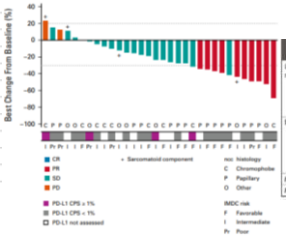
REUNIÓN POST CONGRESO DE LA SOCIEDAD EUROPEA DE ONCOLOGÍA MÉDICA 2024

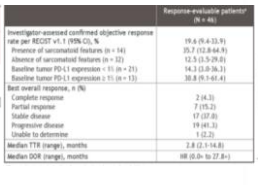
LENVATINIB + PEMBROLIZUMAB (KEYNOTE-B61)	CABOZANTINIB + NIVOLUMAB	AXITINIB + PEMBROLIZUMAB (NEMESIA)	CABOZANTINIB + ATEZOLIZUMAB (COSMIC 021, cohort 10)	NIVOLUMAB + IPILIMUMAB (Checkmate 920, cohort 2)	NIVOLUMAB + IPILIMUMAB + CABOZANTINIB	LENVATINIB + EVEROLIMUS

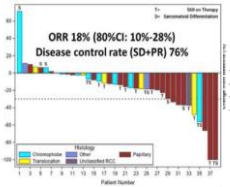


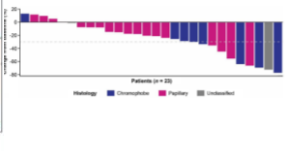












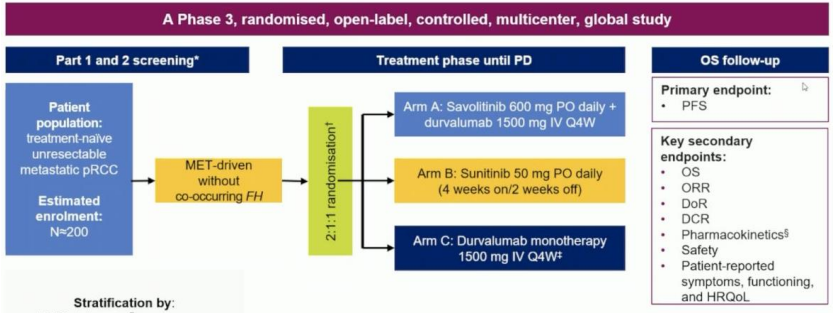
	LEN + PEMBRO	CABO + NIVO	AXI + PEMBRO	CABO + ATEZO	NIVO + IPI	NIVO+IPI+CABO	LEN + EVE
N	158	47	32	32 (pretreated)	46	39	31
ORR	49%	47.5%	43.8%	31%	19.6%	21%	26%
mPFS	18 months	12.5 months	10.8 months	9.5	3.7 months	9.7 months	9.2 months
mOS	Not reached	28 months	-	-	21.2 months	18m OS-rate: 66%	15.6 months

Albiges L, et al. Lancet Oncol. 2023 Aug;24(8):881-891; Lee CH, et al. J Clin Oncol. 2022; 40:2333-2341. ; Stellato M, et al. Int J Mol Sci. 2023 Jan 6;24(2):1096; Pal SK, et al. J Clin Oncol. 2021 Nov 20;39(33):3725-3736; Tykodi SS, et al. J Immunother Cancer. 2022 Feb;10(2):e003844; McGregor B, et al. J Clin Oncol 2023; 41 (16S): 4520; Hutson TE, et al. Eur Urol. 2021 Aug;80(2):162-170; McGregor BA, et al. ESMO 2024..

