

# Tratamiento inmunológico. ¿Cuál es el paciente óptimo?

Enrique Espinosa

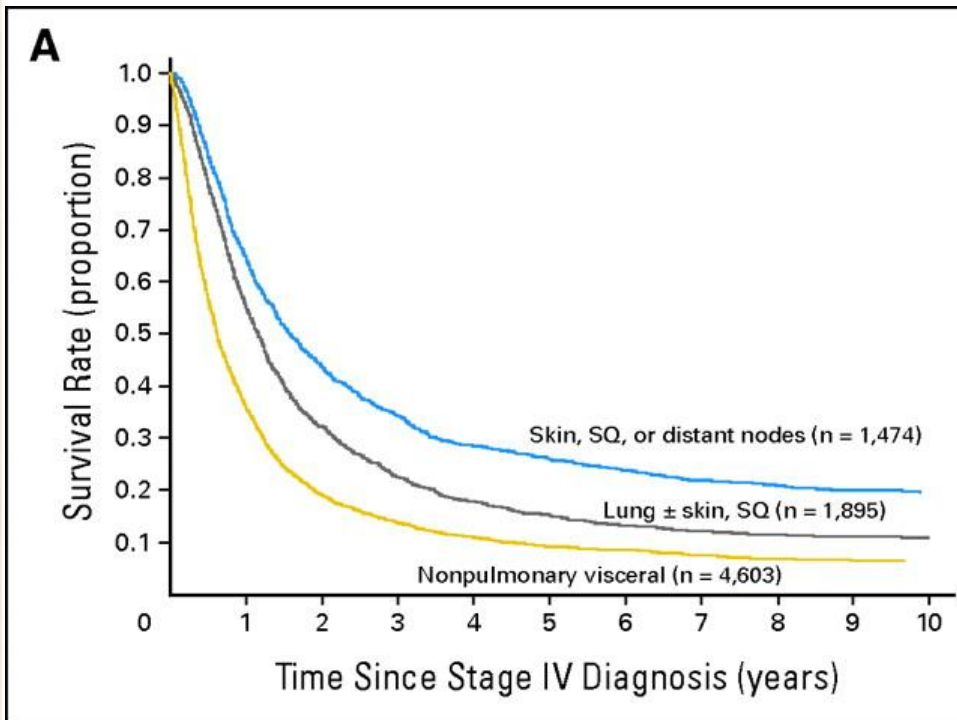


Hospital Universitario La Paz

Comunidad de Madrid



# Datos clásicos



Mediana: 6-7 meses

A 2 años: 13%

Balch, J Clin Oncol 2009

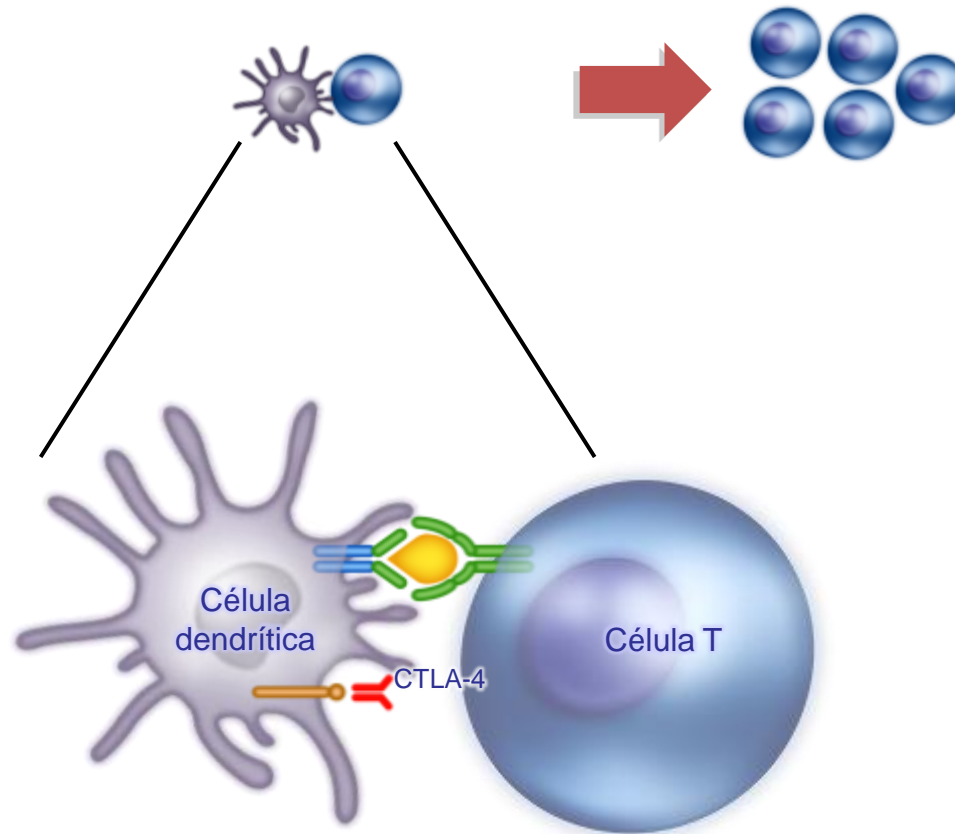


**Anti-CTLA4**

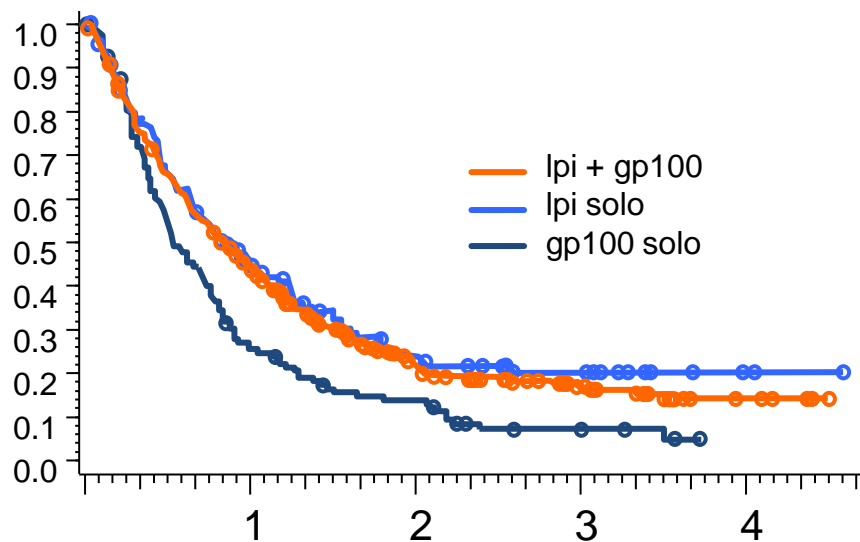


**Anti-PD1**

# Mecanismo acción anti-CTLA4

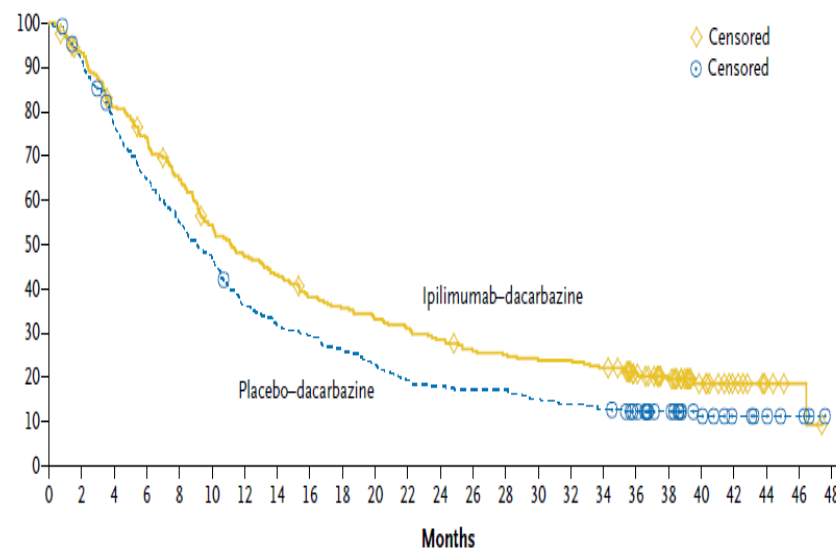


# Ipilimumab



Años

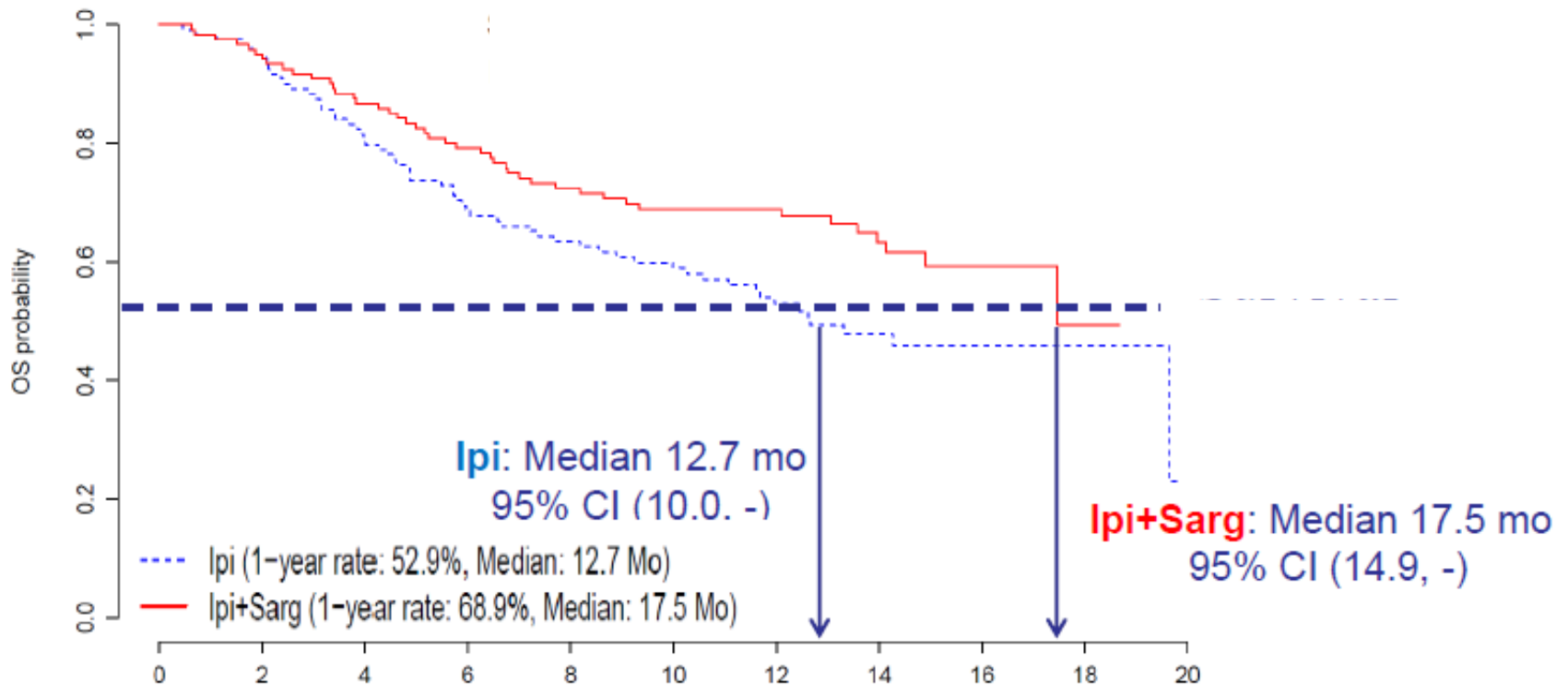
2ª línea  
Hodi, NEJM 2010



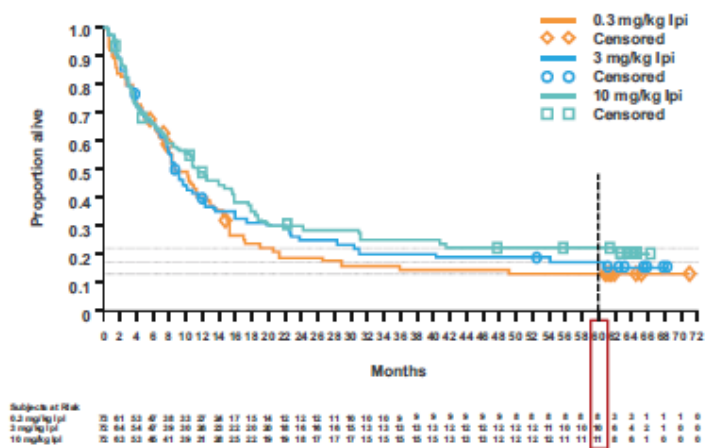
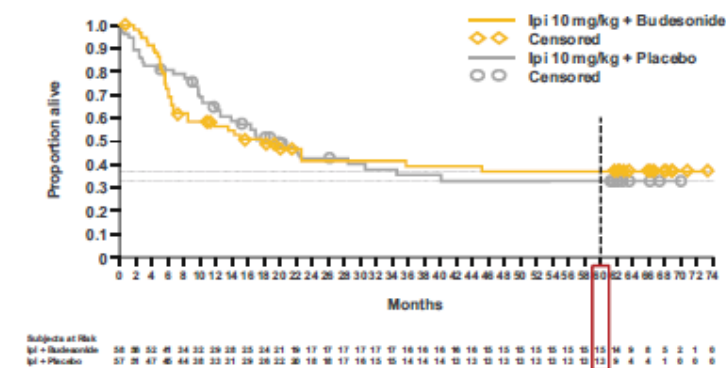
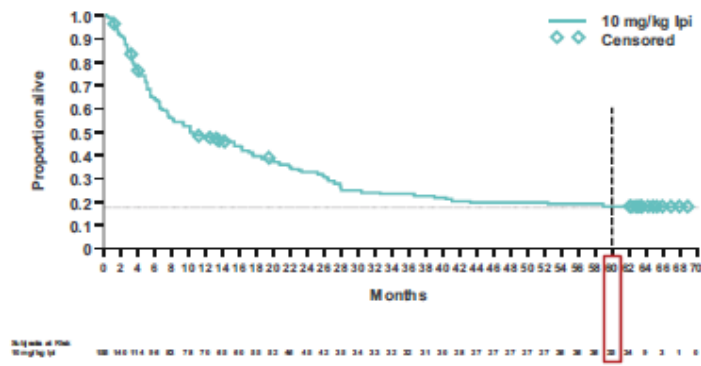
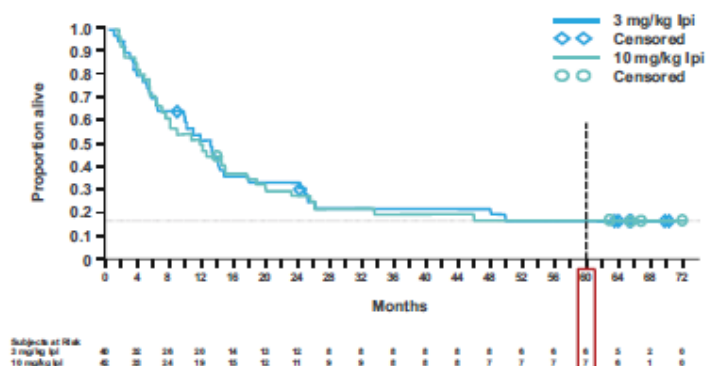
250	230	199	181	157	131	114	104	91	85	79	74	68	61	59	56	56	52	41	31	17	10	4	2	0
252	229	190	160	136	116	89	78	72	64	56	47	44	42	42	37	34	31	26	19	11	7	5	3	0

