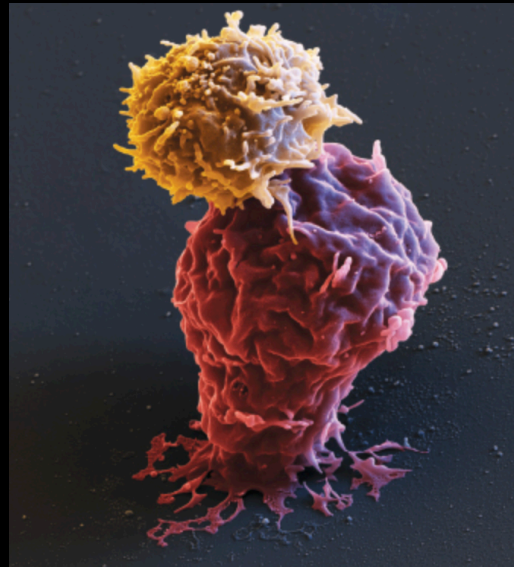


Atual papel da imunoterapia na Oncologia II



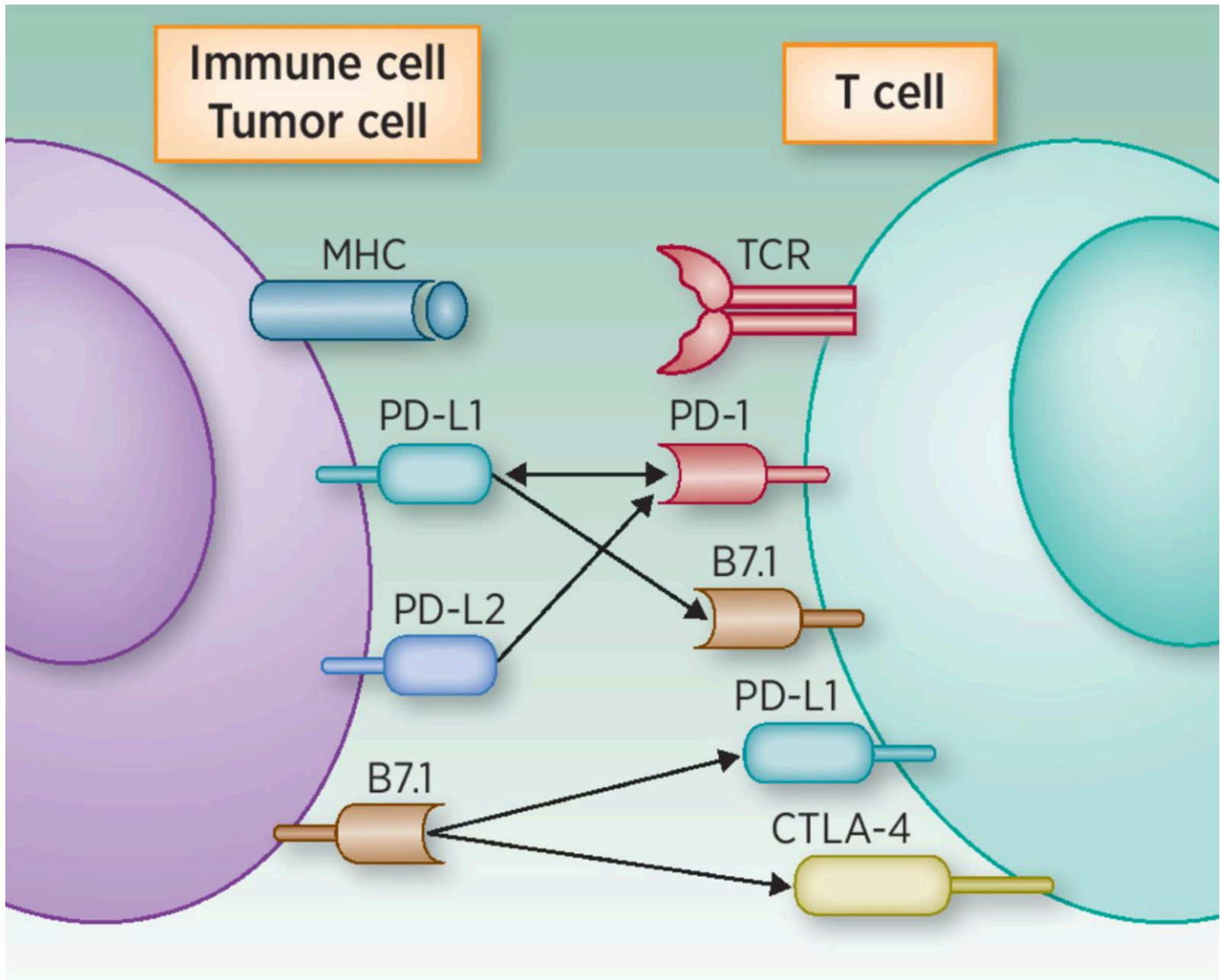
Alexandre A. A. Jácome, MD, PhD

Postdoctoral Fellow no Departamento de Oncologia Clínica Gastrointestinal

MD Anderson Cancer Center

Eventos adversos

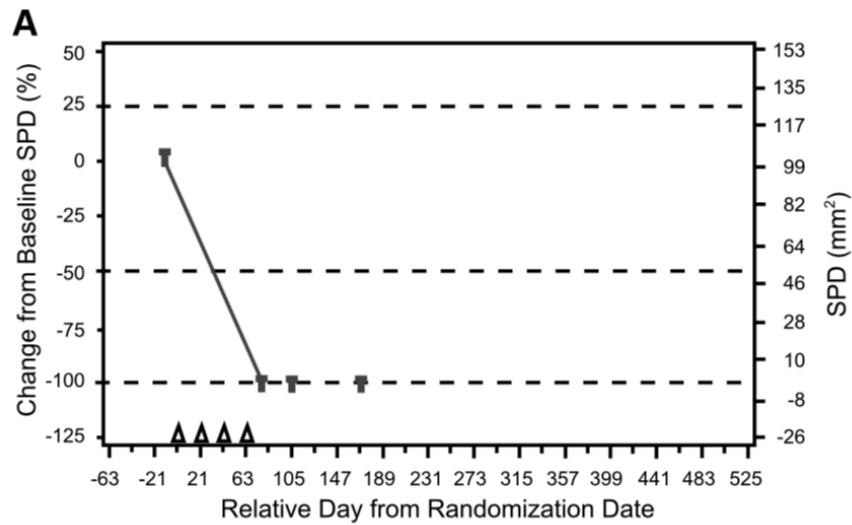