GONORTE
Grupo Oncológico

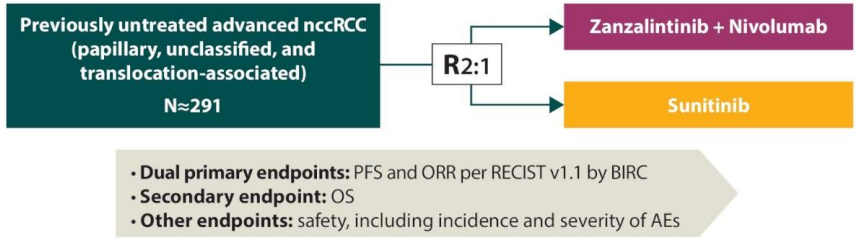
REUNIÓN POST CONGRESO DE LA SOCIEDAD EUROPEA DE ONCOLOGÍA MÉDICA 2024

SAMETA



Choueiri TK, et al. J Clin Oncol. 2022; 40 (16s): TPS4601

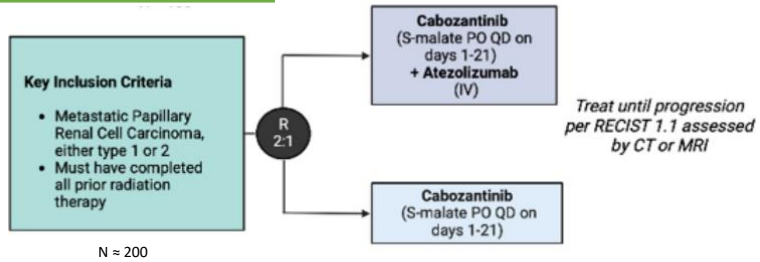
STELLAR 304



AE, adverse event; BIRC, blinded independent radiology committee; nccRCC, non-clear cell renal cell carcinoma; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R, randomized; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1

Pal SK, et al. Ann Oncol. 2023; 34 (2): S1028-S1029

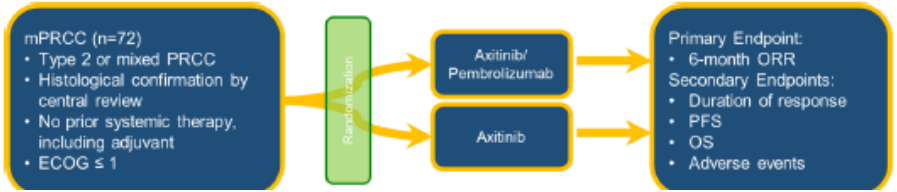
PAPMET2



Primary Endpoint: Compare PFS with metastatic papillary renal cell carcinoma to cabozantinib S-malate with atezolizumab versus cabozantinib alone
Secondary Endpoint: OS, RECIST, ORR, quantitative and qualitative adverse events in each arm

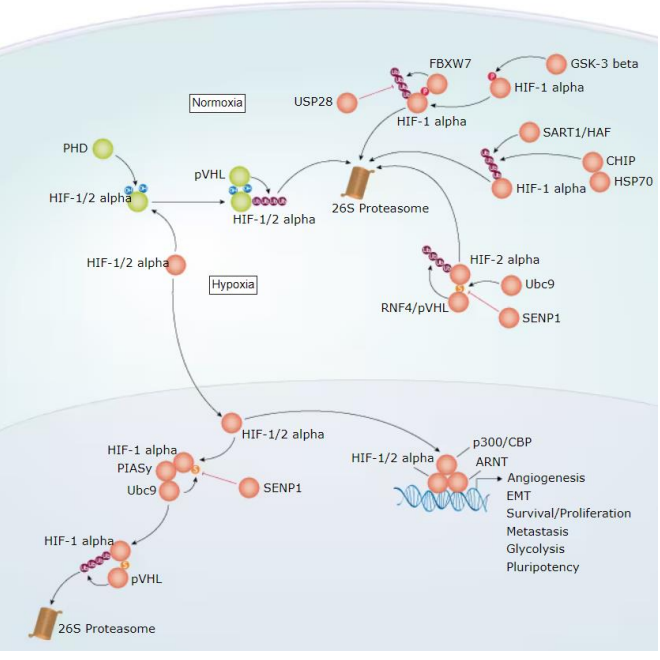
Maughan BL, et al. J Clin Oncol 2024; 42 (4s): TPS493

PAXIPEM



EARLY DATA ON NOVEL DRUGS IN RCC

NOVEL HIF2A inhibitors



NKT2152-101: Ongoing Study of NKT2152 monotherapy in advanced ccRCC

Current Enrollment and Patient Disposition (Data Cut-off June 16, 2024)

Part 1 Dose Escalation
N=60/60

Part 2 Dose Expansion
N=38/40

Clinical Pharmacology Cohorts
N=13/17

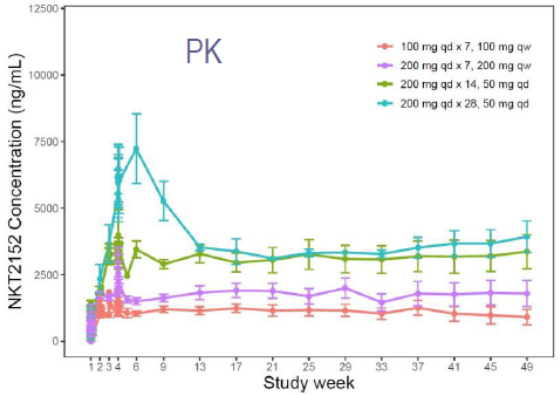
Part 2 Post-Belzutifan
N=2/10

Total Enrolled to Date	113
Ongoing	46 (41%)
Disease/ Clinical Progression	44 (39%)
Adverse Event	14 (12%)
Withdrawal of Consent	5 (4%)
Other	4 (4%)