1ª línea  
Robert, NEJM 2011

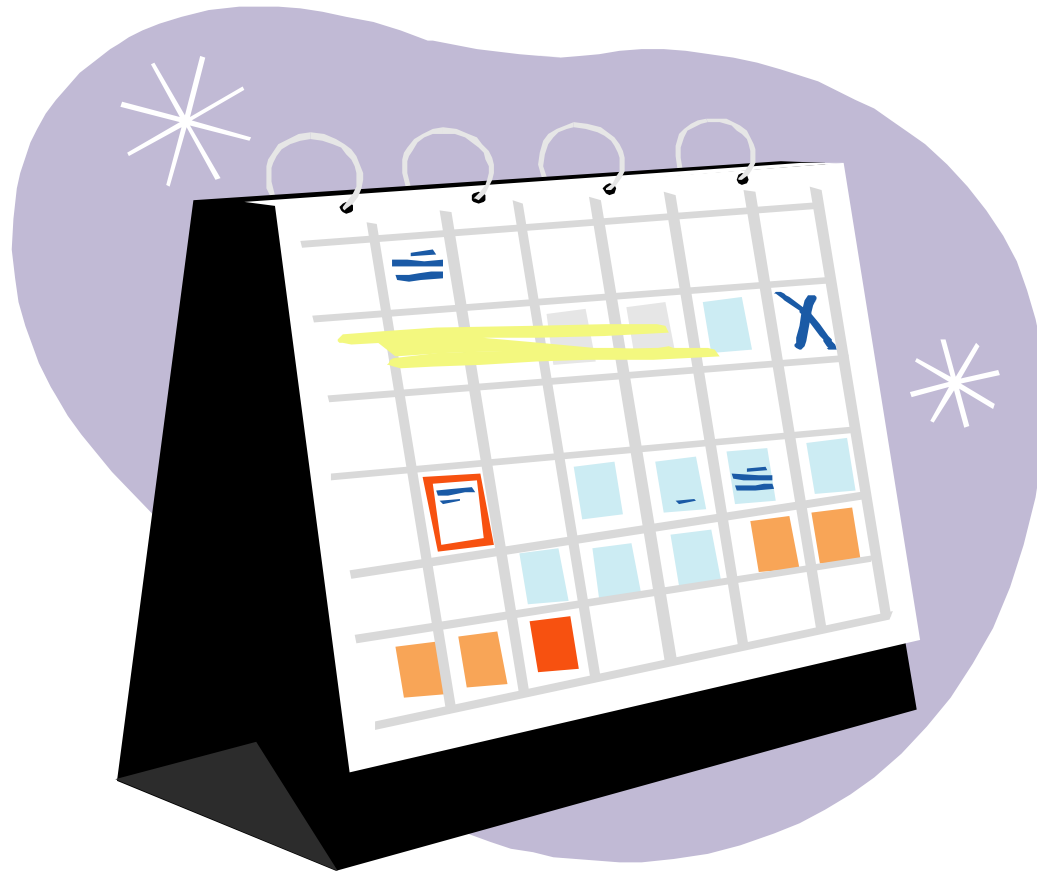
# IPI + GM-CSF



# Ipilimumab a largo plazo

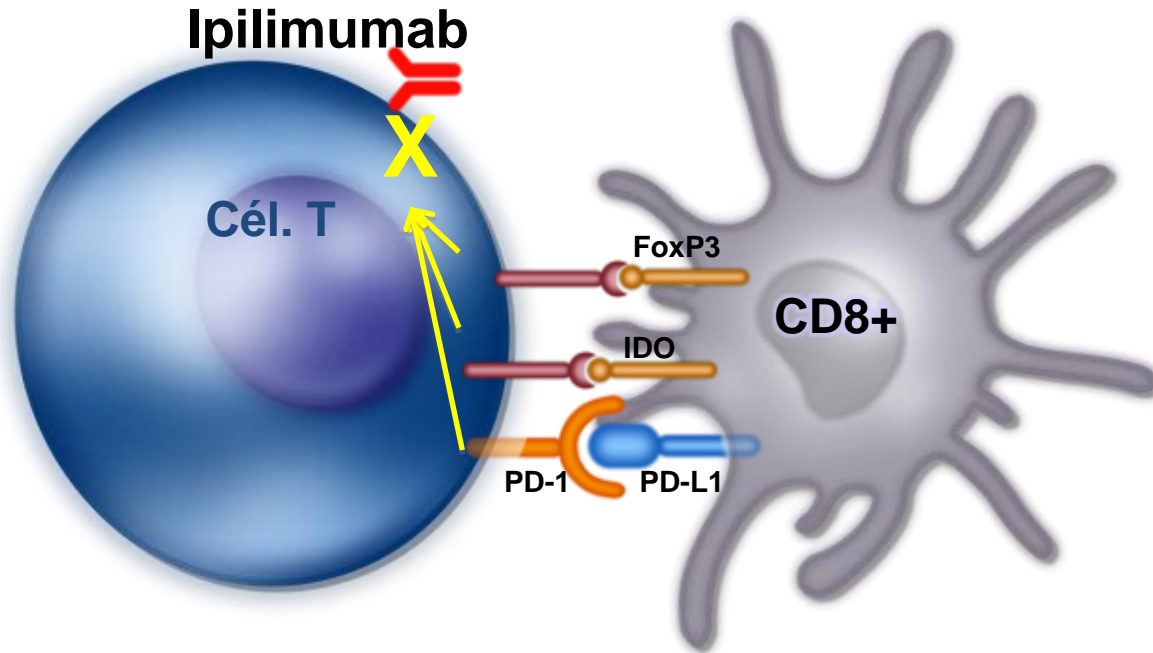


# ¿Paciente óptimo IPI?



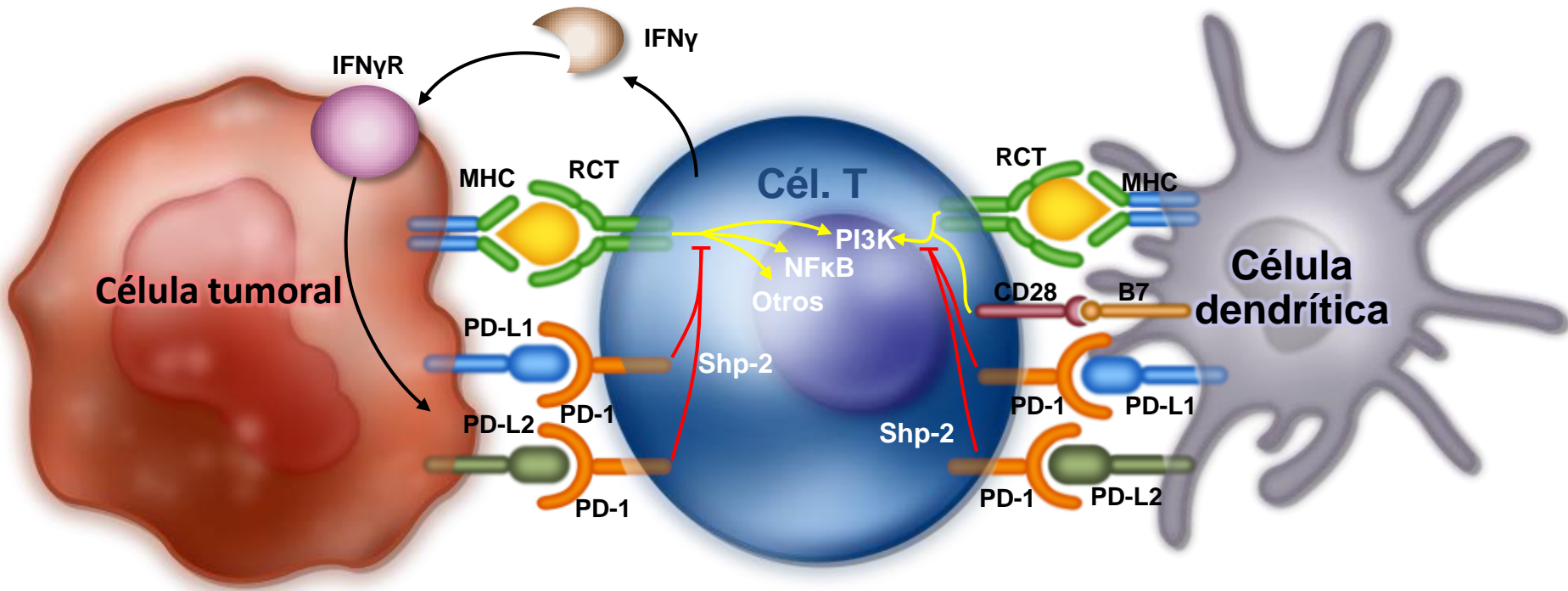


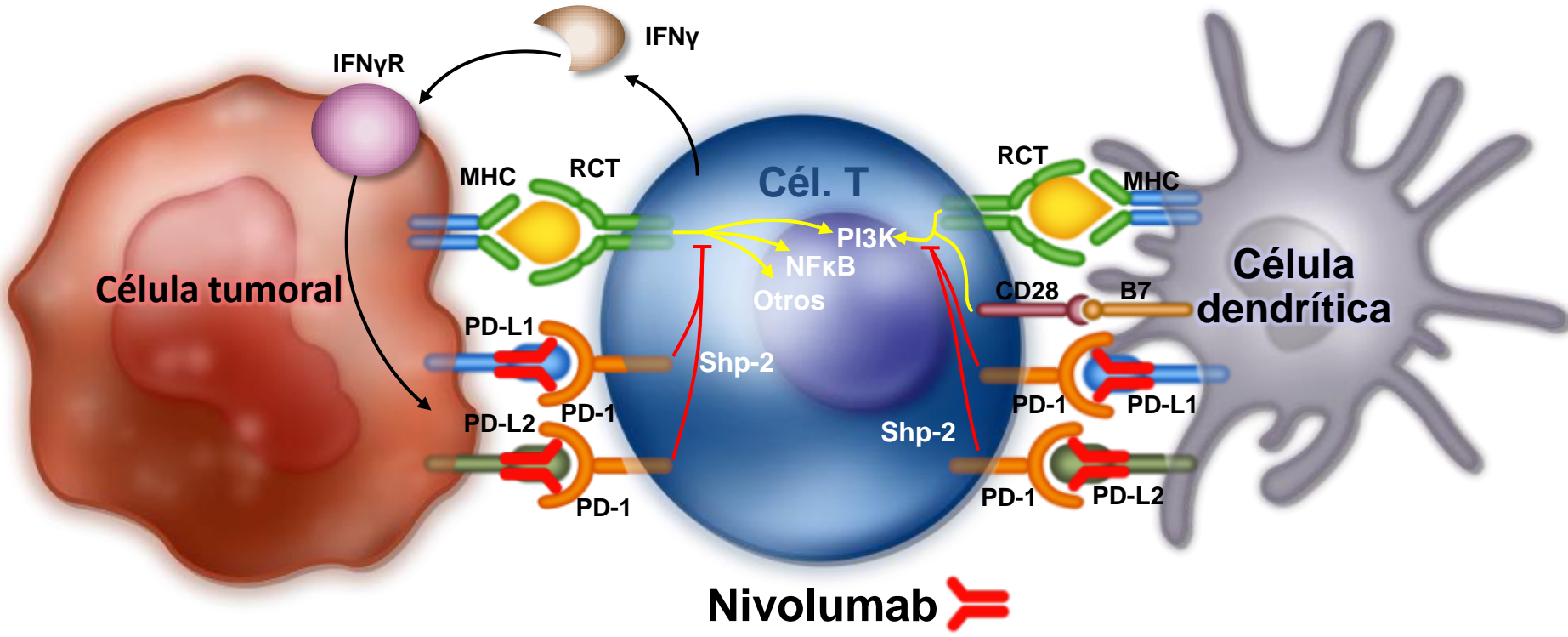
# Predicción respuesta a IPI



Spranger, Sci Transl Med 2013  
Holmgaard, J Exp Med 2013

# Mecanismo acción anti-PD1





# Nivolumab: fase I

0'1 – 0'3 – 1 – 3 – 10 mg/kg / 2 sem.



