

Actualización en el abordaje del feocromocitoma/paraganglioma metastásico

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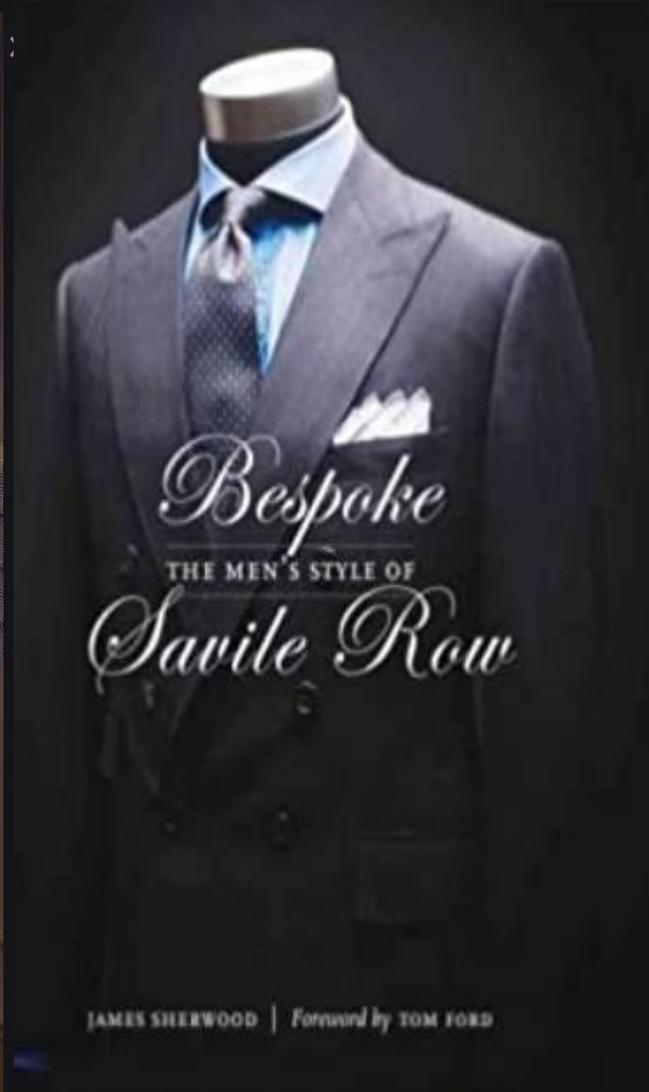


XX SYMPOSIUM
GETNE 2024

14 y 15 de noviembre 2024
Auditorio ABANCA - Santiago de Compostela

GETNE
Grupo Español de Tumores
Neuroendocrinos y Endocrinos

Fundación GETNE
Fundación del Grupo Español
de Tumores Neuroendocrinos y Endocrinos

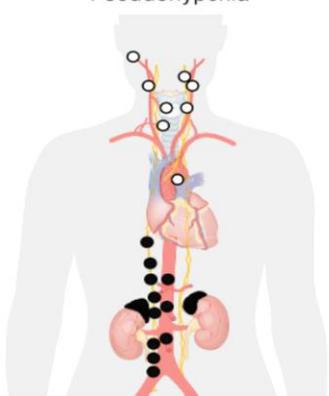
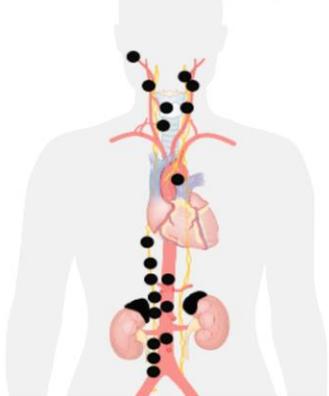
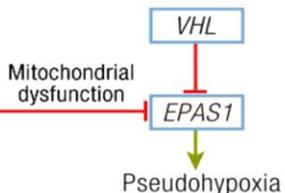
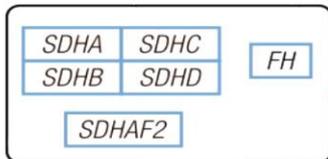


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Pseudohypoxia

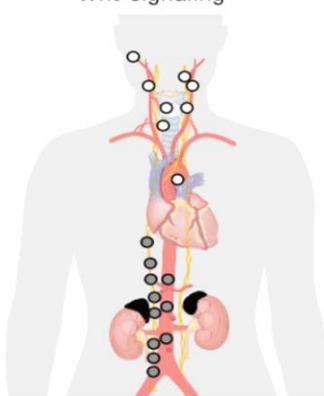
TCA cycle-related
(100%)

VHL/EPAS1-related
(25%)



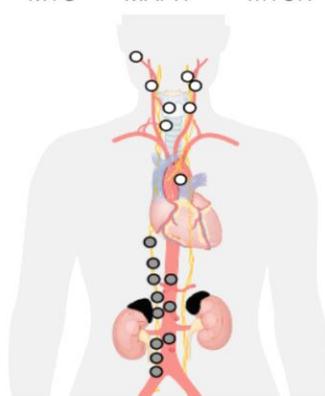
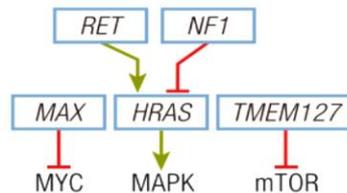
Wnt signaling

CSDE1, MAML3-fusion
(0%)



Kinase signaling

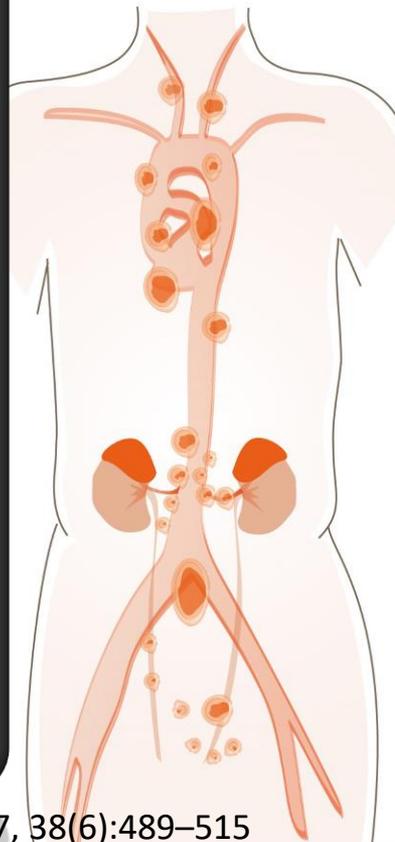
NF1>HRAS>RET>TMEM127>MAX
(20%)



Normetanefrina
Dopamina
Metoxitiramina
Metástasis

Diferenciación celular

Metanefrina



Características Prequirúrgicas y Postsquirúrgicas de PPGL Potencialmente Agresivos