	Ipi + Nivo	Ipi	Nivo	Pembro	Atezo
	G3-4	G3-4	G3-4	G3-4	G3-4
Diarreia	9%	6%	3%	4%	2%
Rash	3%	2%	< 1%	4%	1%
ALT / AST	9%	2%	1%	< 1%	3%
Pneumonite	1%	< 1%	< 1%	3%	< 1%
Descontinuação	30%	14%	8%	5%	8%



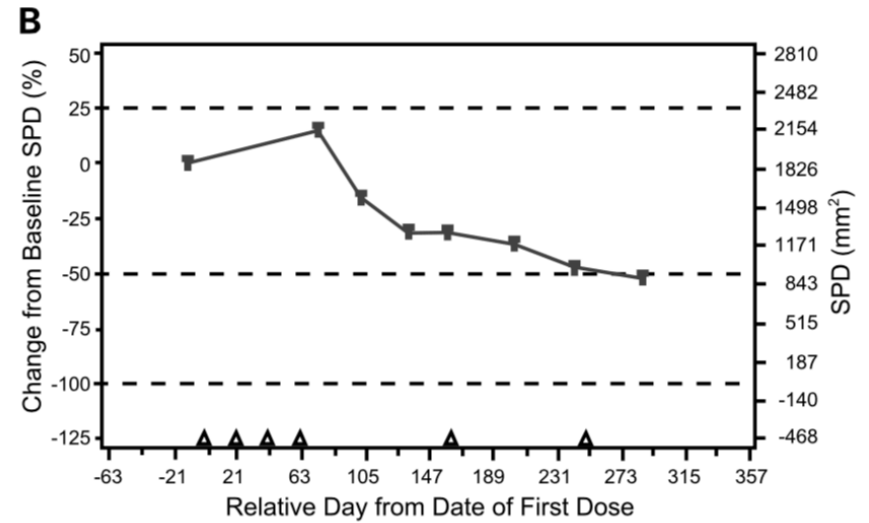
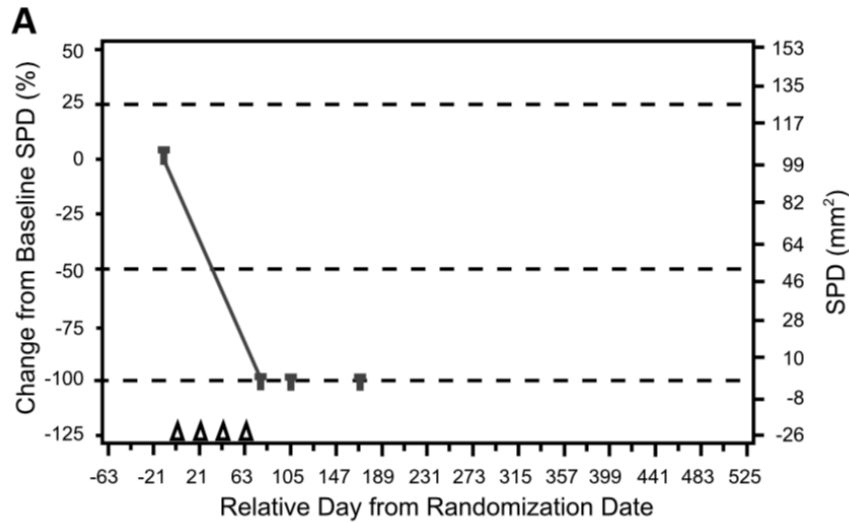
Imunoterapia