Characteristic	All Patients (N=113)	Part 1 Patients (N=60)
ECOG PS at baseline 0/1/2, n (%)	48 (42.9) / 62 (55.4) / 2 (1.8)*	28 (47.5) / 30 (50.8) / 1 (1.7)*
IMDC Risk: Favorable/Intermediate/Poor, n (%)	6 (5.3) / 66 (58.4) / **41 (36.3)**	3 (5.0) / 36 (60.0) / **21 (35.0)**
Number of prior lines of therapy		
1/2/3/4 or more, n (%)	15 (13.3) / 31 (27.4) / 29 (25.7) / **38 (33.6)**	6 (10.0) / 12 (20.0) / 19 (31.7) / **23 (38.3)**
Median (range)	3 (1-9)	3 (1-8)
Prior VEGF TKI, n (%)	106 (93.8)	59 (98.3)
Prior I/O therapy, n (%)	110 (97.3)	59 (98.3)
Prior mTOR inhibitor, n (%)	32 (28.3)	25 (41.7)

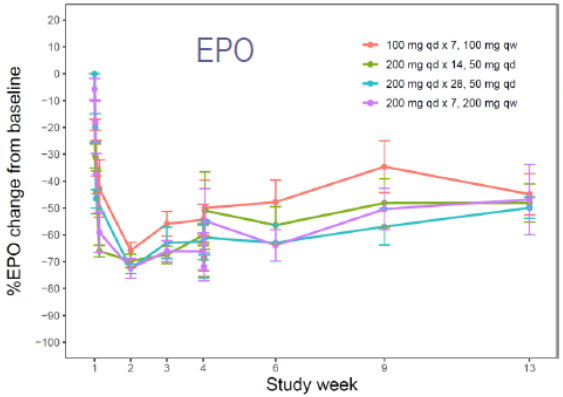
Jonasch E, et al. ESMO 2024

Pharmacokinetic and Pharmacodynamic Profiles support Loading and Maintenance Dosing of NKT2152



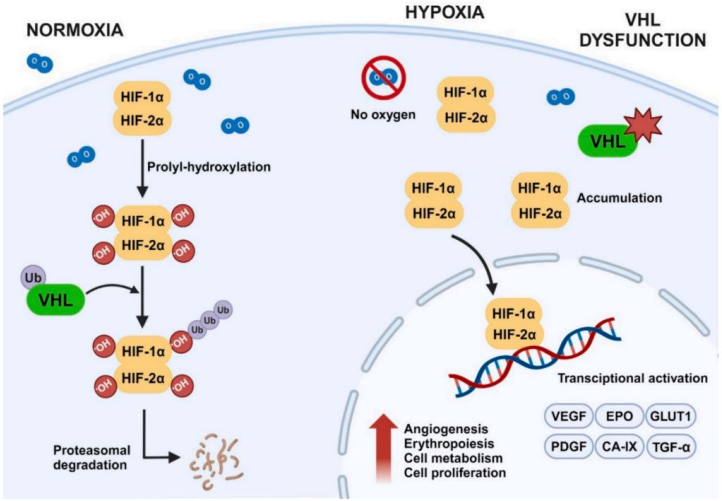
The PK is dose linear and time independent with an estimated median $t_{1/2}$ of 38 days based on a 2-compartment population PK model.

EPO, erythropoietin; PK, pharmacokinetics; PD, pharmacodynamics; $t_{1/2}$, half-life.