Tamaño grande: >5 cm (adrenal) > 4 cm extraadrenal

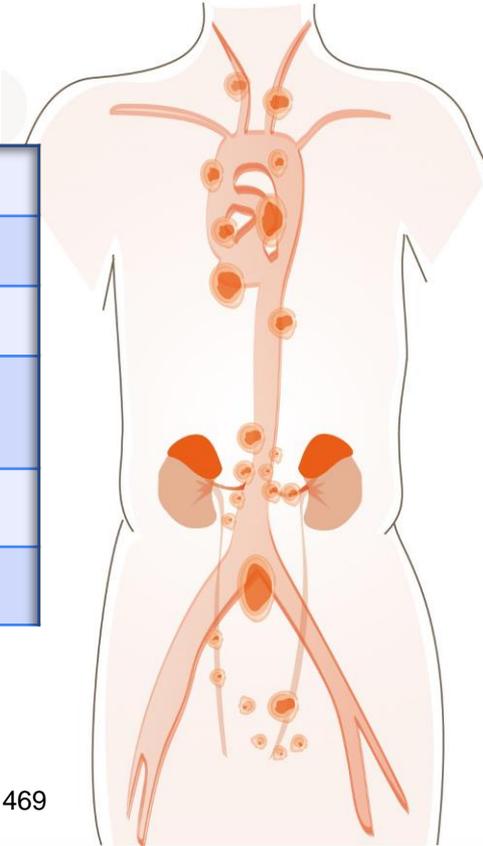
Invasión vascular evidente

Variante patogénica germinal SDHB

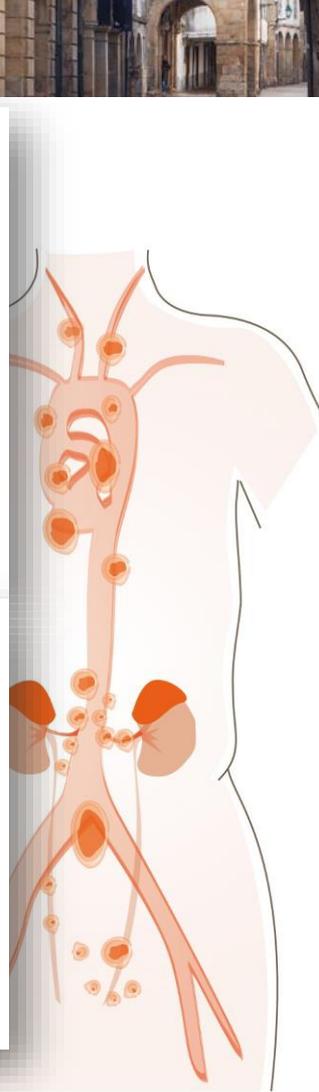
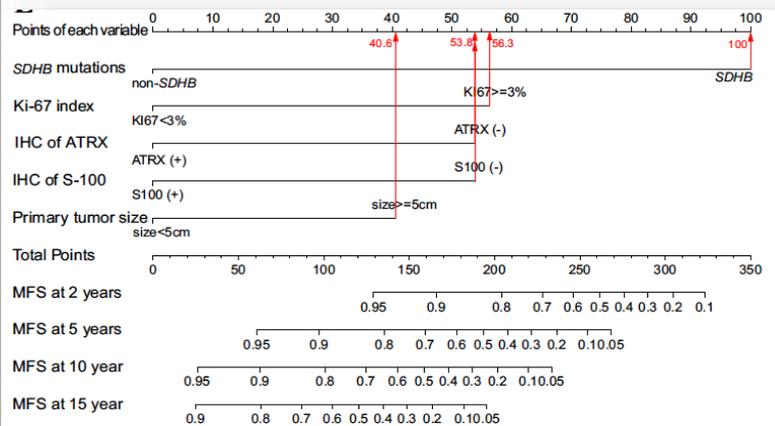
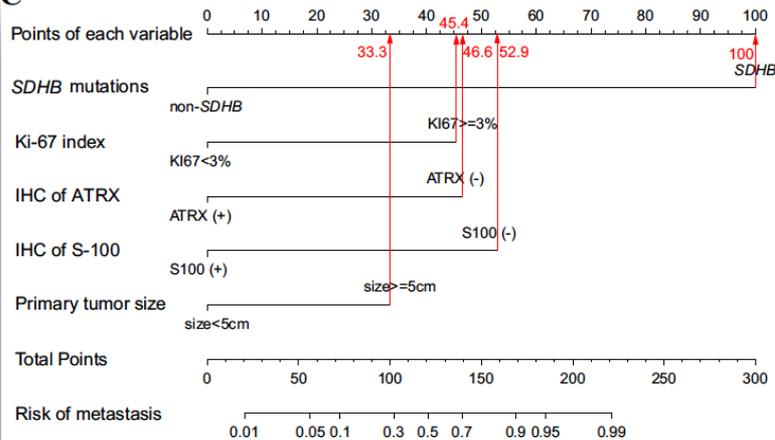
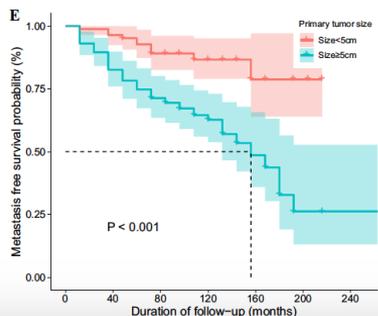
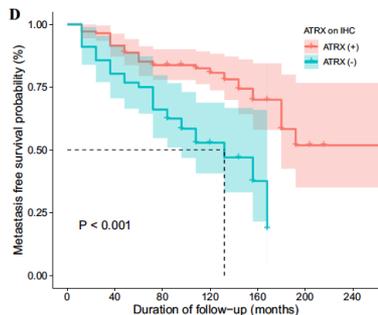
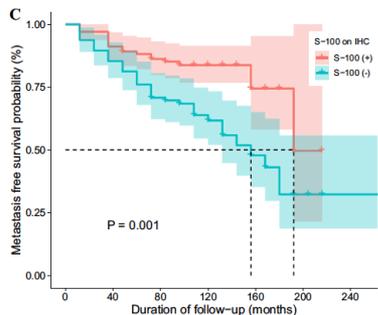
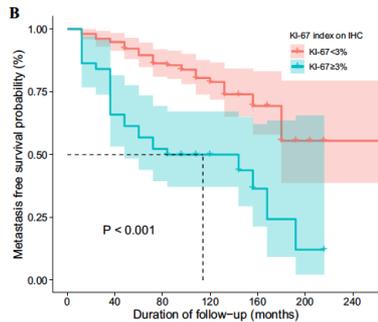
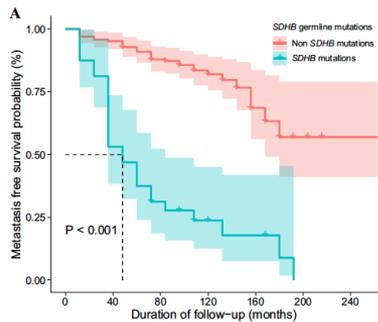
Tumor con compromiso de ganglios adyacentes

Niveles persistentemente elevados de metanefrinas tras cirugía

Índice de Ki-67 o mitótico >2 o 5%

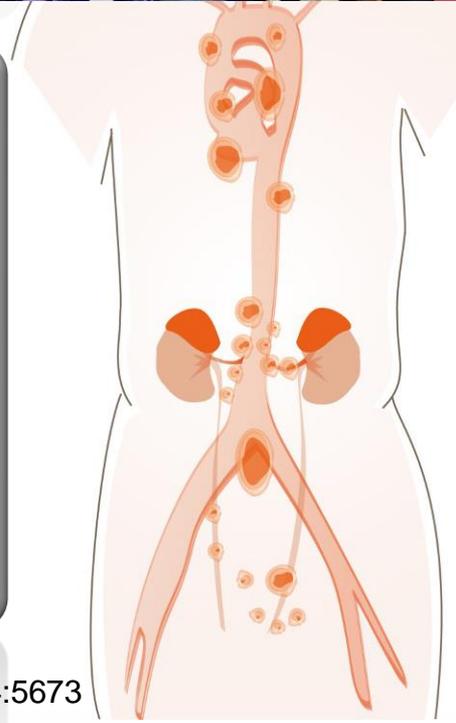
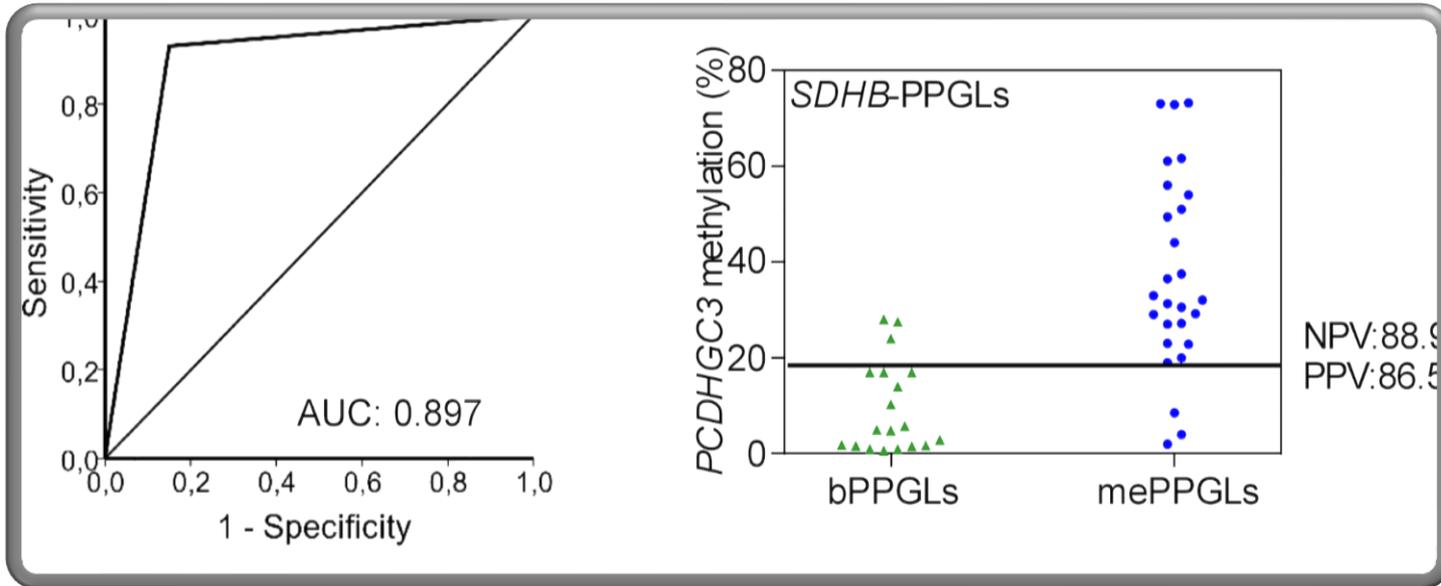