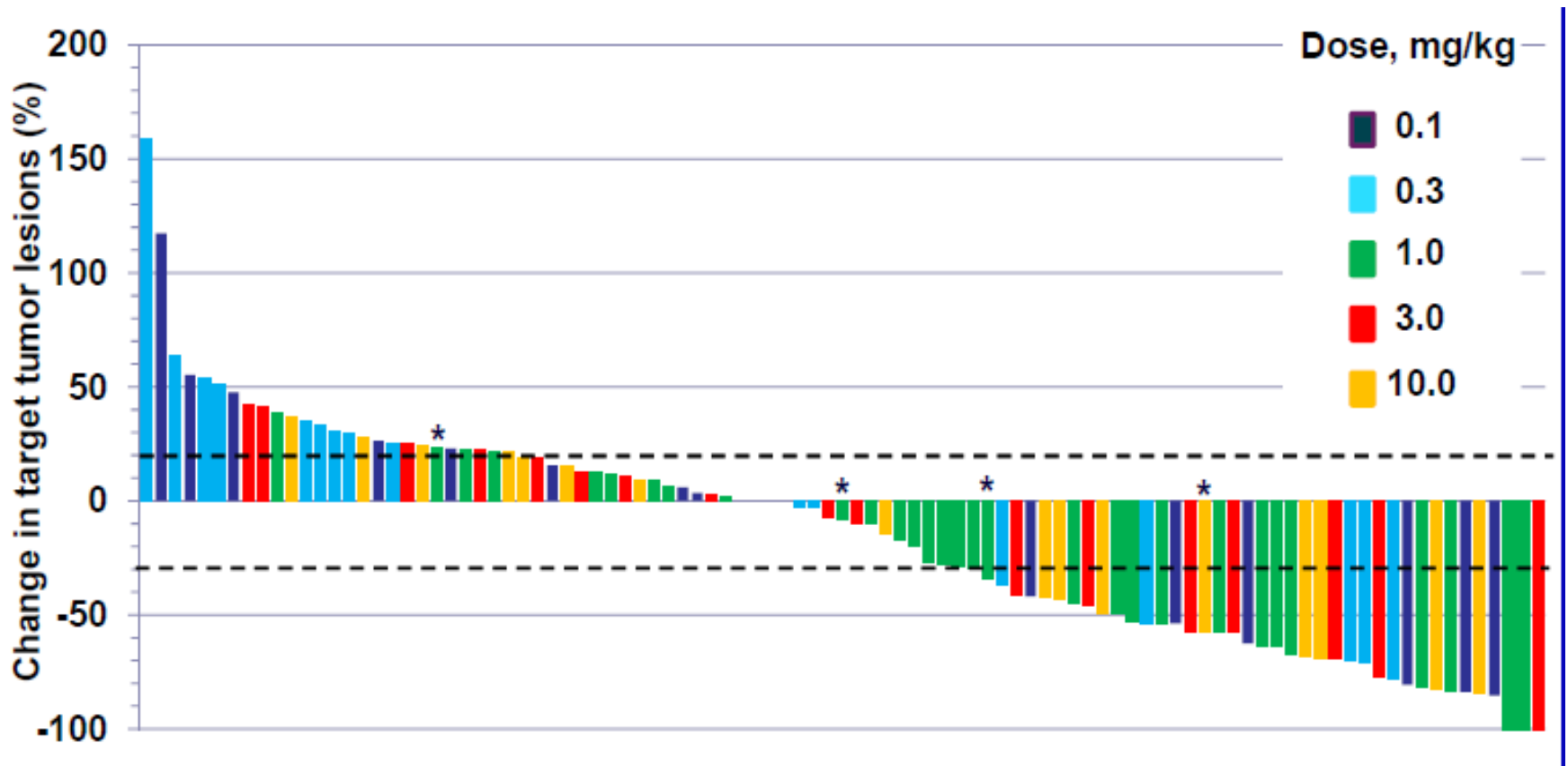
N=107

97% ECOG 0-1

36% LDH elevada

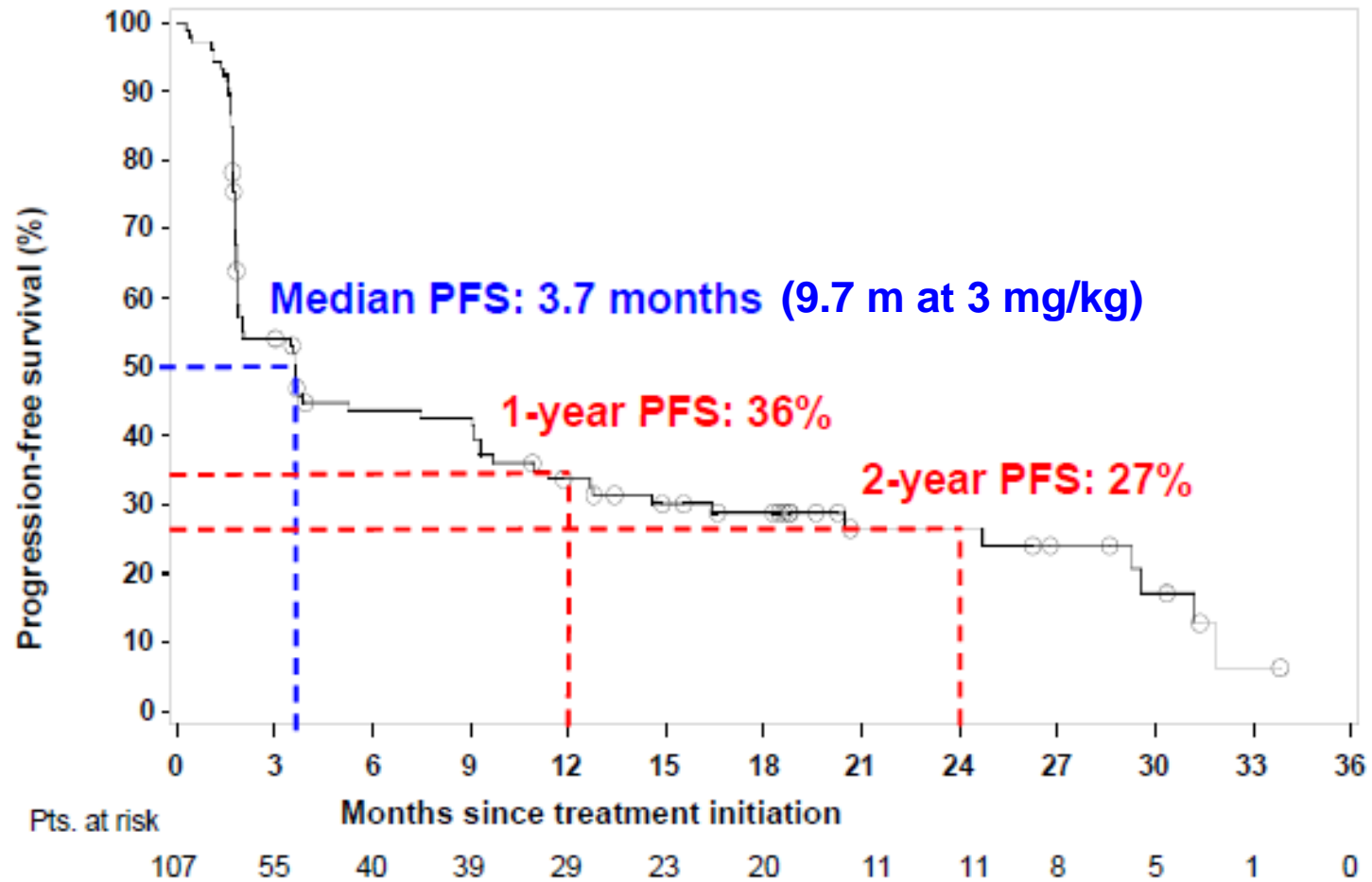
66% dos o más líneas previas

# Nivolumab fase I

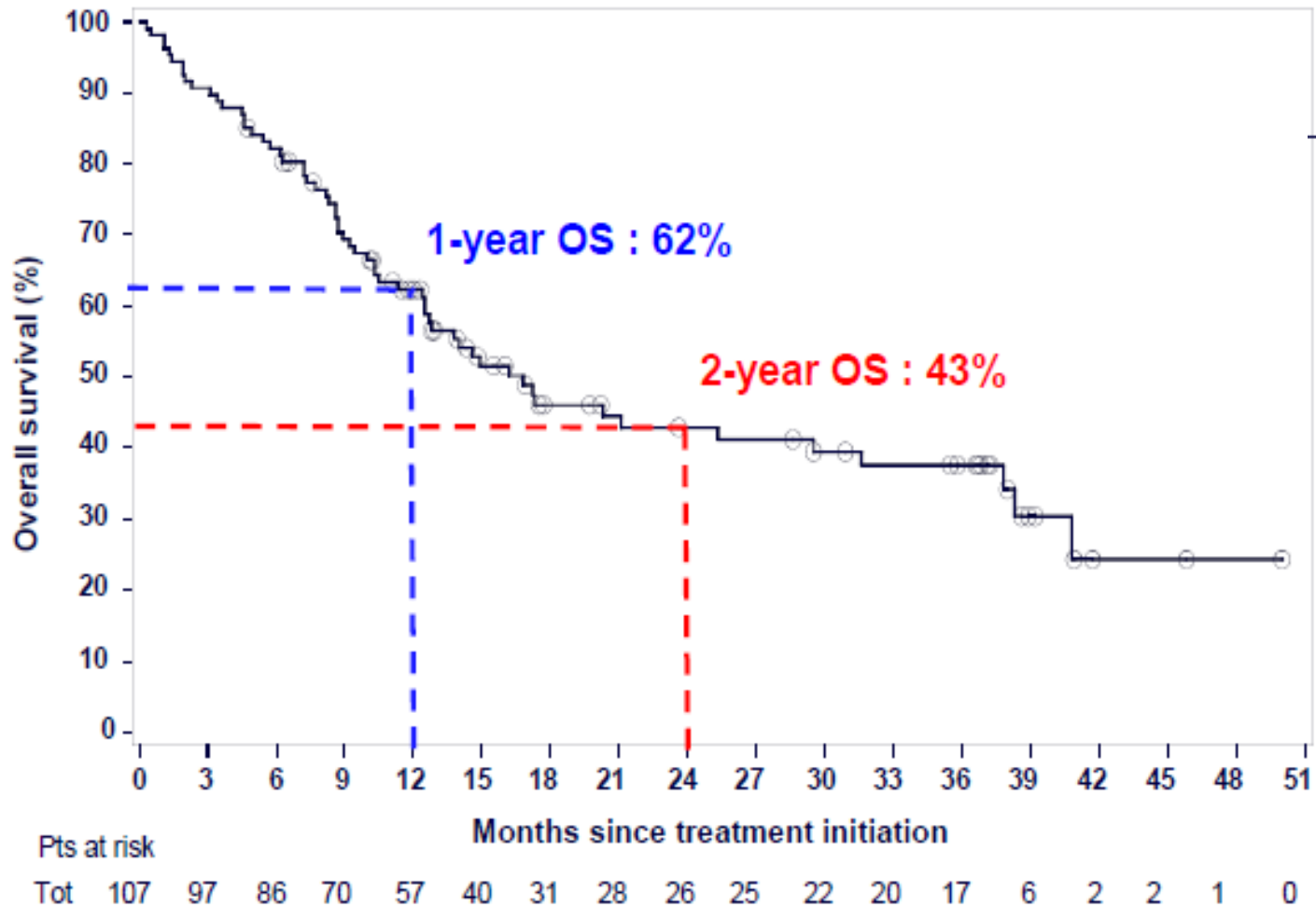


ORR 31% (41% at 3 mg/kg)