- ✓ Mecanismos de evasão imune
- ✓ Mecanismos de ação dos inibidores de checkpoint
- ✓ Eficácia
- ✓ Eventos adversos imuno-relacionados
- ✓ Avaliação de resposta
- ✓ Biomarcadores preditivos
- ✓ Perspectivas

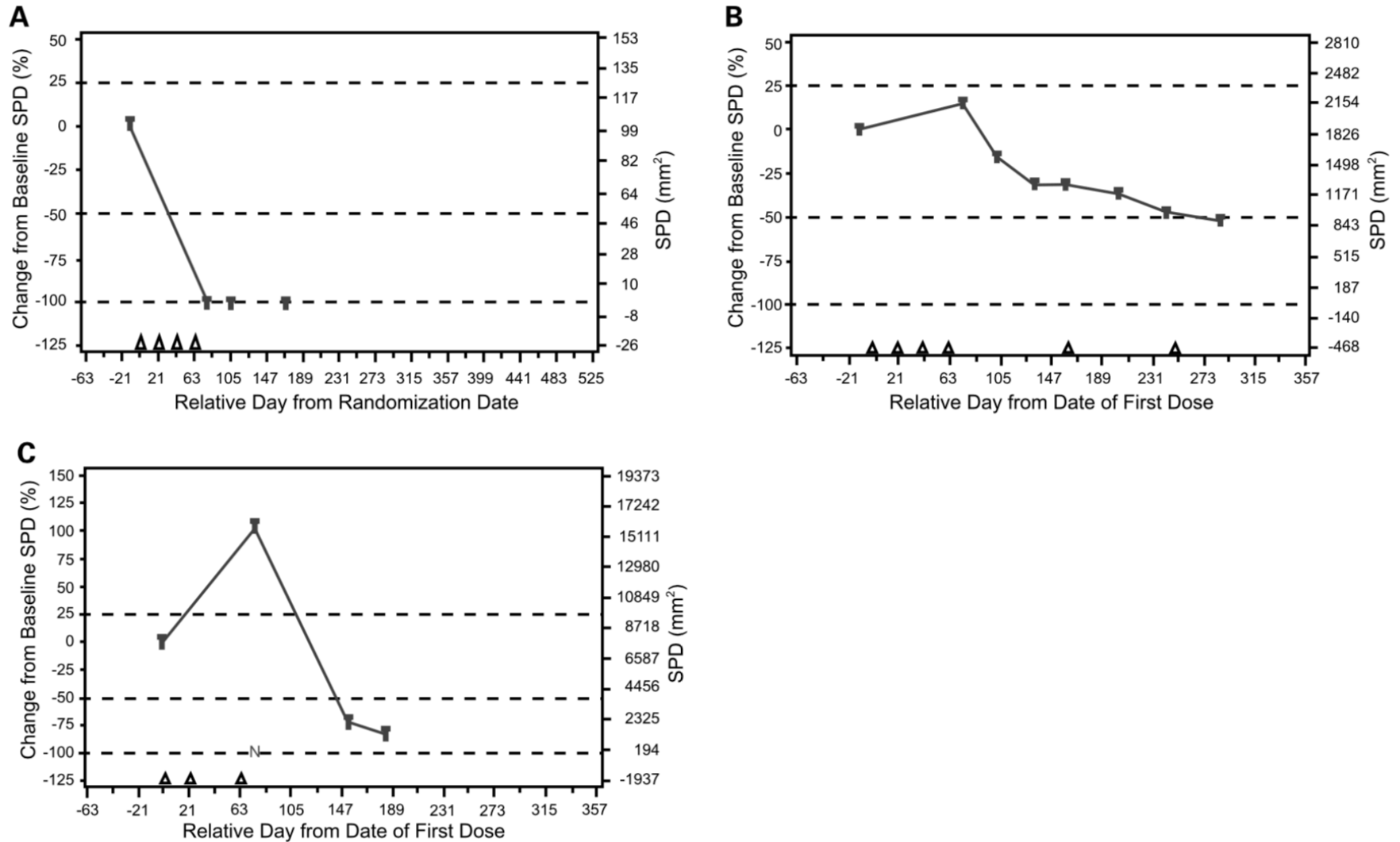
Padrões de resposta



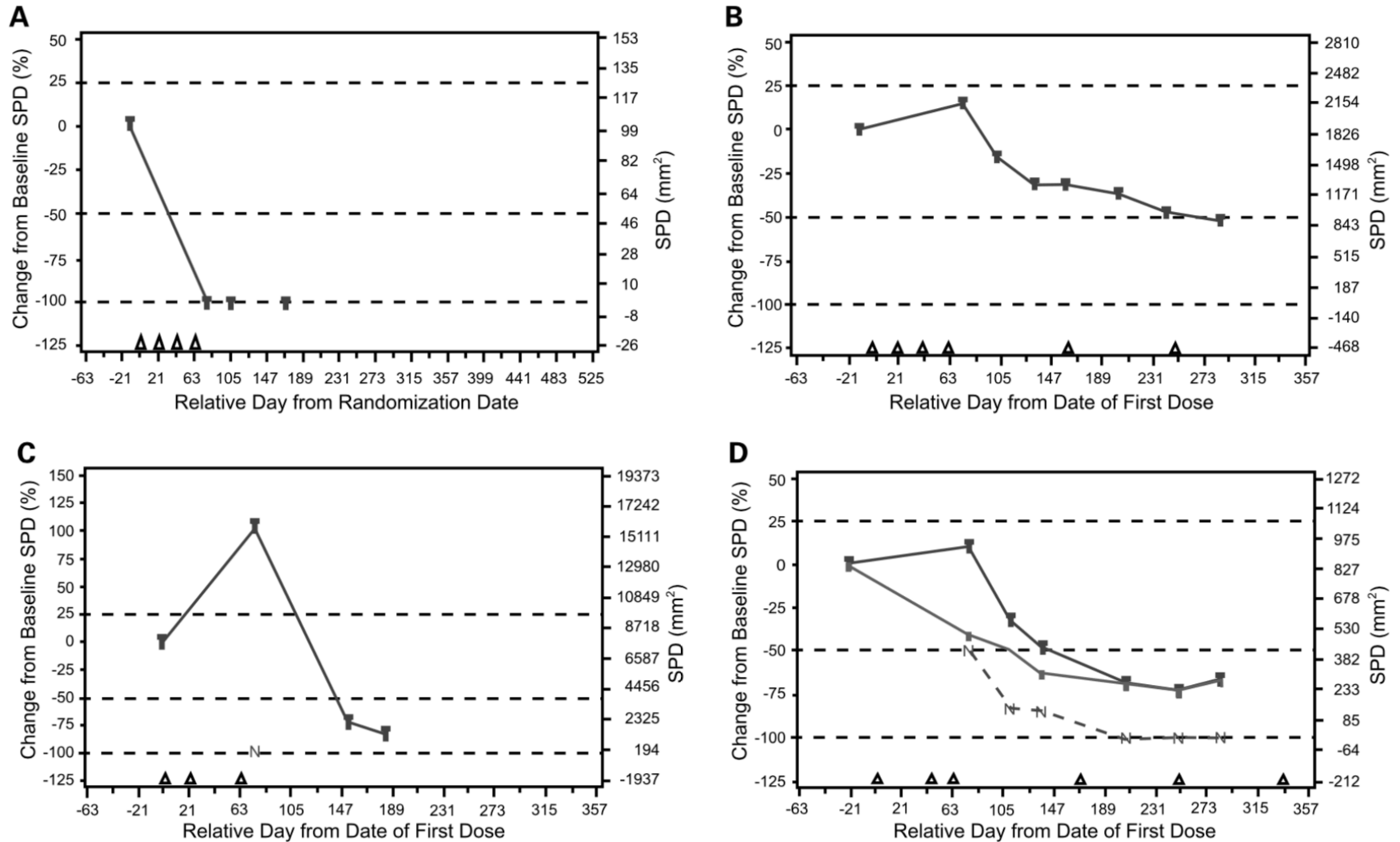
Padrões de resposta