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Metilación de Protocadherina GC3 asociada con metástasis de SDHB PPGLs

BECA GETNE 2015



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- Referral to Center of Excellence/specialized high-volume center
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- Blood pressure control
- Consider de-bulking surgery
- Loco-regional approaches for tumor control (radiotherapy, ablation, embolization)
- Bone-targeted agents

Stable disease & low tumor burden

Slow progression or medium tumor burden

Rapid progression or high tumor burden or uncontrolled symptoms

Radiographic & biochemical surveillance

Progression

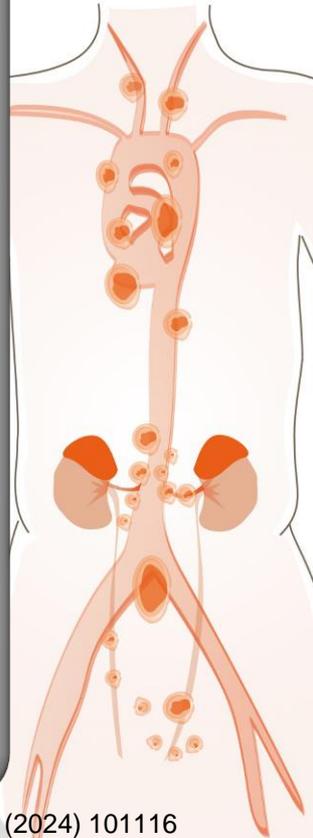
- Clinical trials
- I-131-MIBG (HSA/Conventional)
- Lu-177 dotatate PRRT
- RTK inhibitors: Sunitinib/Cabozantinib

Progression

- CVD chemotherapy for 6-9 cycles followed by consideration of temozolomide as maintenance
- Capecitabine + Temozolomide

Progression

- Clinical Trials of HIF2A targeted agents: Belzutifan
- Multi-receptor tyrosine kinase (RTK) inhibitors: Sunitinib or Cabozantinib (+/- anti-PD-1 immunotherapy)



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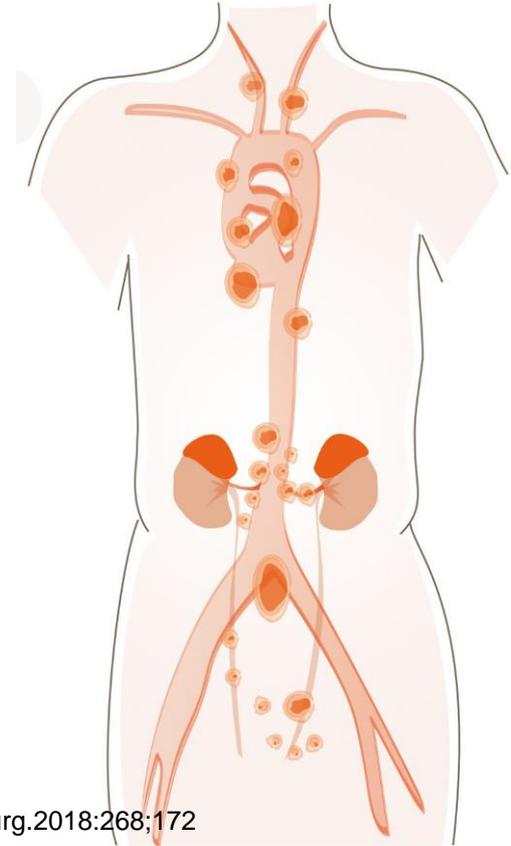
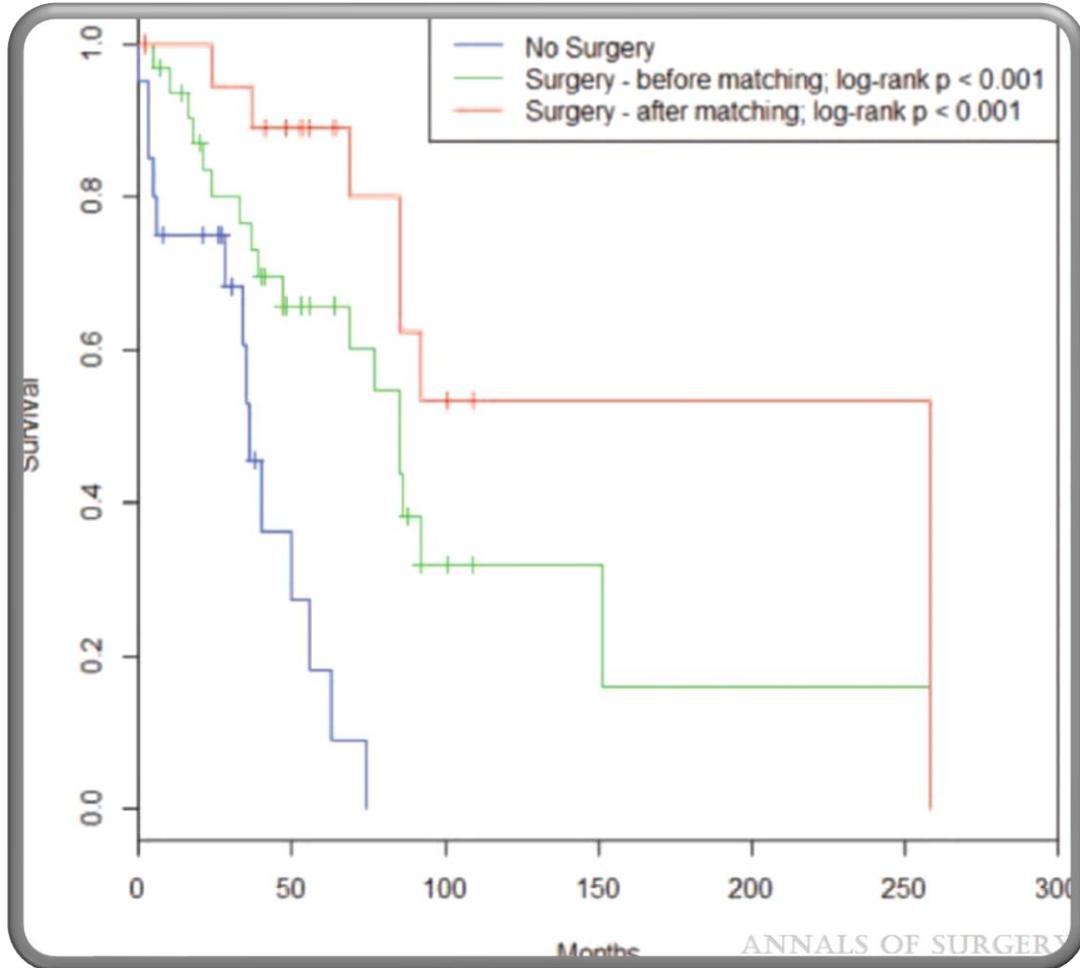