# Nivolumab fase I



# Nivolumab fase I



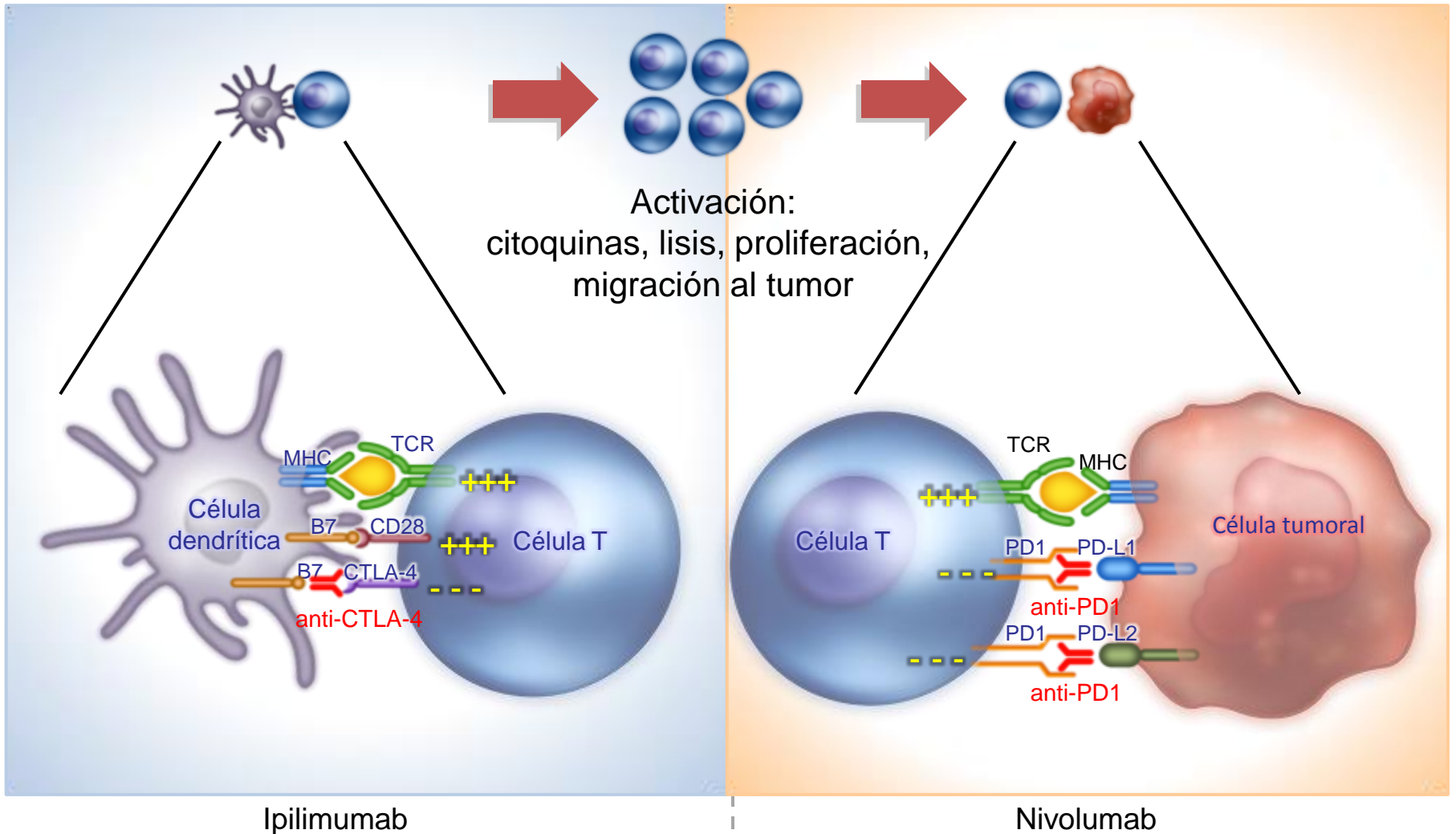
# NIVO + vacuna

Un 25% de pacientes refractarios a IPI  
puede responder a NIVO

PD-L1 no es un marcador fiable de  
respuesta a nivolumab



# Bloquear CTLA-4 y PD1

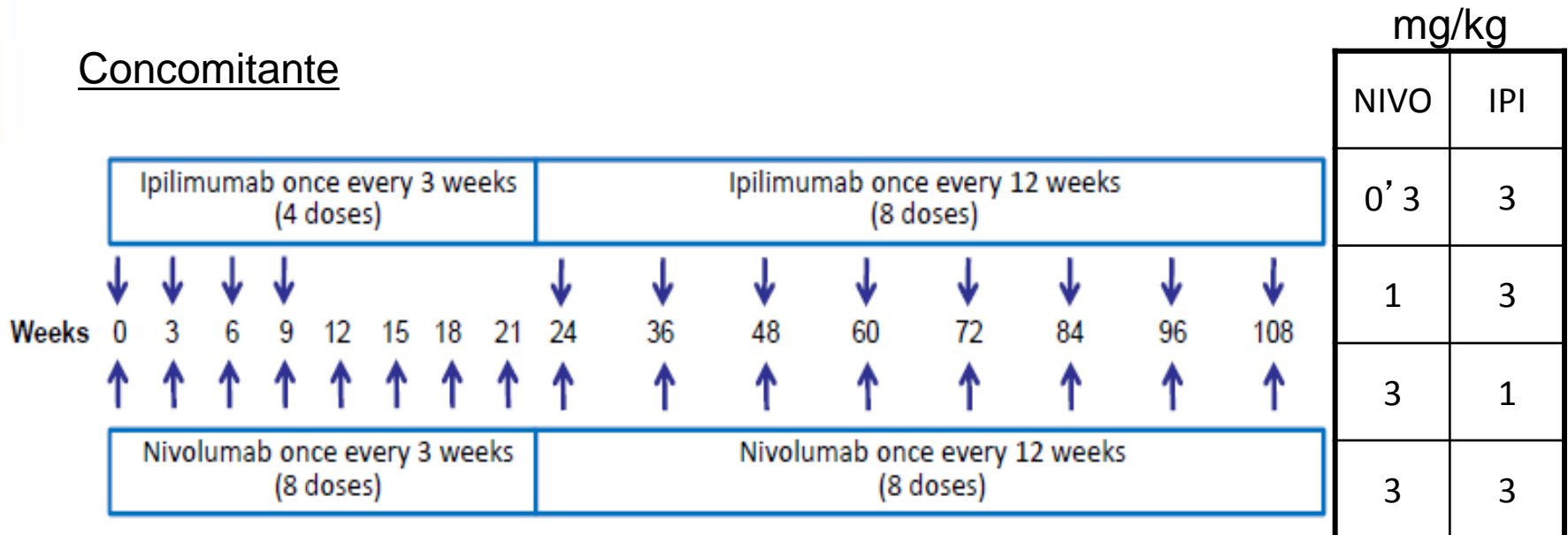


# NIVO + IPI fase I

## Secuencial

Tras IPI, nivolumab /2 sem., máximo 48 sem. (dosis 1 y 3 mg/kg)