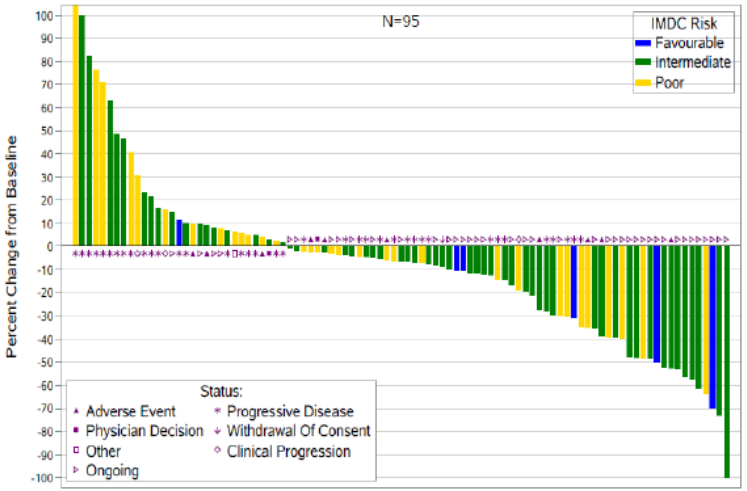


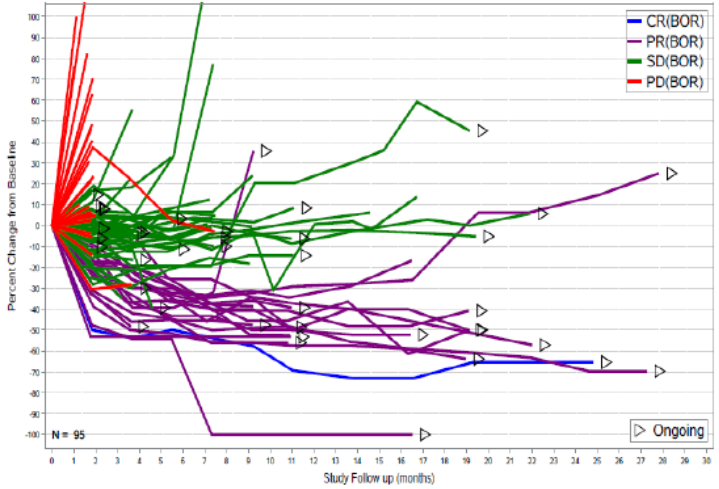
Significant and sustained EPO suppression is observed at all dose levels.

- Maximal fractional inhibition of EPO production (I_{max}): 72%
- Plasma NKT2152 concentration for 50% maximal inhibition (IC_{50}): 16.4 ng/mL



Rioja P, et al. Cancer Treat Rev.2024
Jonasch E, et al. ESMO 2024





	All Patients (N=100)	Part 1 Patients (N=57)
Best Overall Response, n (%)		
CR	1 (1.00)	1 (1.75)
PR	19 (19.0)	14 (24.6)
SD	52 (52.0)	28 (49.1)
PD	28 (28.0)	14 (24.6)

There are 5 patients without any post-baseline response assessments, who were efficacy evaluable due to clinical progression or death.

Disease Control Rate (DCR) is the proportion of patients who had CR, PR, or durable SD (8+ weeks) as assessed by Investigator per RECIST 1.1.

Eric Jonasch, MD

Median TTR (range), months	3.7 (1.6-9.1)
Median DOR (95% CI)	NE (8.31, NE)
DCR (95% CI)	60% (50%, 70%)

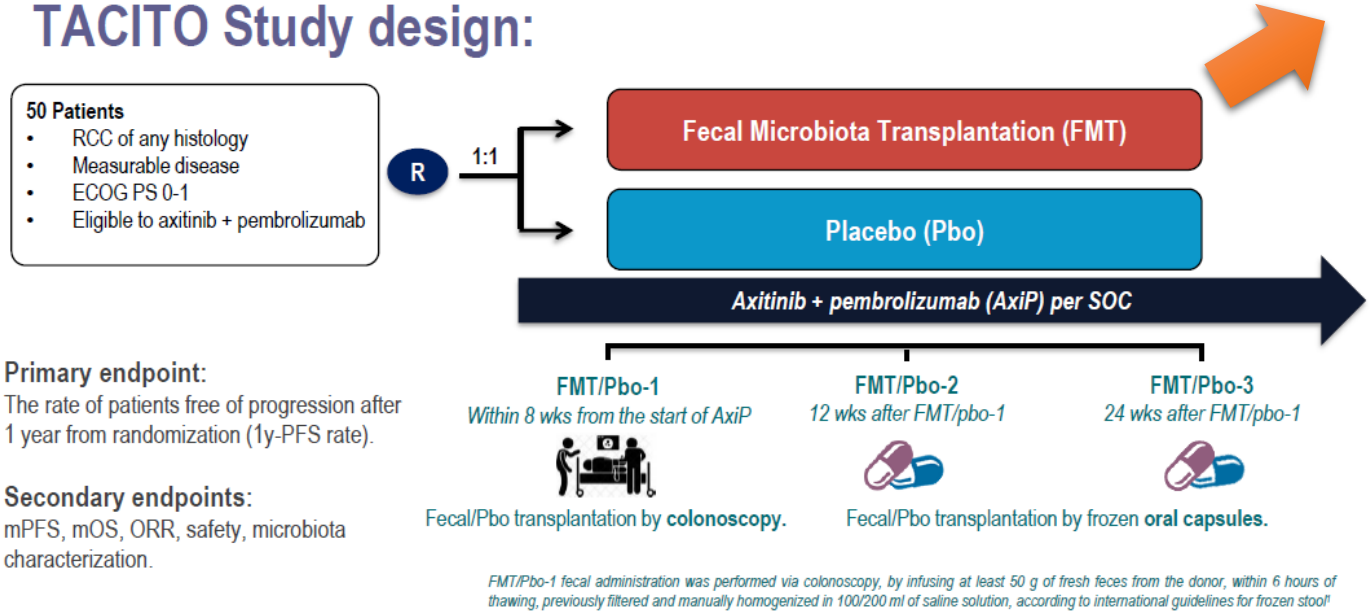
- Overall, in 100 efficacy evaluable patients: ORR 20% and mPFS 7.4 m
- In Part 1 (n=57) with longer follow up: ORR 26.3% and mPFS 9.2 m