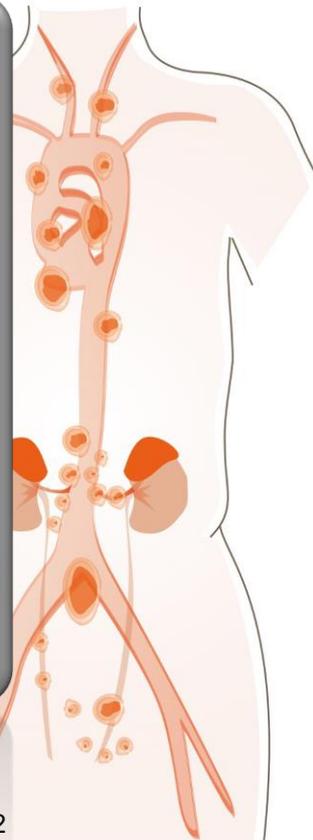
TABLE 3. Multivariate Cox Proportional Hazards Model for OS Using Propensity Score Weighting in Patients With Synchronous Metastases

Variable	HR	95% CI	P
Surgery: yes vs no	0.222	(0.106, 0.464)	<0.001
Location: PGL vs PHEO	4.777	(2.272, 10.044)	<0.001
Tumor Burden*: high vs low	2.442	(1.091, 5.467)	0.03
Bone metastases: yes vs no	3.033	(1.088, 8.455)	0.034
Primary tumor size: ≥ 5 cm vs < 5 cm	9.606	(3.407, 27.087)	<0.001

0 50 100 150 200 250 300

Months

ANNALS OF SURGERY



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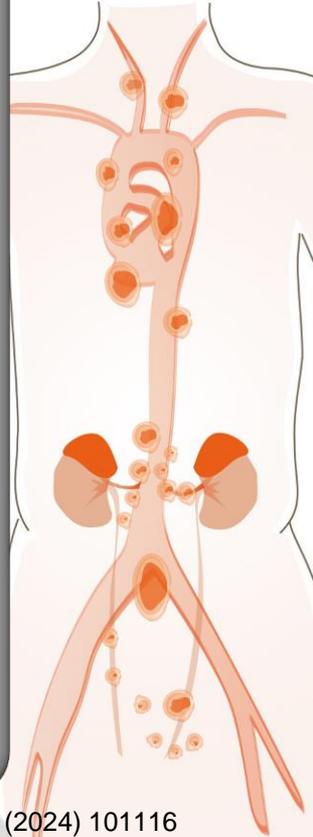
Progression

Rapid progression or high tumor burden or uncontrolled symptoms

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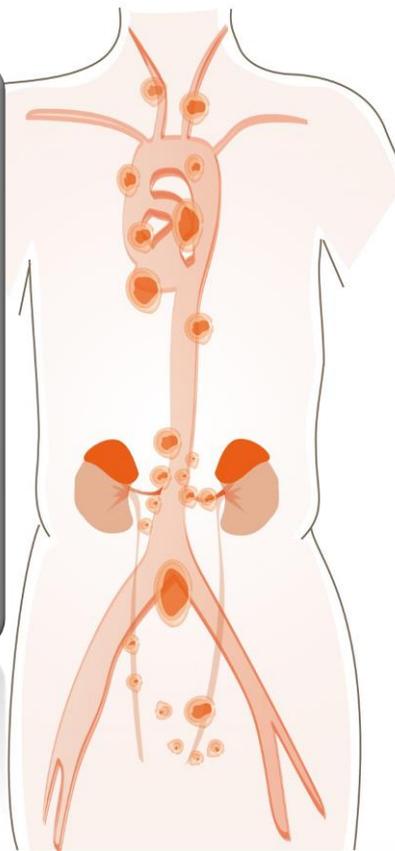
Progression

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- Multi-receptor tyrosine kinase (RTK) inhibitors: Sunitinib or Cabozantinib (+/- anti-PD-1 immunotherapy)



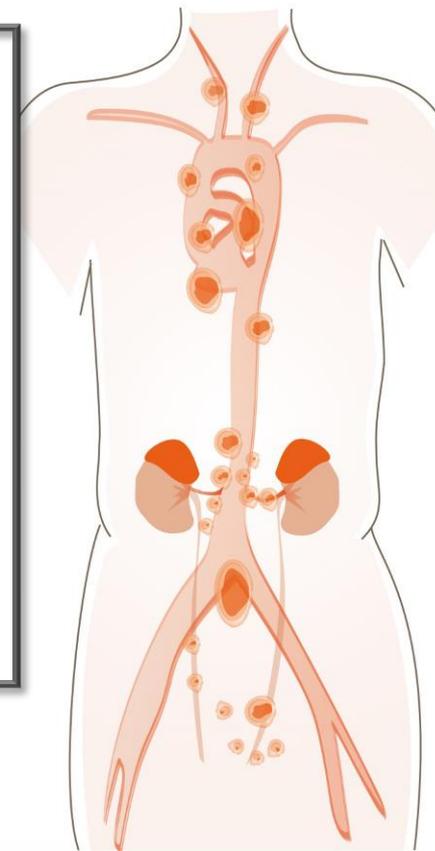
Tratamiento con ^{131}I -MIBG

Parameter	One therapeutic dose (<i>n</i> = 18)	Two therapeutic doses (<i>n</i> = 50)	At least 1 therapeutic dose (<i>n</i> = 68)
Reduction of all antihypertensive medications by $\geq 50\%$ for ≥ 6 mo (<i>n</i>)			
Yes	1 (6%) (95% CI, 0–28)	16 (32%) (95% CI, 21–46)	17 (25%) (95% CI, 16–34)
No	17 (94%)	34 (68%)	51 (75%)
Best confirmed overall tumor response by RECIST 1.0 (<i>n</i>)			
Evaluated patients	14	50	64
CR	0	0	0
PR	0	15 (30%)	15 (23%)
Stable disease	10 (71%)	34 (68%)	44 (69%)
Progressive disease	2 (14%)	1 (2%)	3 (5%)
No assessment	2 (14%)	0	2 (3%)