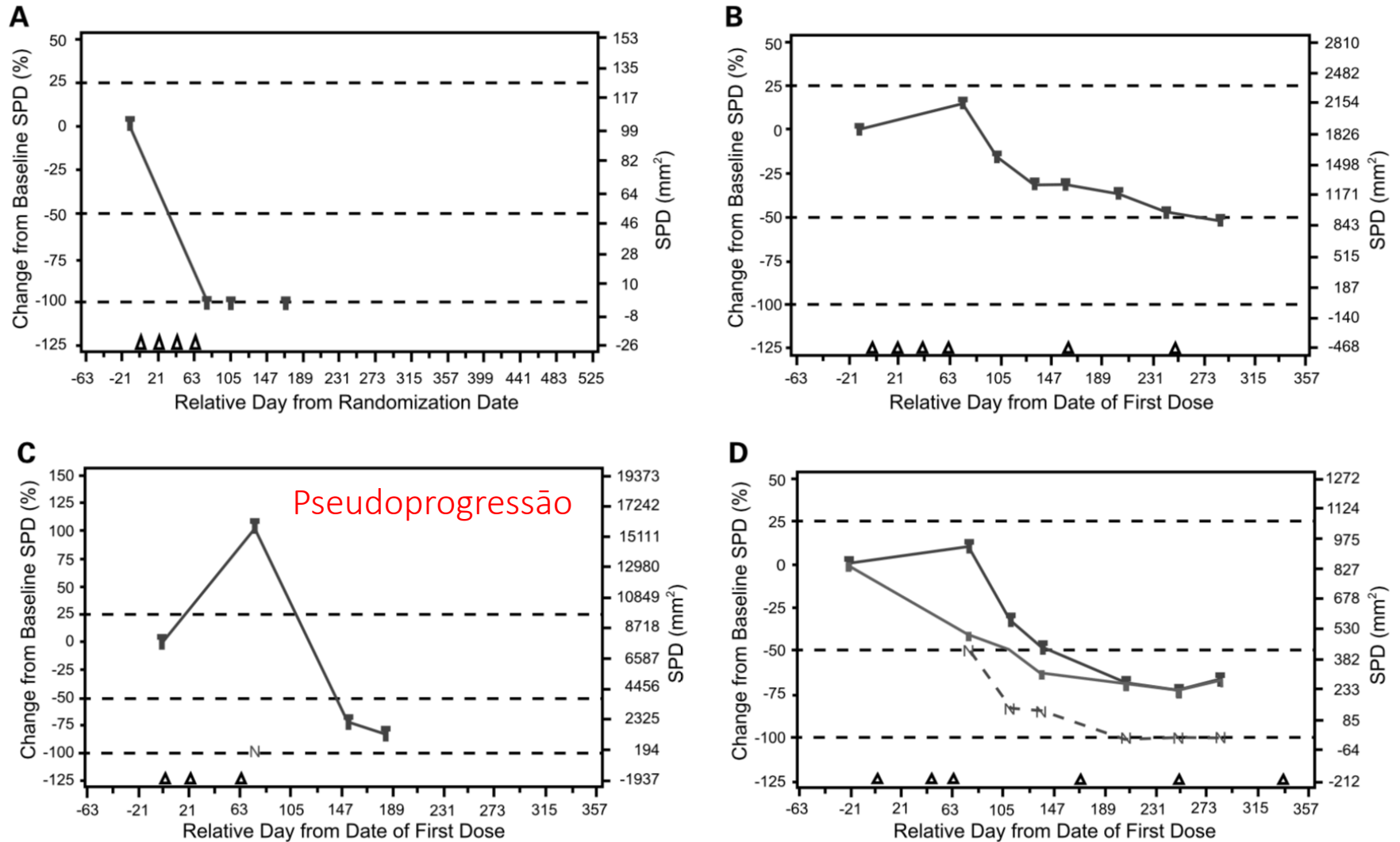
Padrões de resposta



Padrões de resposta



Padrões de resposta

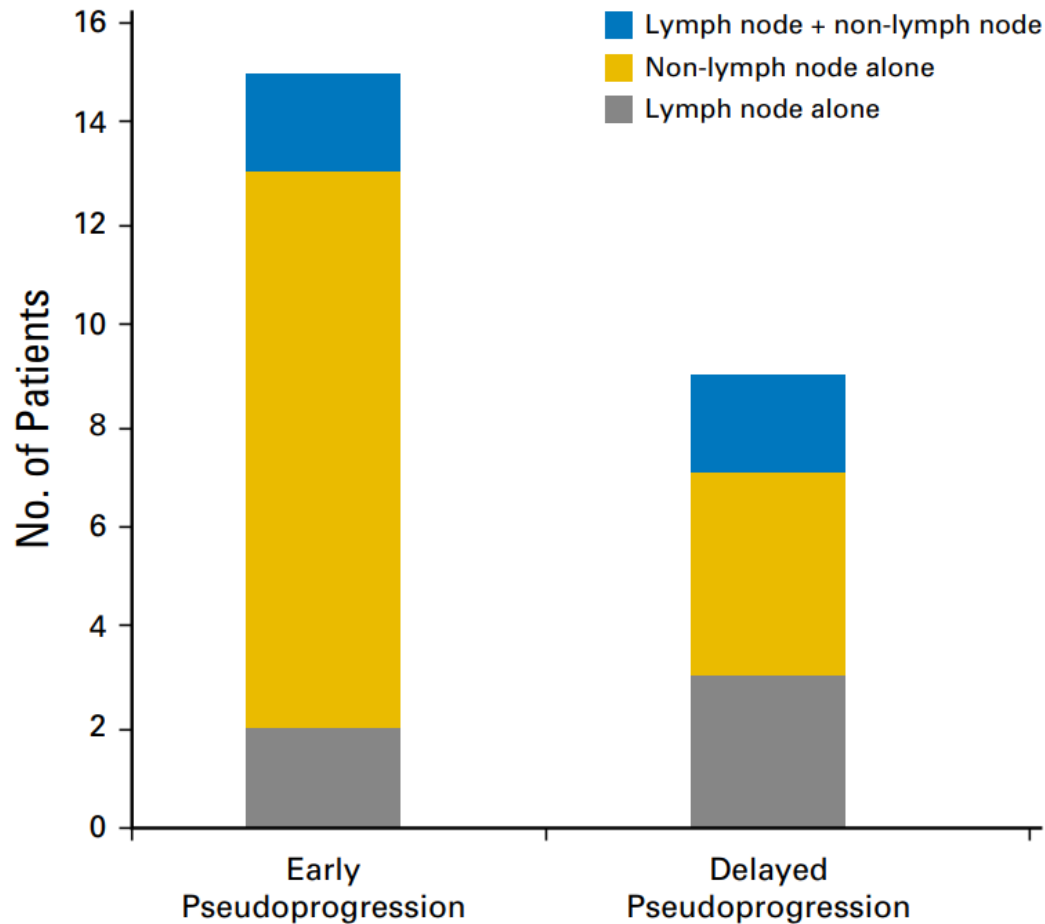


Pseudoprogressão