Jonasch E, et al. ESMO 2024

Modulating GUT MICROBIOTA

CR in APR/2020 to nivolumab + ipilimumab mRCC

TACITO Study design:



Primary endpoint:
The rate of patients free of progression after 1 year from randomization (1y-PFS rate).

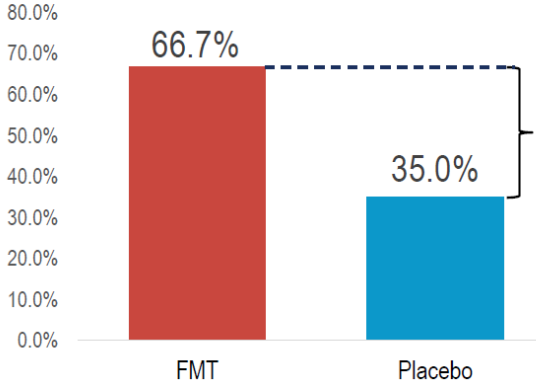
Secondary endpoints:
mPFS, mOS, ORR, safety, microbiota characterization.

FMT/Pbo-1 fecal administration was performed via colonoscopy, by infusing at least 50 g of fresh feces from the donor, within 6 hours of thawing, previously filtered and manually homogenized in 100/200 ml of saline solution, according to international guidelines for frozen stool[1]

Ciccarese Ch, et al. ESMO 2024

Primary endpoint

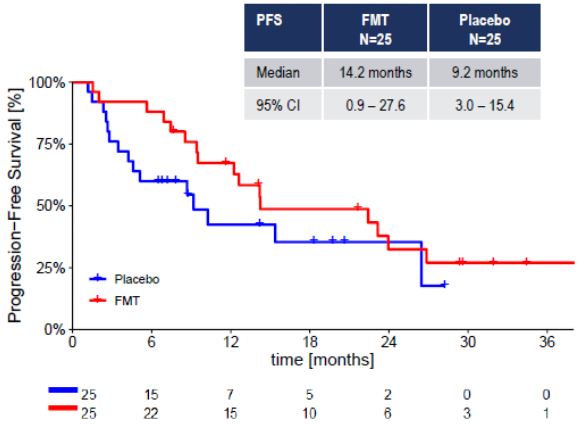
Rate of patients free of progression after 1 year from randomization:

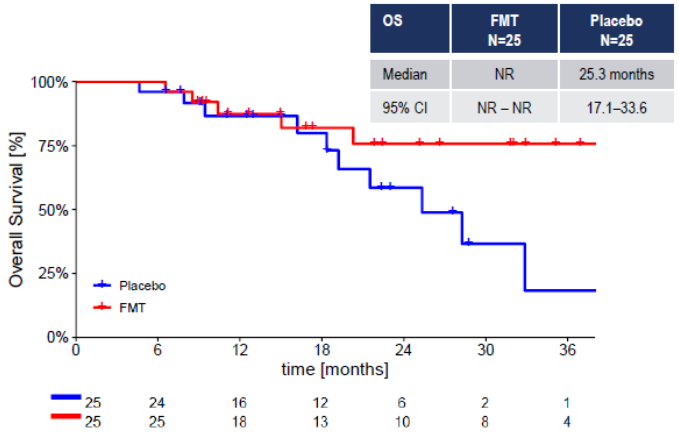


FMT increased the 1-y PFS rate of 31.7% compared to Pbo (p = 0.036)

The primary endpoint was met.