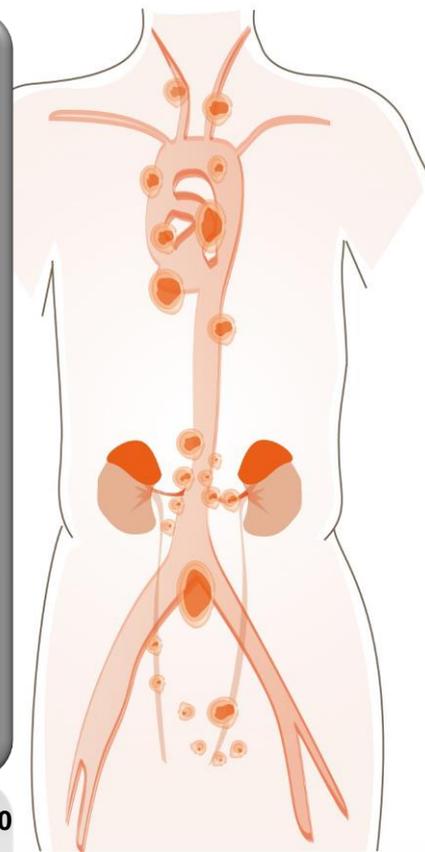
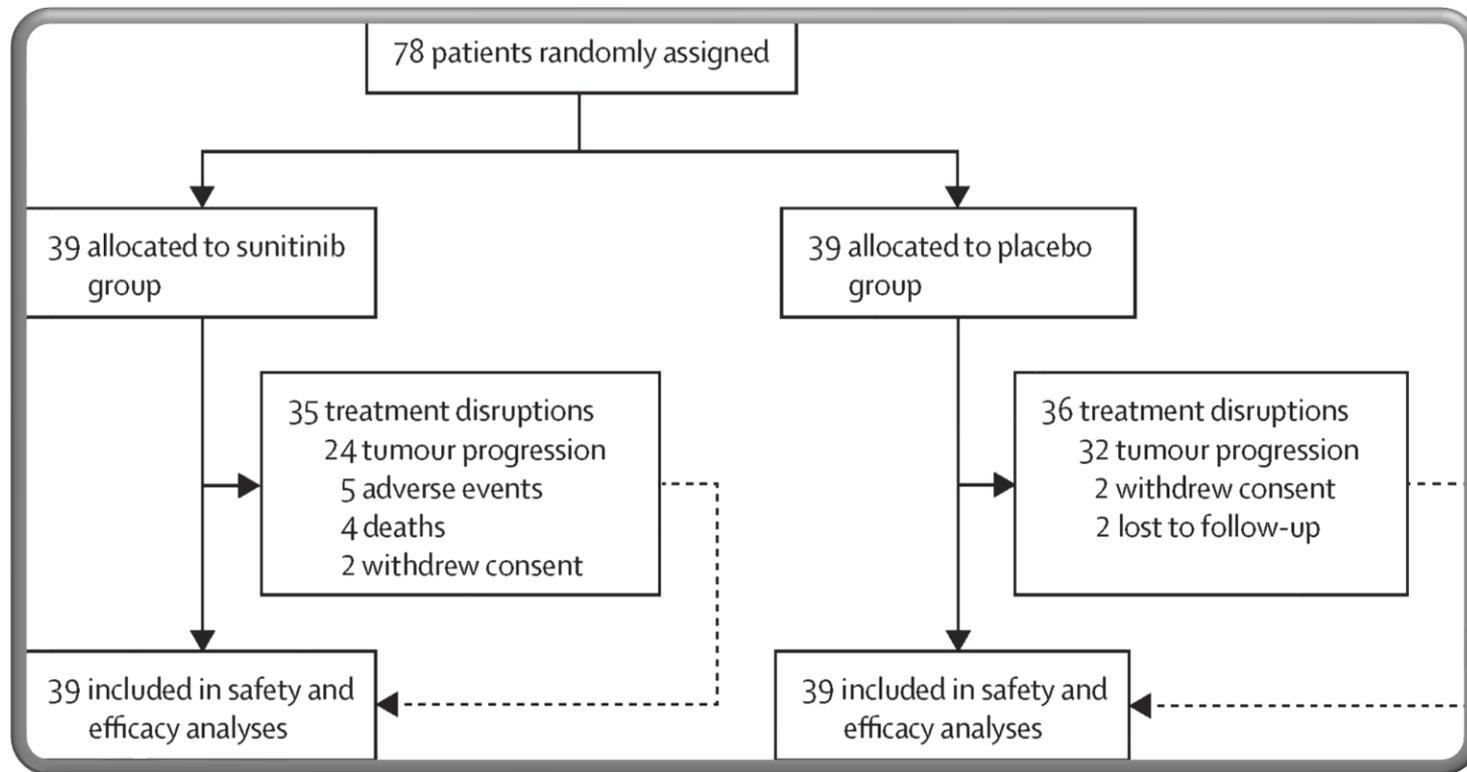


Tratamiento con radionúclidos con ^{177}Lu -DOTATATE

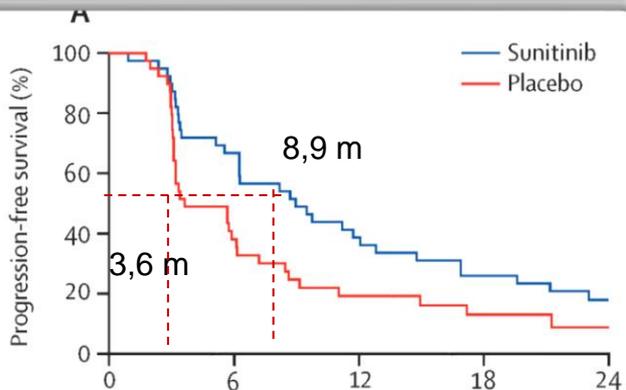
	All (n=30)	TNM stage	
		Localised [†] (n=13)	Metastatic [†] (n=17)
Best response, n (%)			
Partial response	7 (23.3)	1 (7.7)	6 (35.3)
Stable disease	20 (66.7)	12 (92.3)	8 (47.1)
Progressive disease	3 (10.0)	0	3 (17.6)
Disease control rate, n (%) [*]	17 (85.0)	6 (100)	11 (78.6)
Survival, months [*]	20	6	14
Median follow-up, months	52.5	87	44
Primary events	14	1	13
Median PFS (months)	30	n.r.	13
Deaths	9	0	9
Median OS (months)	n.r.	n.r.	23



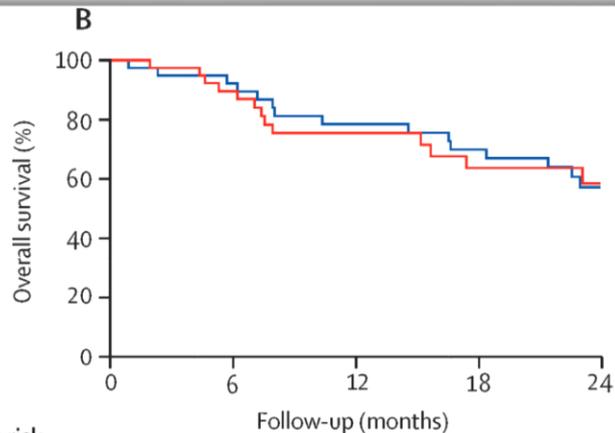
FIRSTMAPPP: sunitinib



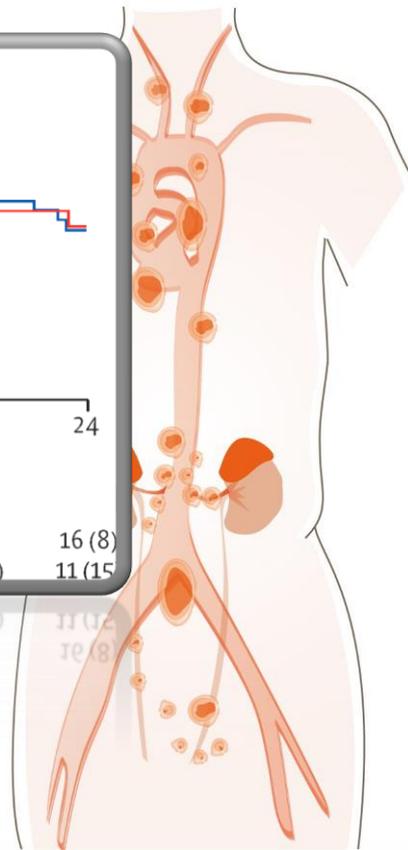
FIRSTMAPPP: sunitinib



Number at risk number censored)		0	6	12	18	24
Sunitinib	39 (0)	26 (0)	14 (0)	10 (0)	5 (2)	
Placebo	39 (0)	14 (1)	7 (1)	4 (2)	2 (3)	

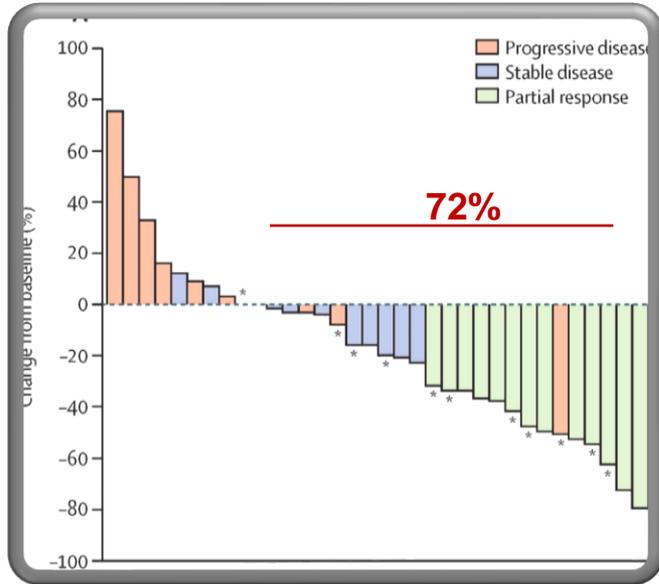


Number at risk number censored)		0	6	12	18	24
Sunitinib	39 (0)	34 (2)	27 (4)	24 (4)	16 (8)	
Placebo	39 (0)	33 (2)	24 (6)	16 (11)	11 (15)	