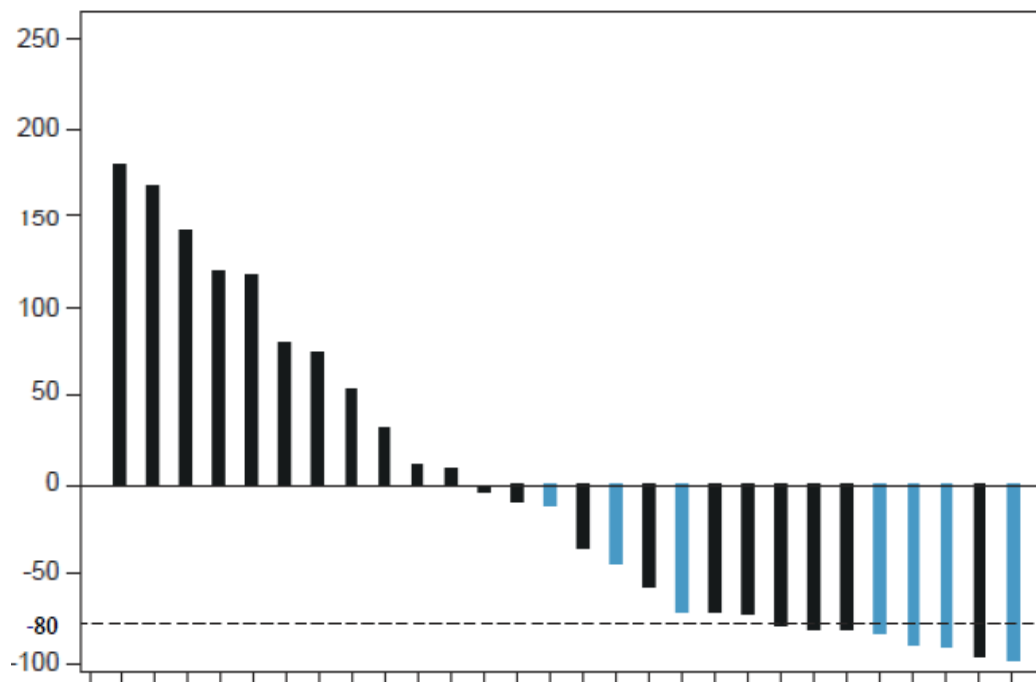
## Concomitante



Wolchok, NEJM 2013

# NIVO + IPI fase I

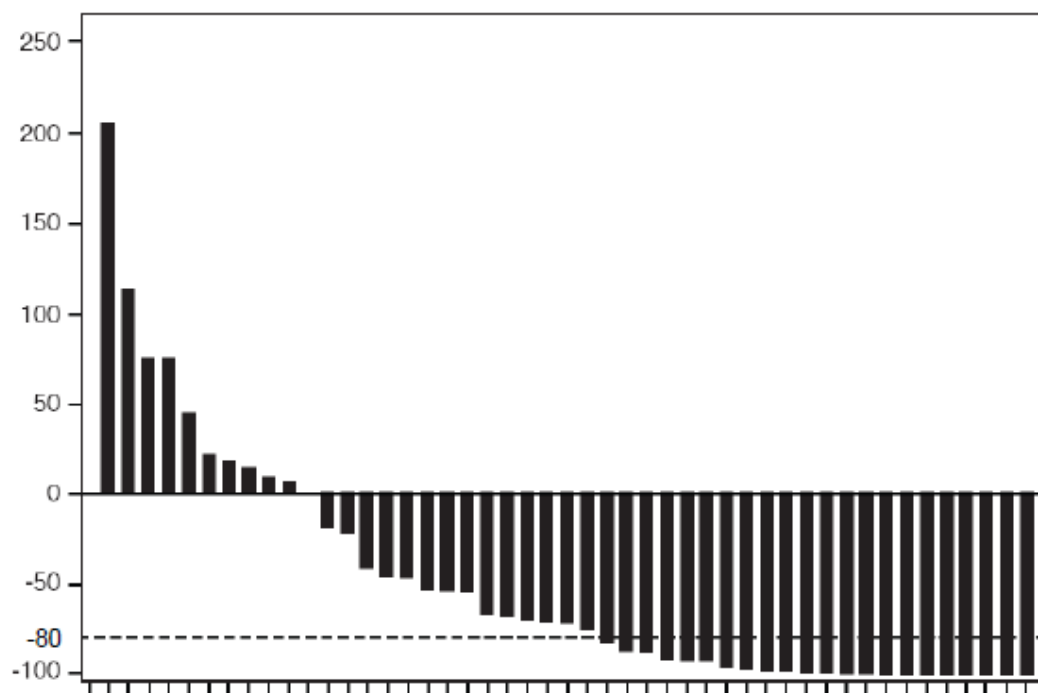
## Secuencial



NIVO	IPI	N	RG
1		16	38%
3		14	0
Global		30	20%

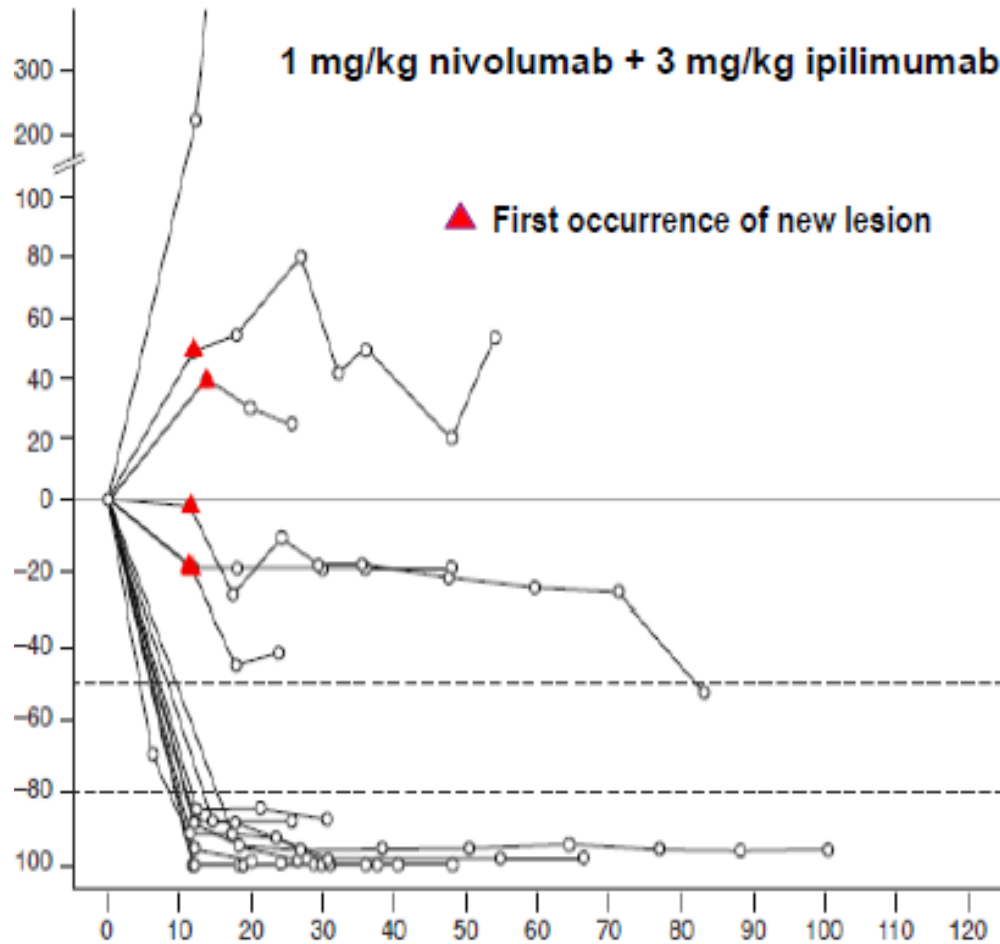
# NIVO + IPI

## Concomitante



NIVO	IPI	N	RG
0'3	3	14	21%
1	3	17	53%
3	1	15	40%
3	3	6	50%
Global		52	40%

# NIVO + IPI fase I



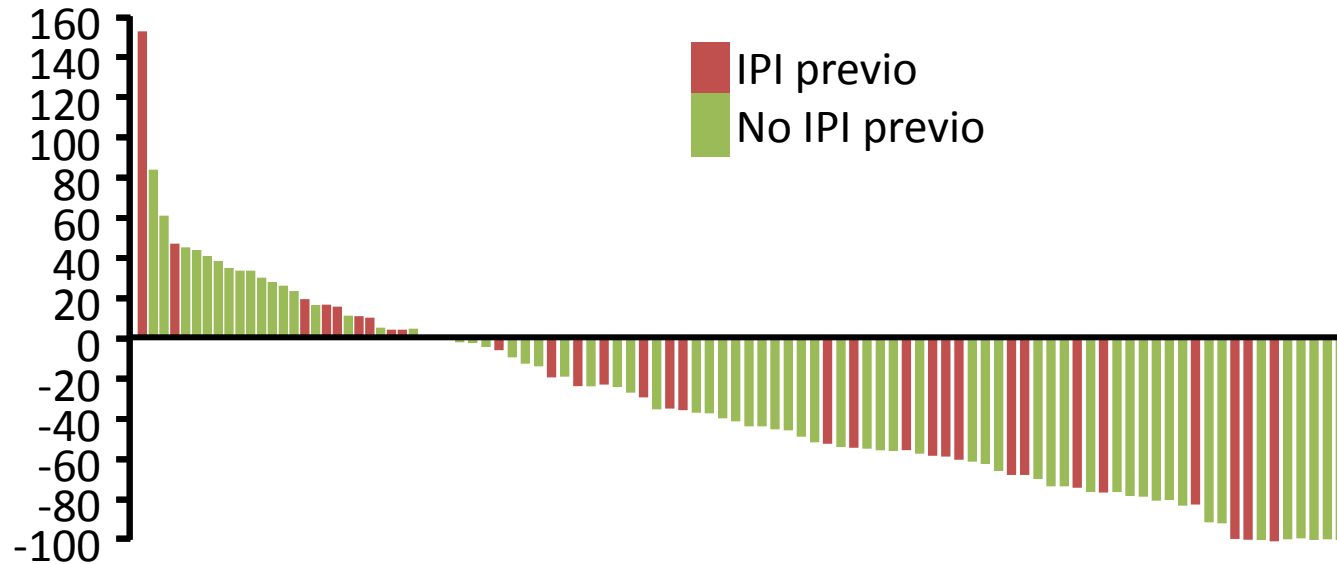
# MK3475 fase I

10 mg/kg/2s - 10 mg/kg/3 s – 2 mg/kg/2s