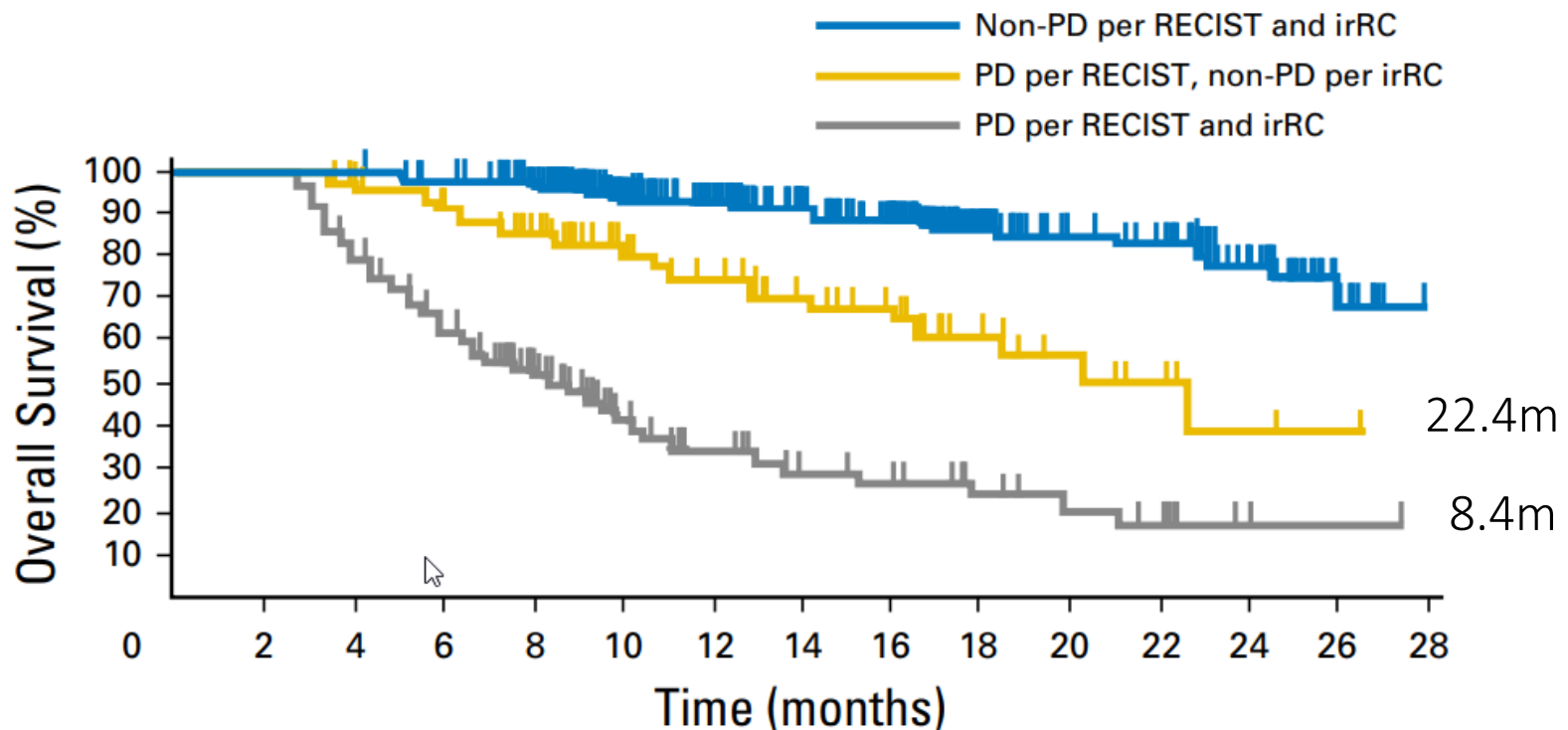
Aumento $\geq 25\%$ na carga tumoral não confirmada por segunda avaliação em 4 semanas
Precoce: ≤ 12 semanas
Tardia: > 12 semanas