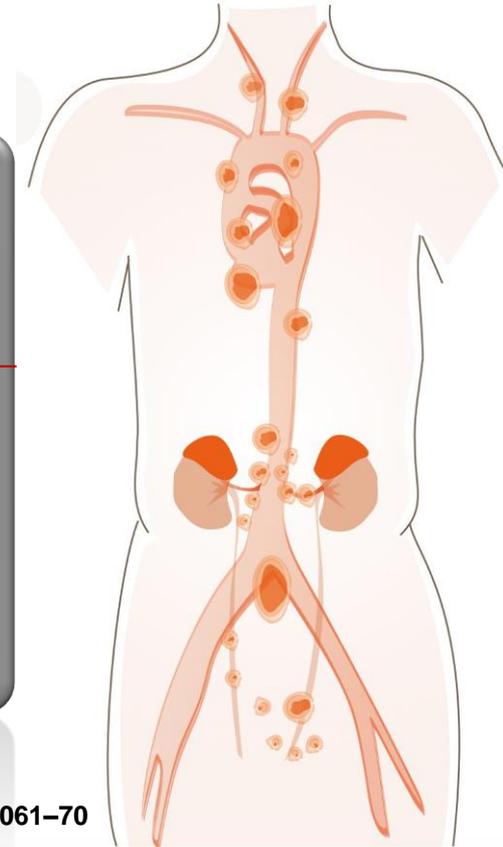
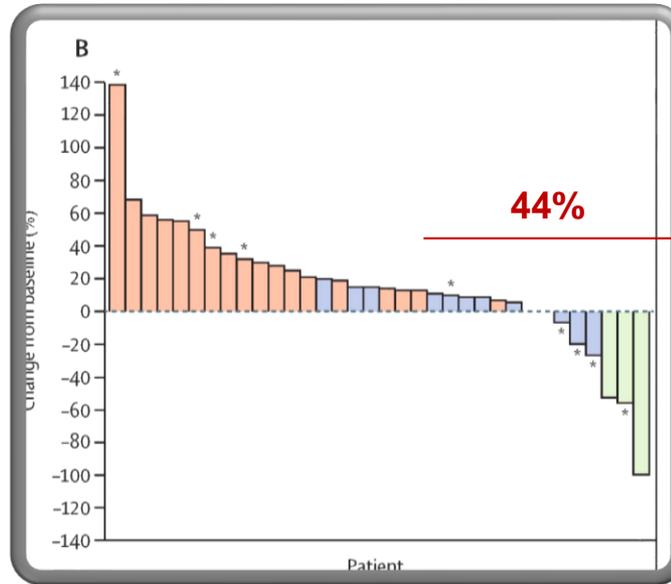


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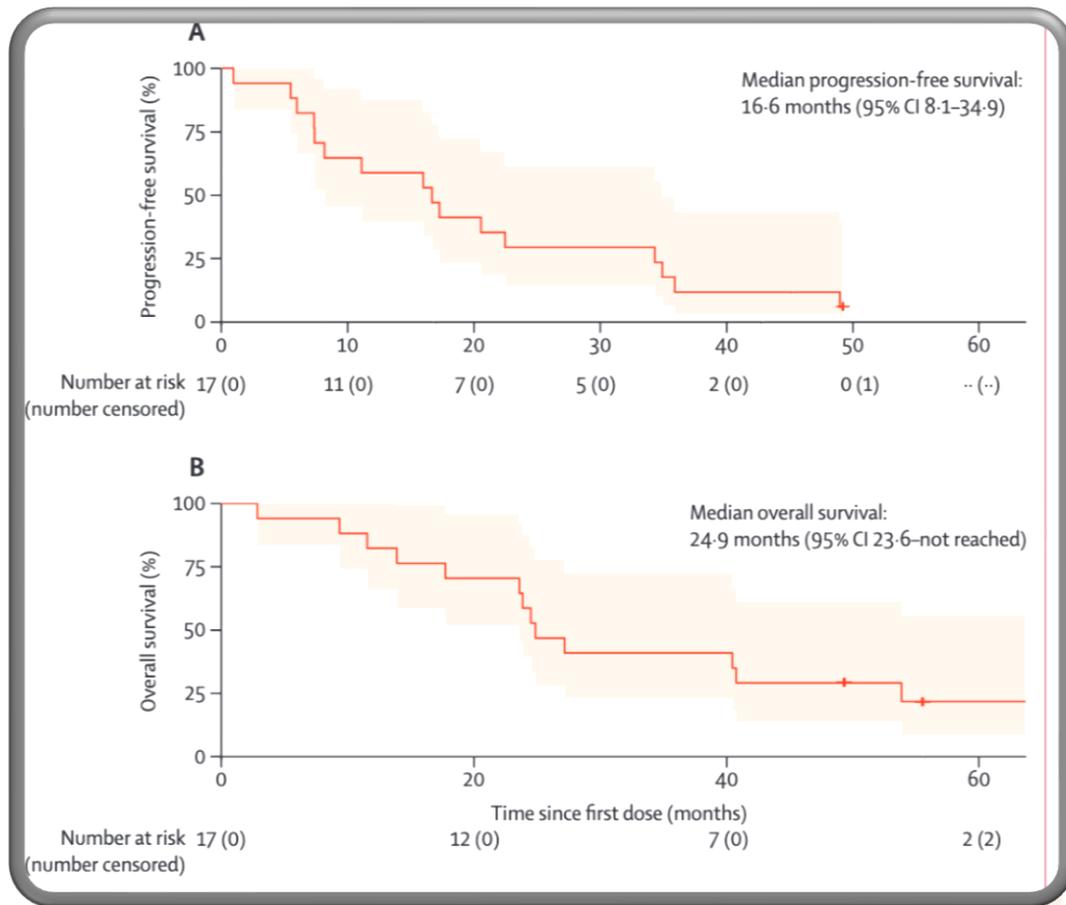
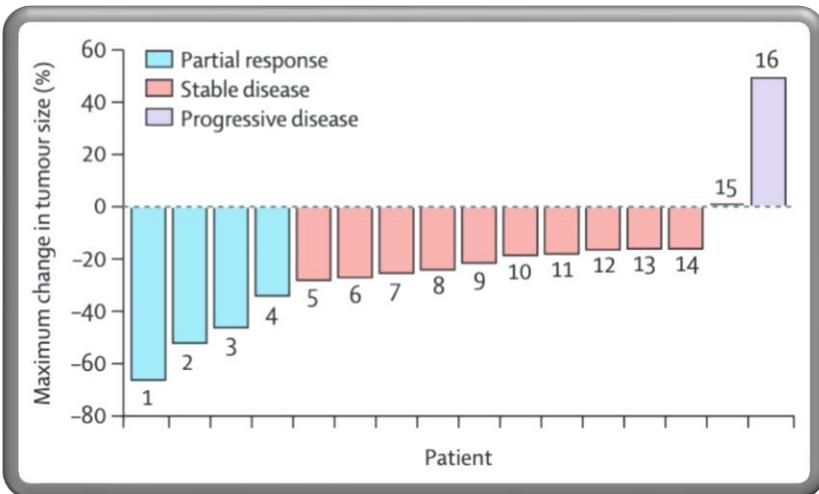
SUNITINIB