N=135  
48 IPI previo

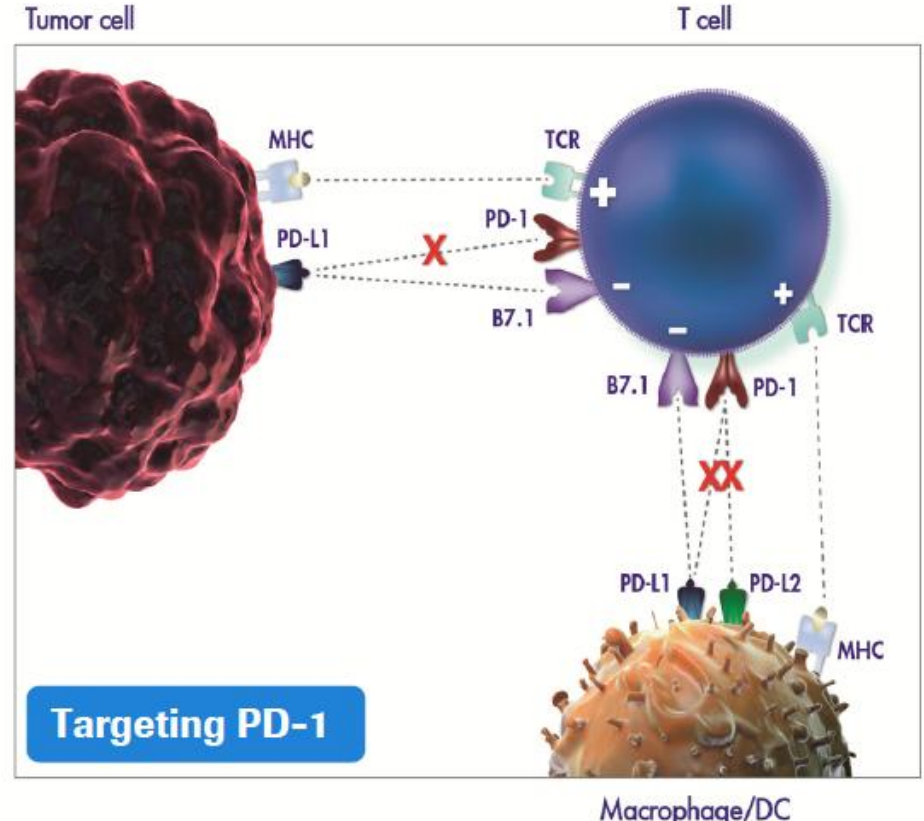
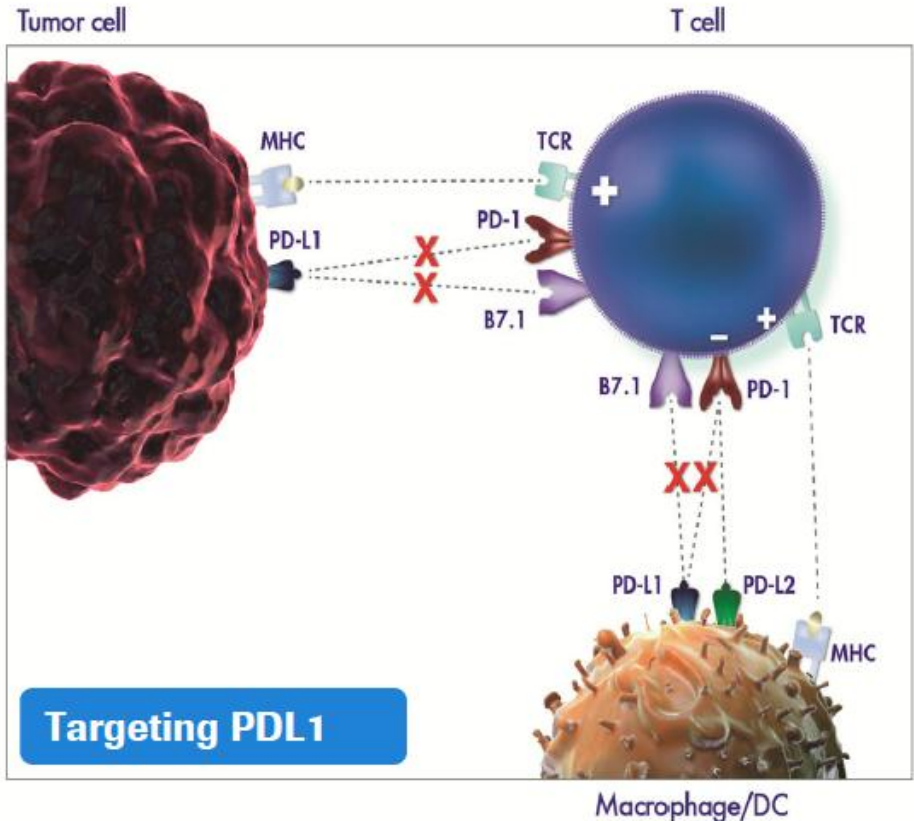
# MK3475 fase I



## Respuestas RECIST

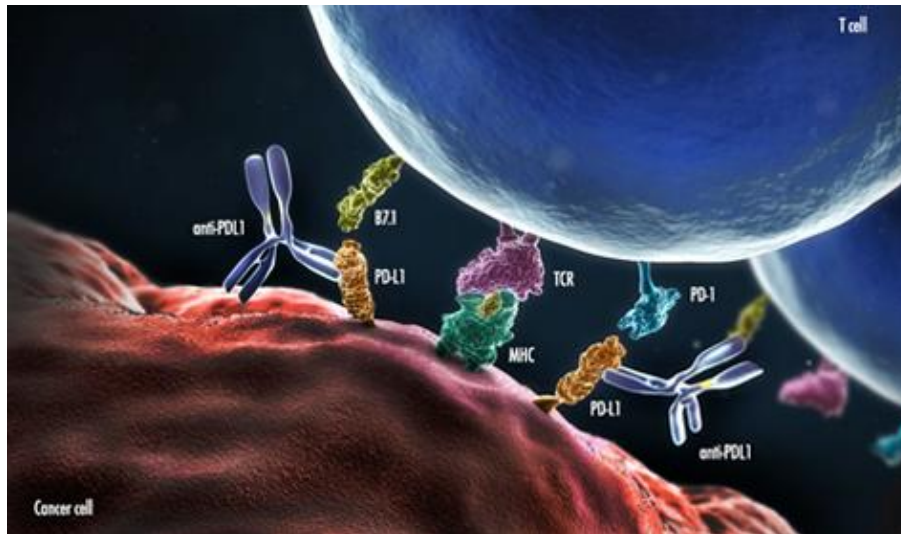
	No IPI previo	IPI previo
10 mg/kg /2w (n = 52)	49	62
10 mg/kg /3w (n = 45)	26	27
2 mg/kg /3w (n = 20)	25	--

Hamid, NEJM 2013





# MPDL3280A fase I



RG 29%

SLP a 24 semanas 43%

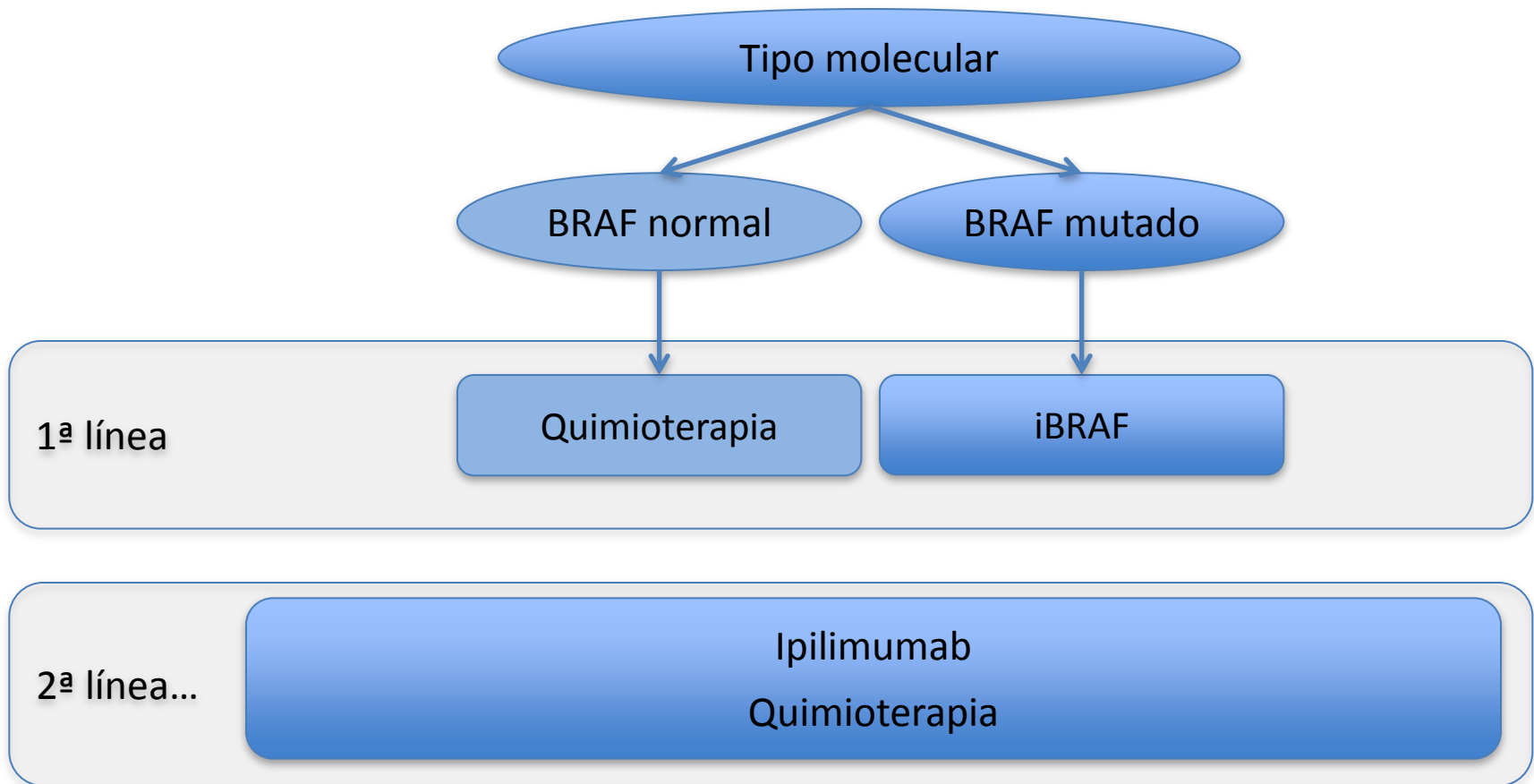
# ¿Paciente óptimo anti-PD1?