Pseudoprogressão



Keynote-001
n: 327
Incidência: 7.3%

Pseudoprogressão



Sobrevida global 2 anos: 77.6% vs 37.5% vs 17.3%

RECIST 1.1 vs irRC

	RECIST 1.1	irRC
Medida	Unidimensional	Bidimensional
Lesões-alvo	5	15
Lesões novas	Progressão	Adicionadas ao baseline
Resposta parcial	Redução $\geq 30\%$	Redução $\geq 50\%$
Progressão de doença	Aumento $\geq 20\%$	Aumento $\geq 25\%$
Confirmação em 4s	Desnecessária	Necessária

RECIST 1.1 vs irRC

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Confirmação em 4s	Desnecessária	Necessária

RECIST 1.1 vs irRC

Estima-se que o uso do RECIST na avaliação de resposta em imunoterapia subestime o benefício do tratamento em cerca de **15%** dos pacientes

Imunoterapia

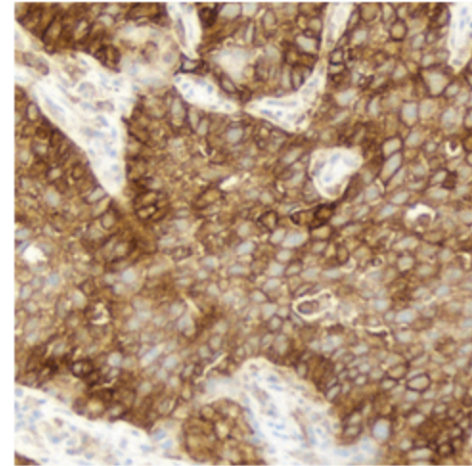
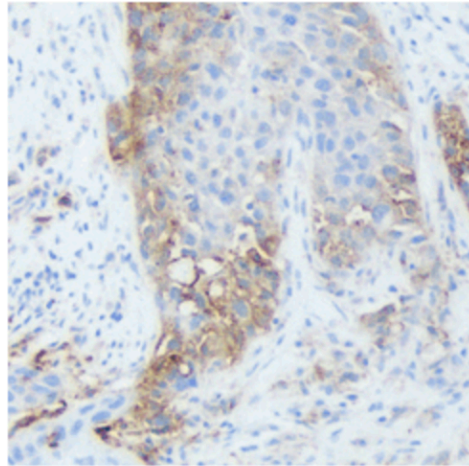
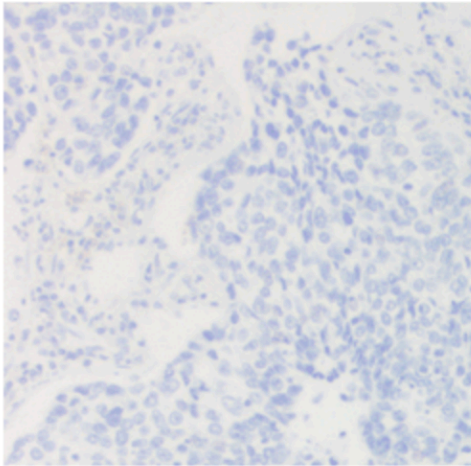
- ✓ Mecanismos de evasão imune
- ✓ Mecanismos de ação dos inibidores de checkpoint
- ✓ Eficácia
- ✓ Eventos adversos imuno-relacionados
- ✓ Avaliação de resposta
- ✓ Biomarcadores preditivos
- ✓ Perspectivas

PD-L1

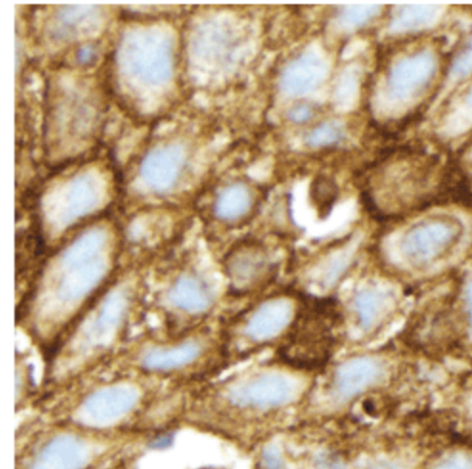
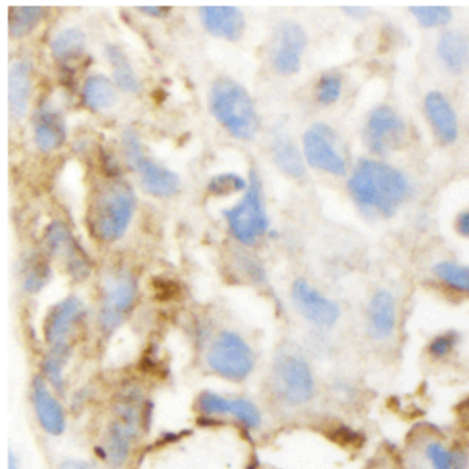
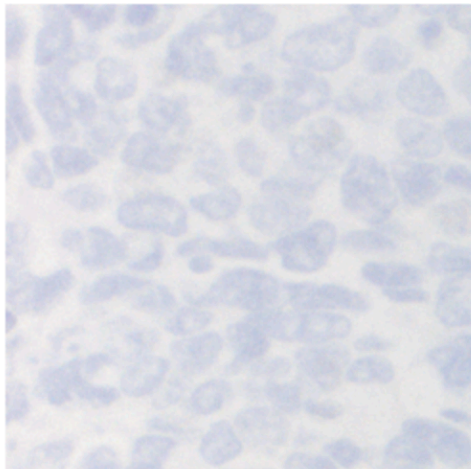
PS <1%