Tumor Response*	FMT N=25 (%)	Placebo N=25 (%)
Overall Response Rate	13 (52.0%)	7 (28.0%)
Complete response	0	0
Partial response	13 (52.0%)	7 (28.0%)
Stable disease	9 (38.0%)	11 (44.0%)
Progressive disease	2 (8.0%)	7 (28.0%)
Not evaluable	1 (4.0%)	0

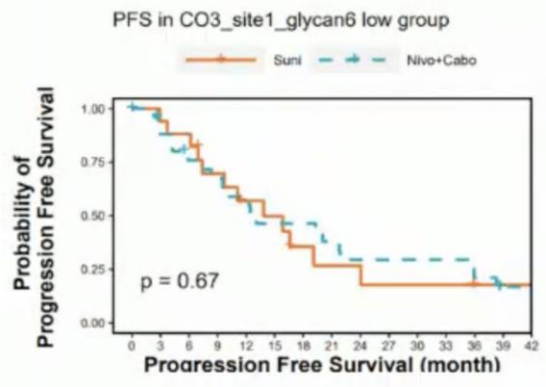


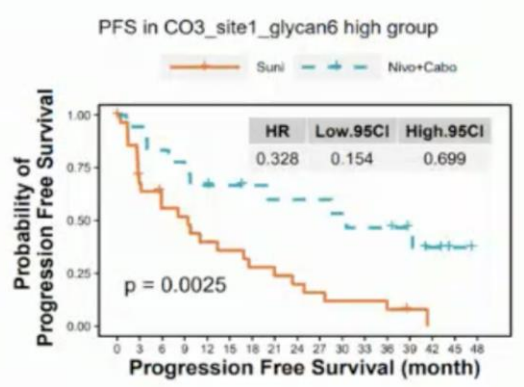


Ciccarese Ch, et al. ESMO 2024

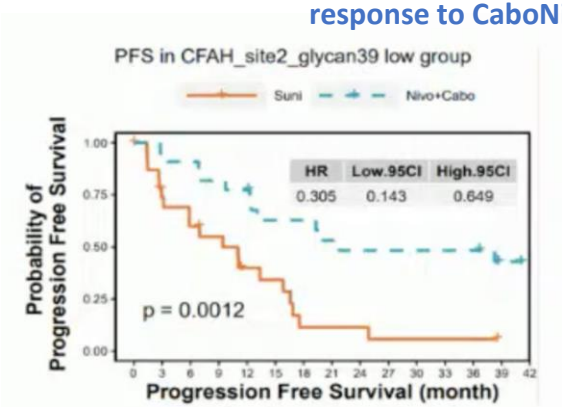
ANYTHING NEW IN BIOMARKERS?

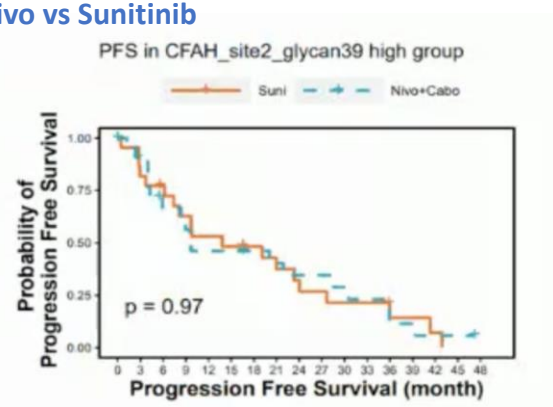
High serum levels of CO3 glycopeptide are potentially predictive of favorable response to CaboNivo vs Sunitinib





Low serum levels of CFAH glycopeptide are potentially predictive of favorable response to CaboNivo vs Sunitinib





Braun D et al. ESMO 2024

CONCLUSIONS

- IO rechallenge (PD-1/PD-L1 inhibition) is discouraging in RCC
- TKI in second line after IO based combination remains standard of care
- Belzutifan does not improve OS in pretreated population but benefits in objective response rate, duration of response, progression free survival, duration of therapy, and less need for subsequent therapies with more time to deterioration
- There are no clear biomarkers predictive of response in metastatic disease. The results of pivotal studies do not seem reproducible.