PLACEBO



Natalie Trial: cabozantinib



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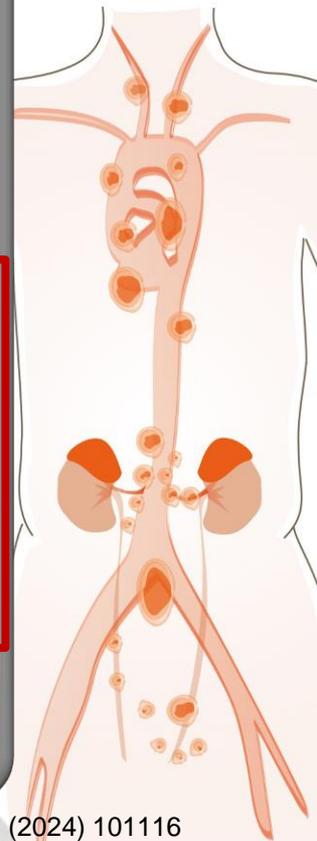
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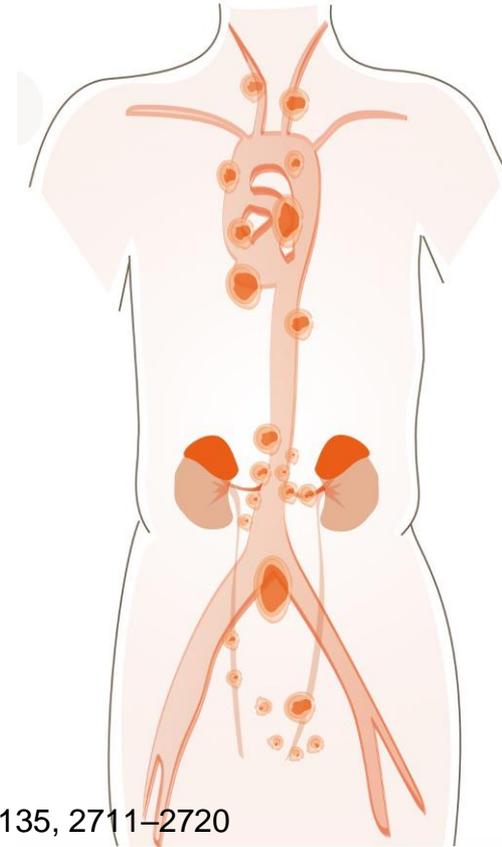
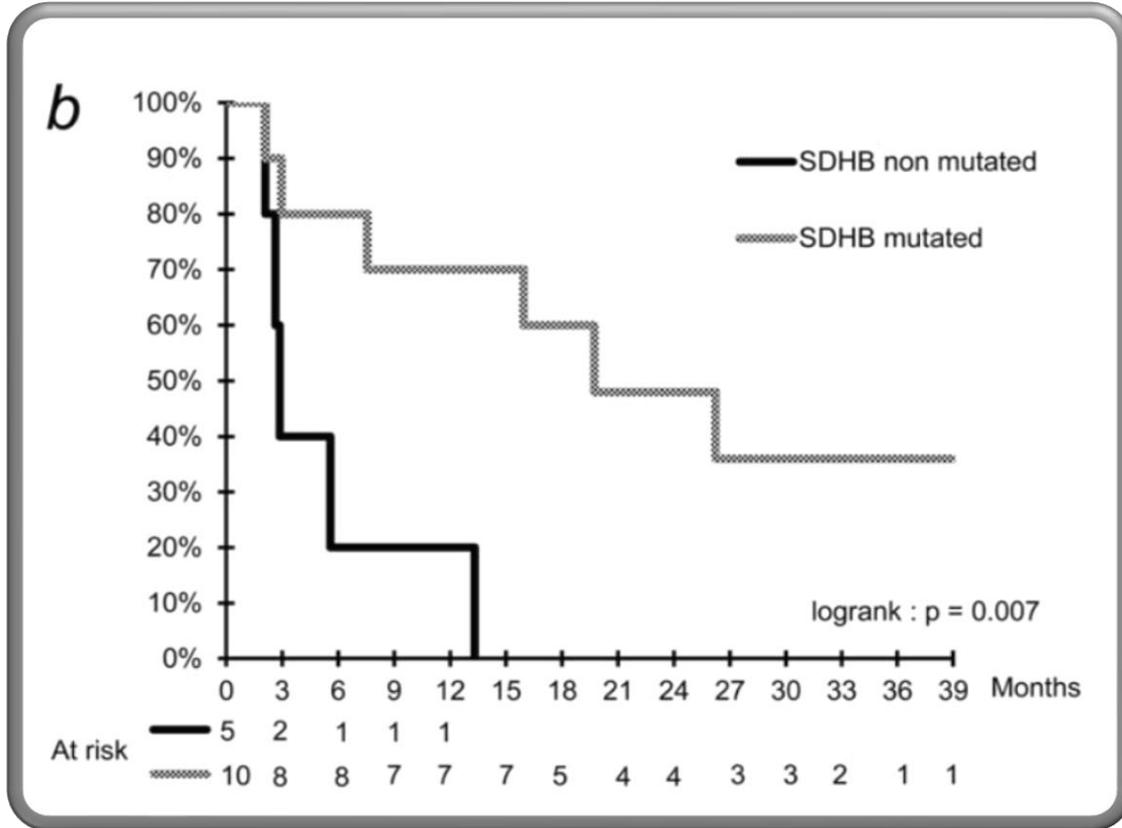
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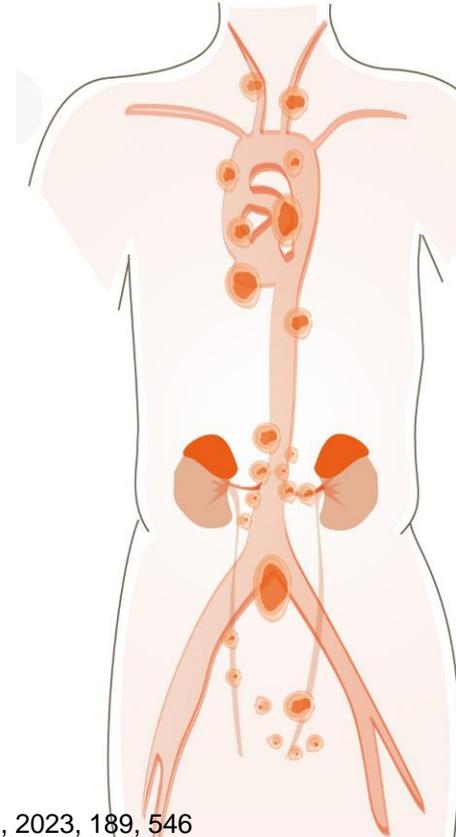
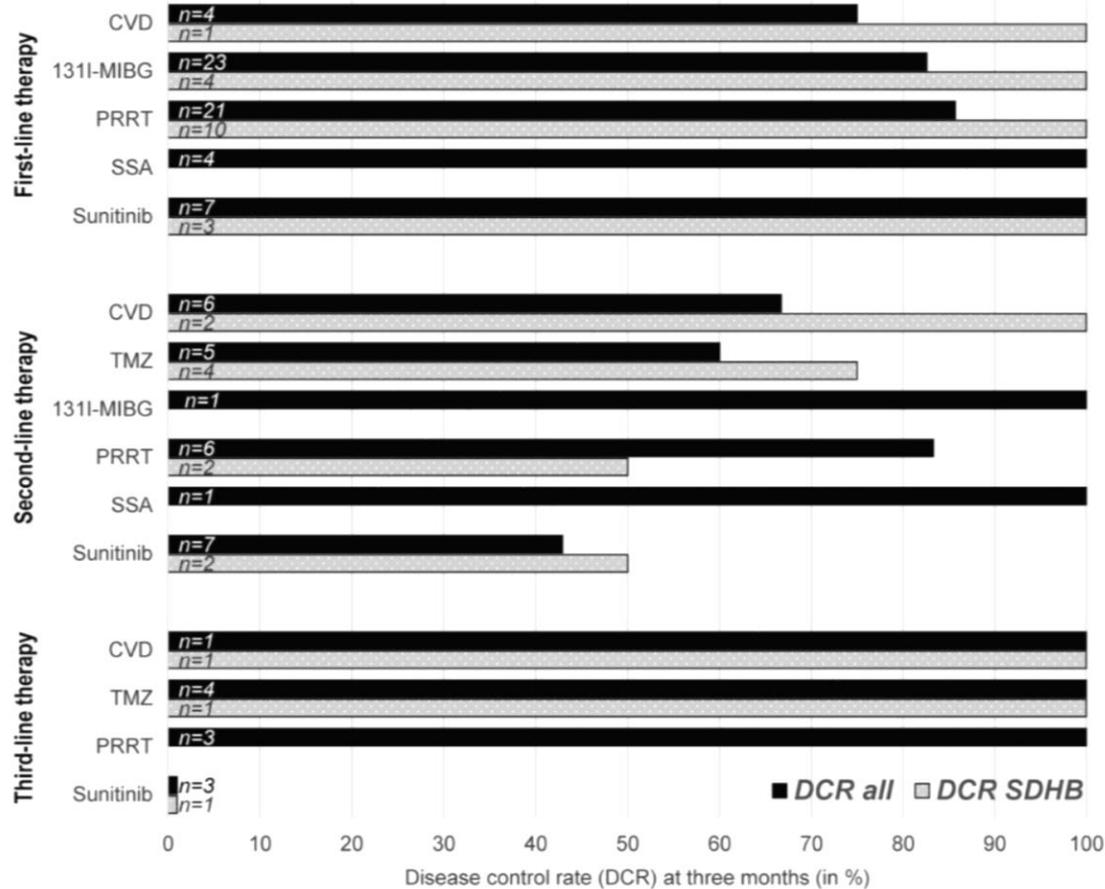
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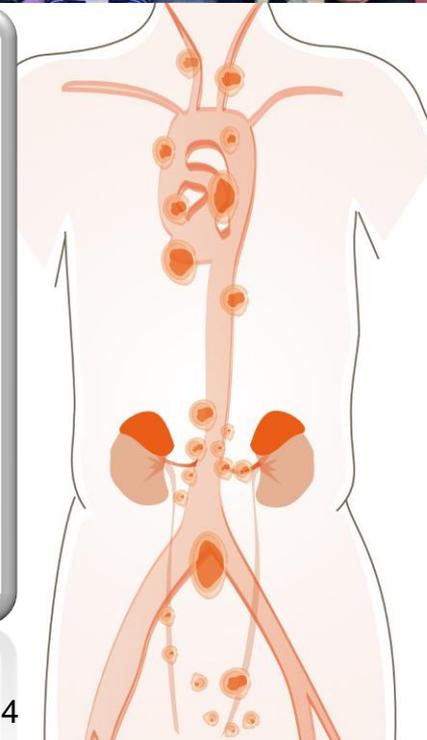
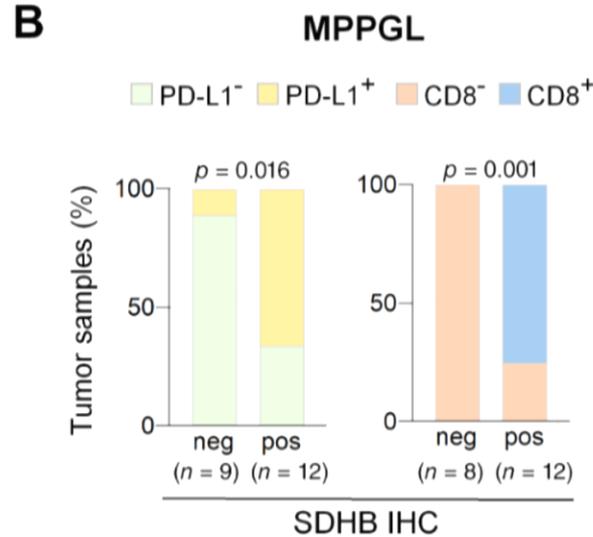
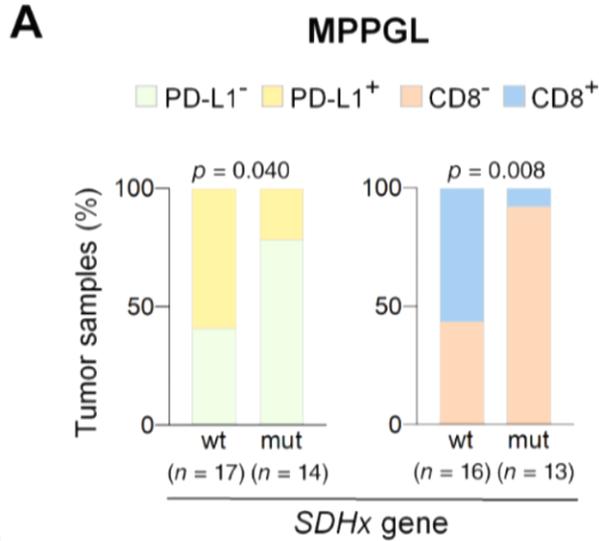
Temozolamida