## ENSAYOS CLÍNICOS

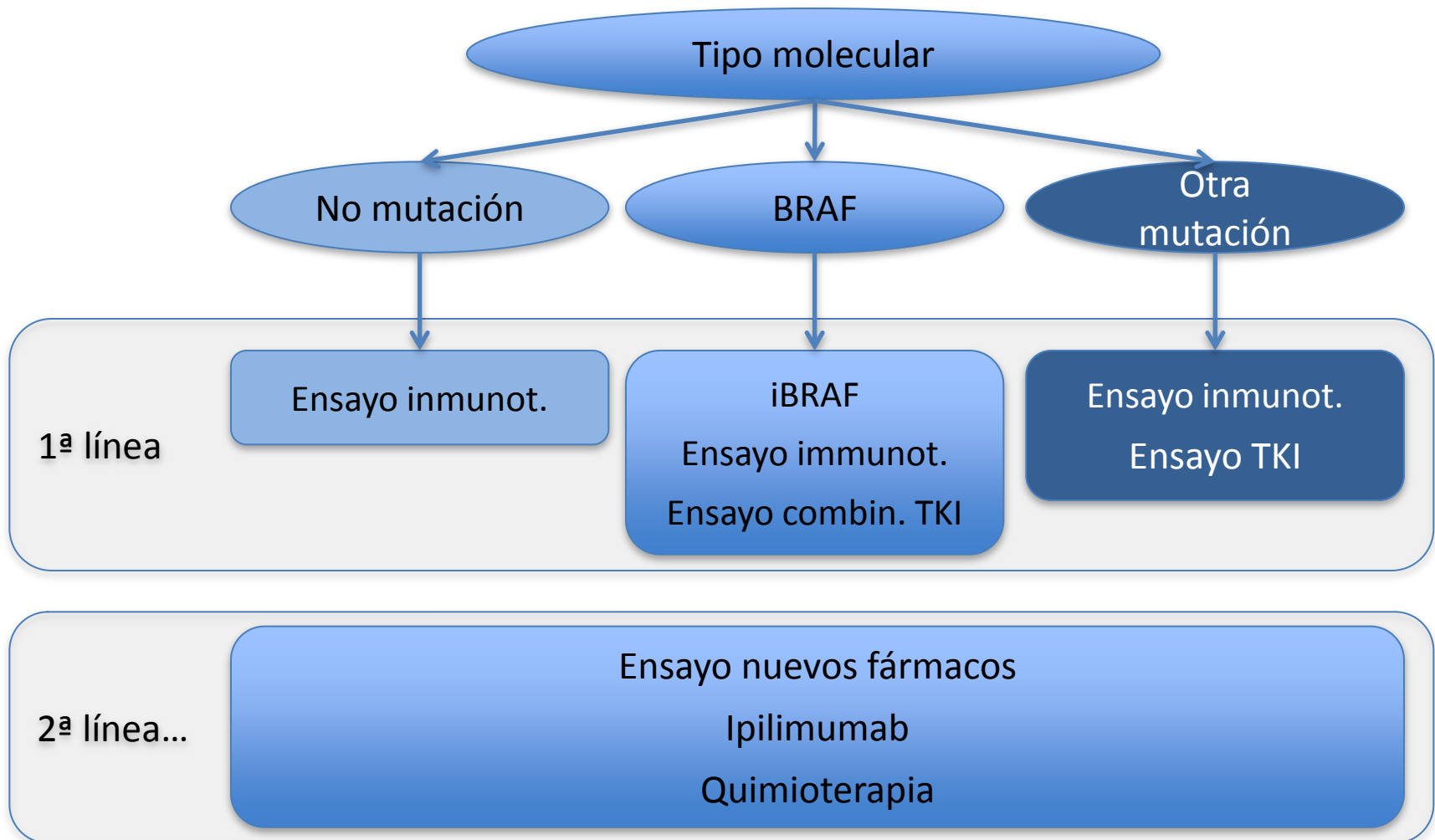
Criterios de inclusión

Criterios de exclusión

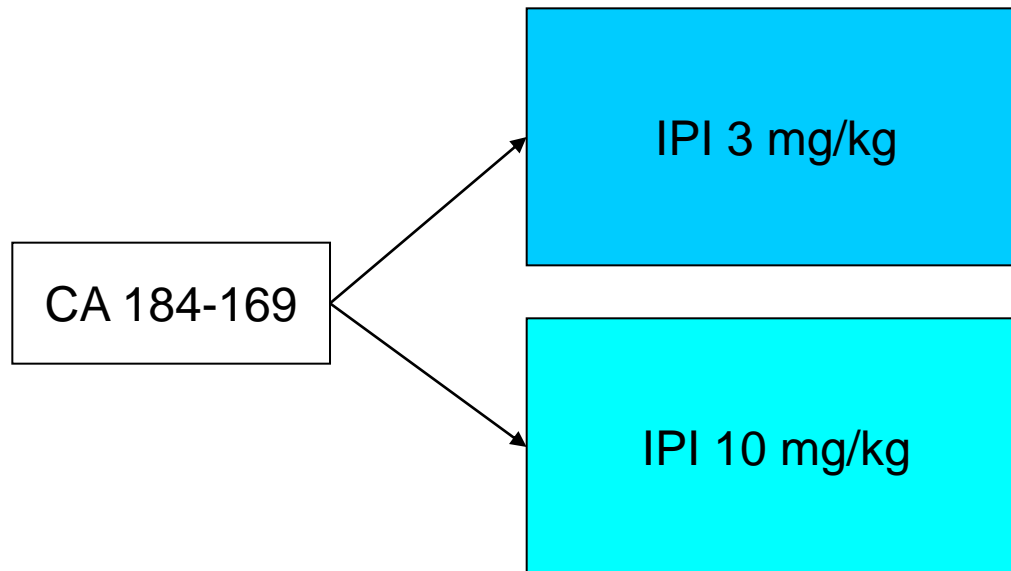
# Algoritmo terapéutico



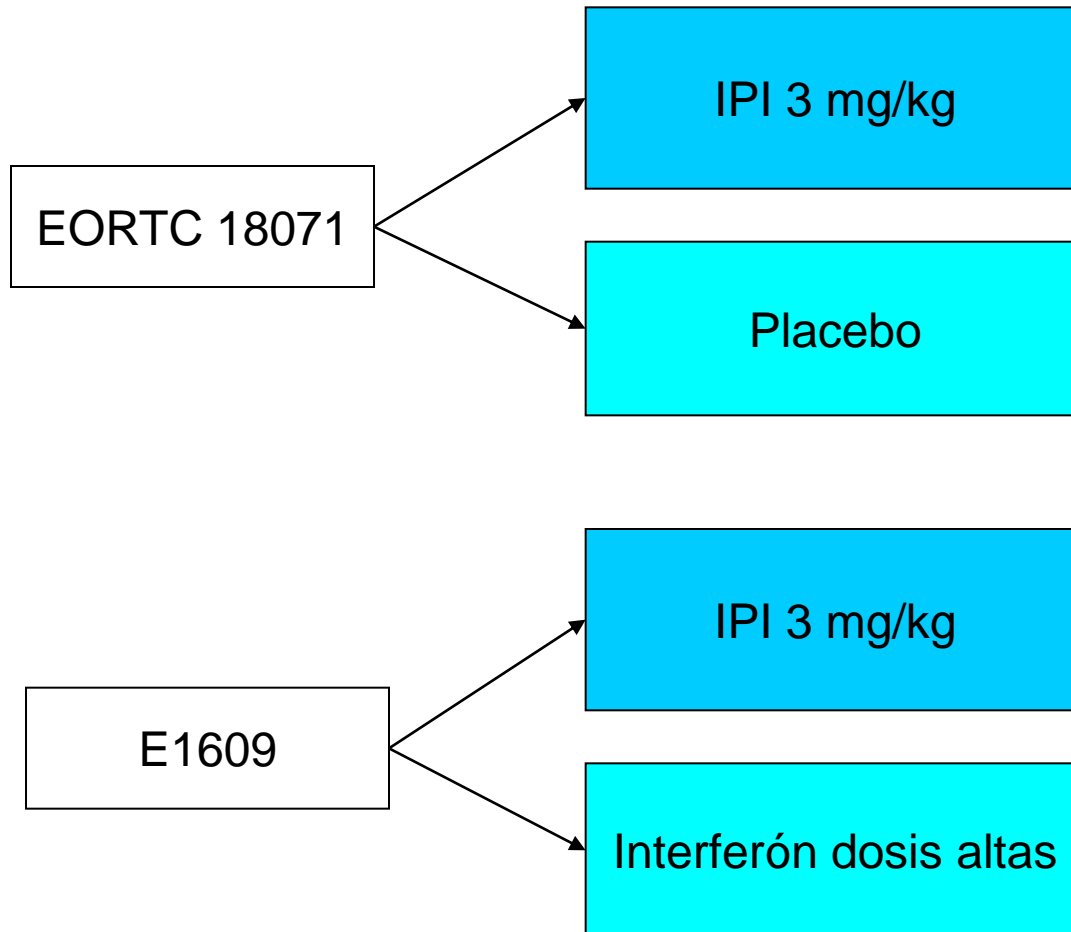
# Algoritmo terapéutico



# ¿Dosis óptima de IPI?

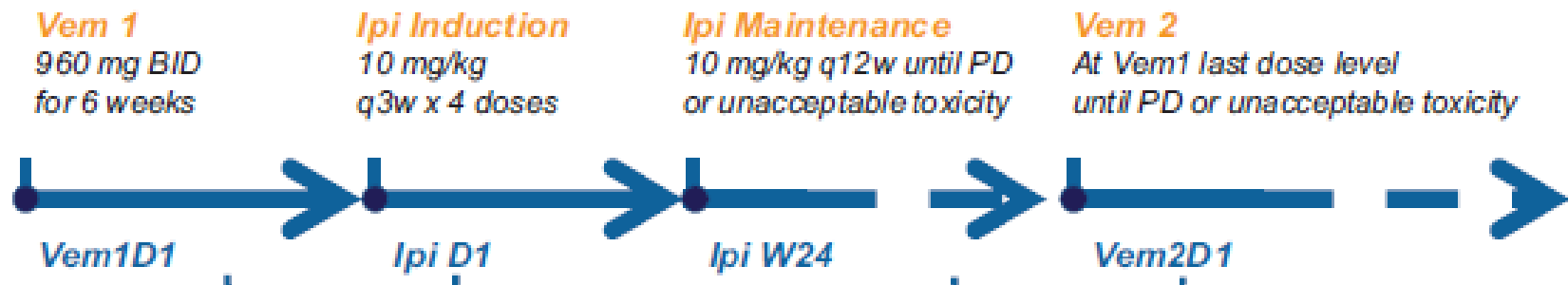


# IPI en adyuvancia

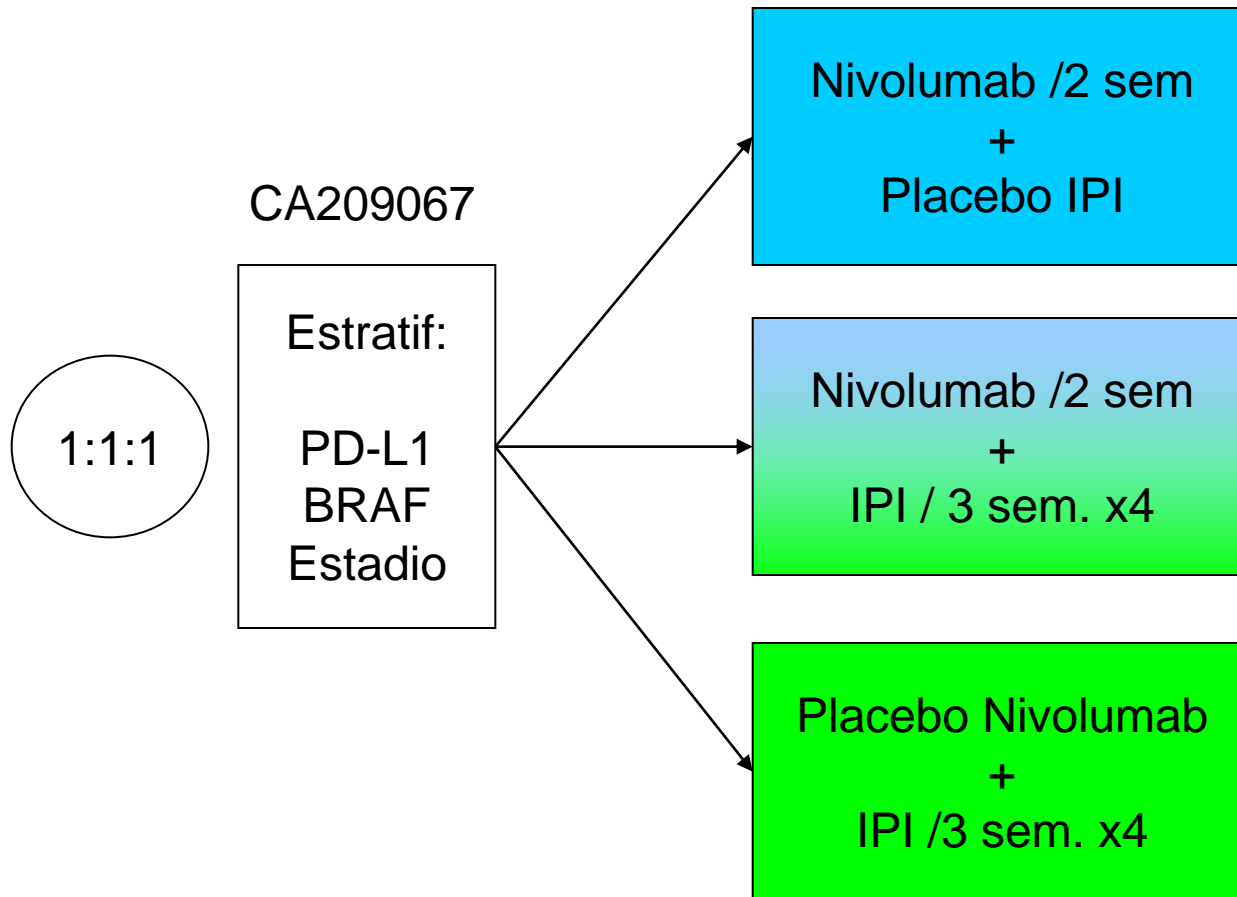


# IPI y vemurafenib

CA 184-240

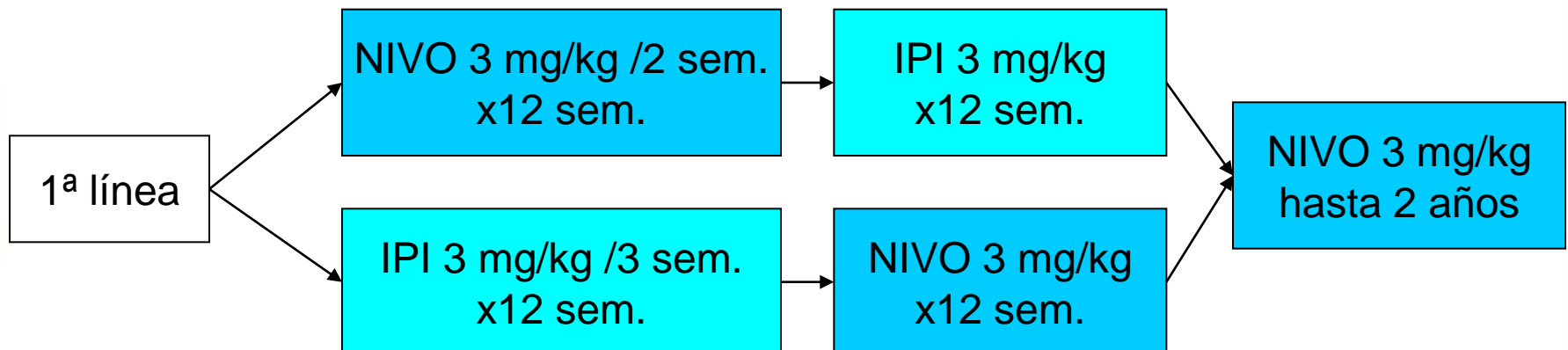
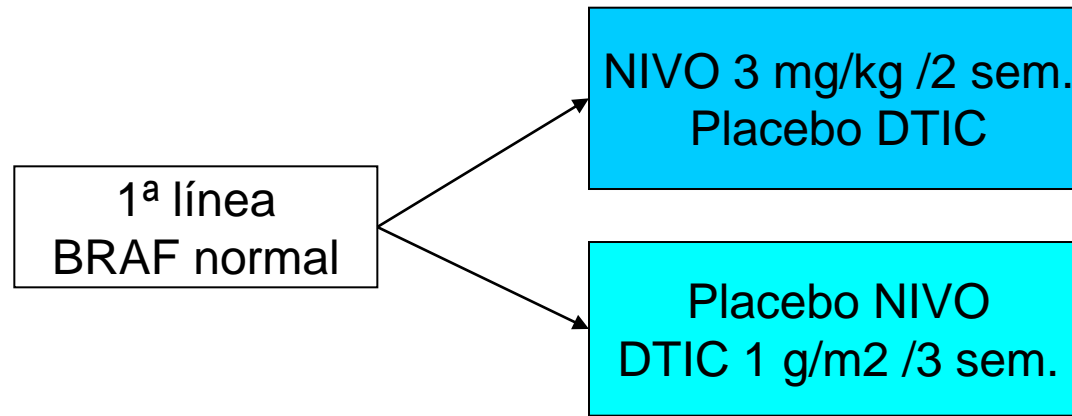


# NIVO / IPI

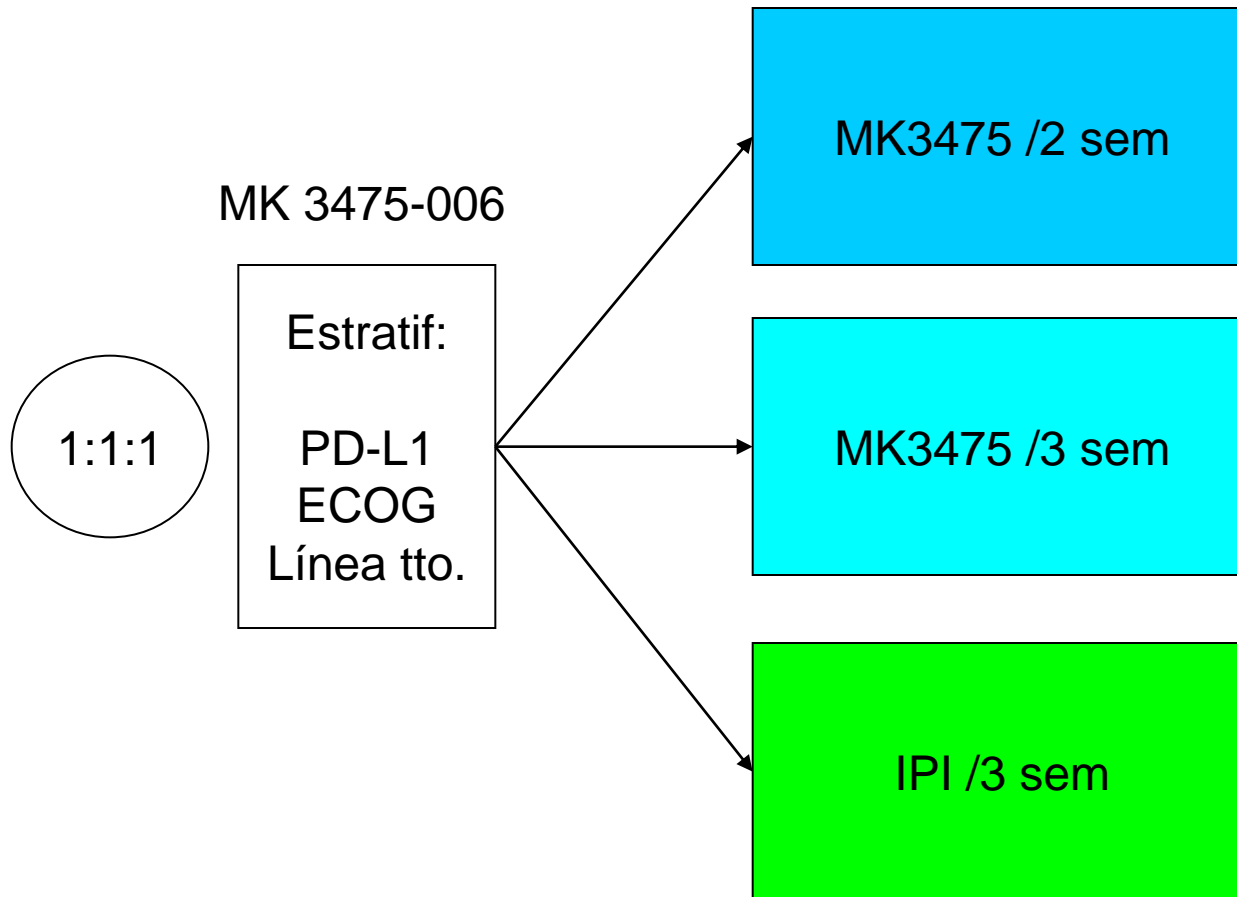




# Otros ensayos NIVO



# MK3475/IPI



# Conclusiones

IPI necesita tiempo

Predicción respuesta incierta

IPI y anti-PD1: ensayos clínicos

[www.groupgem.org](http://www.groupgem.org)