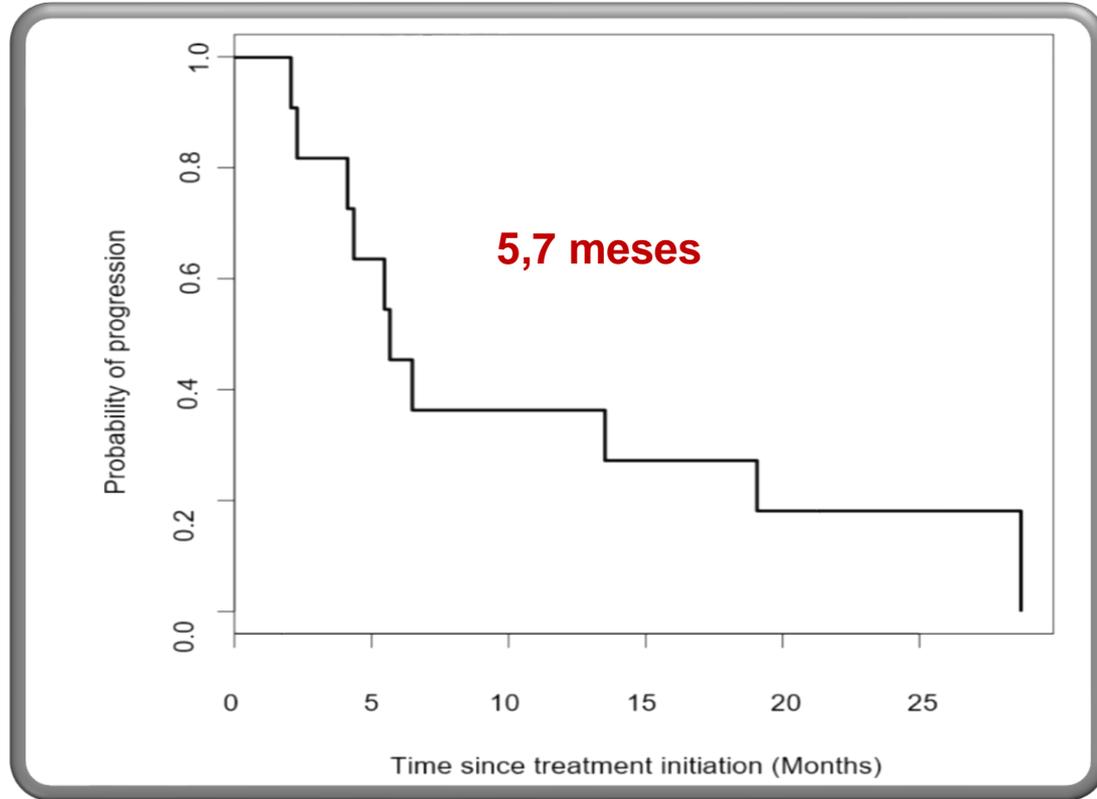
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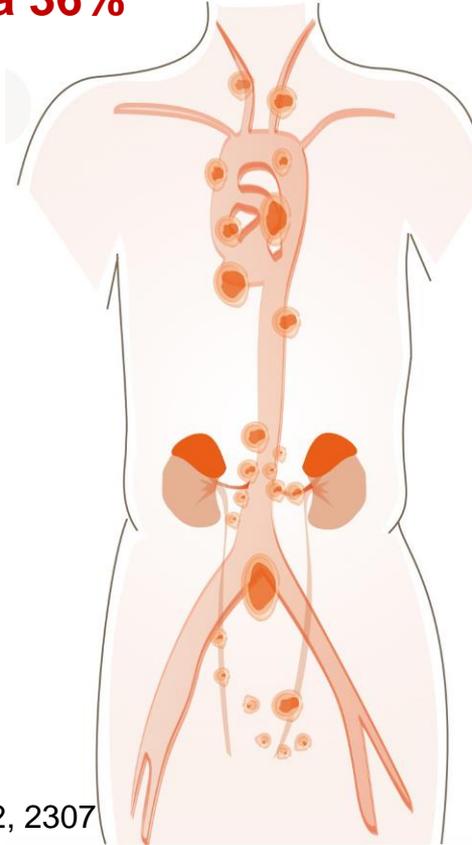
Fenotipo immunosupresivo



Pembrolizumab



Respuesta 36%



Muchas gracias

A photograph of four men in suits walking outdoors. The man on the far left is wearing a grey double-breasted suit. The man in the center is wearing a blue checkered suit. The man on the far right is wearing a dark blue suit. The man in the middle-right is wearing glasses and a dark suit. They are all looking forward with neutral expressions.

“Si no fuera por la gran variabilidad clínica entre pacientes, la medicina podría ser considerada como una *ciencia* y no como un *arte*” W.Osler, 1892