PS 1-49%

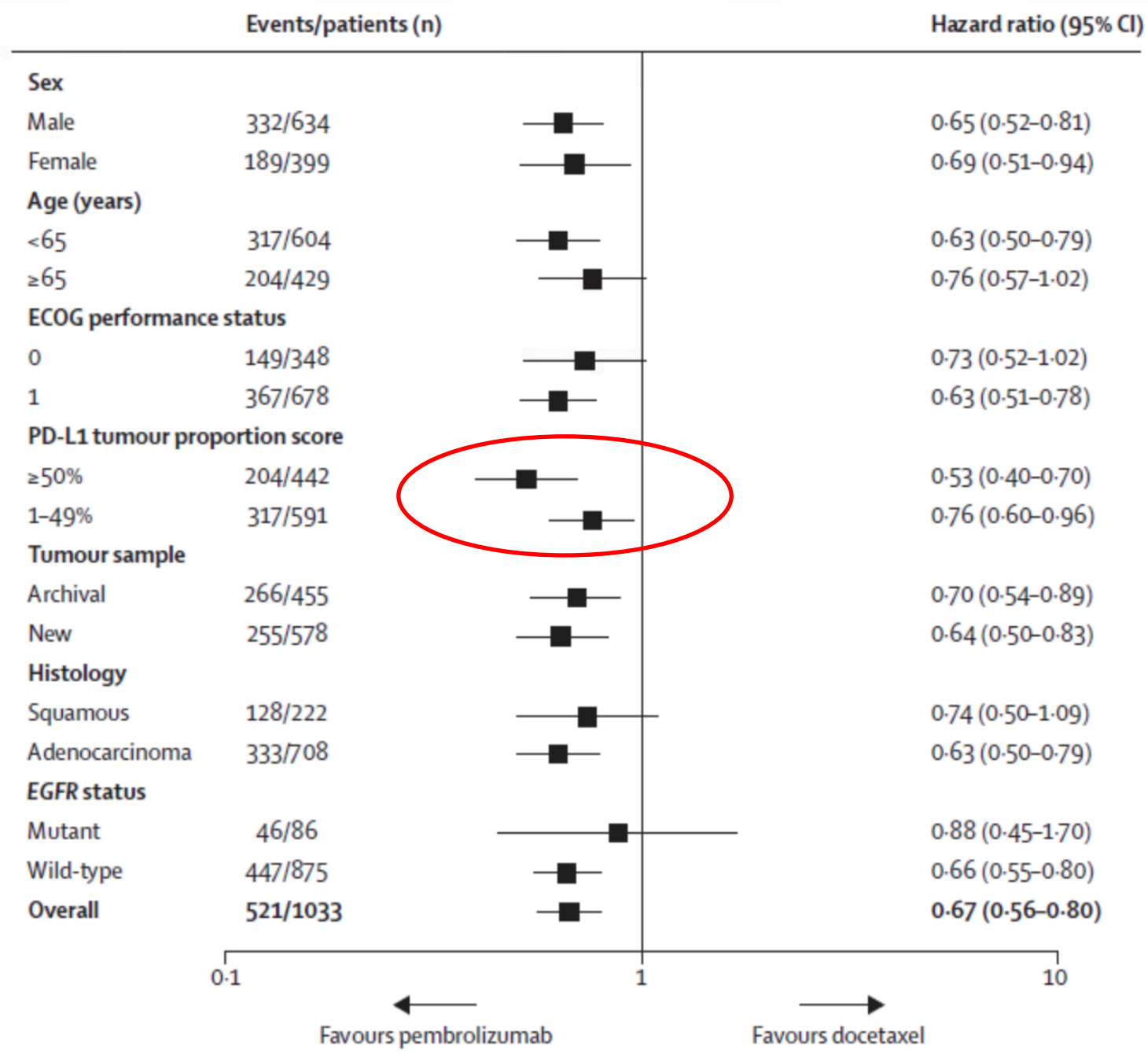
PS ≥50%



**5x
magnification**

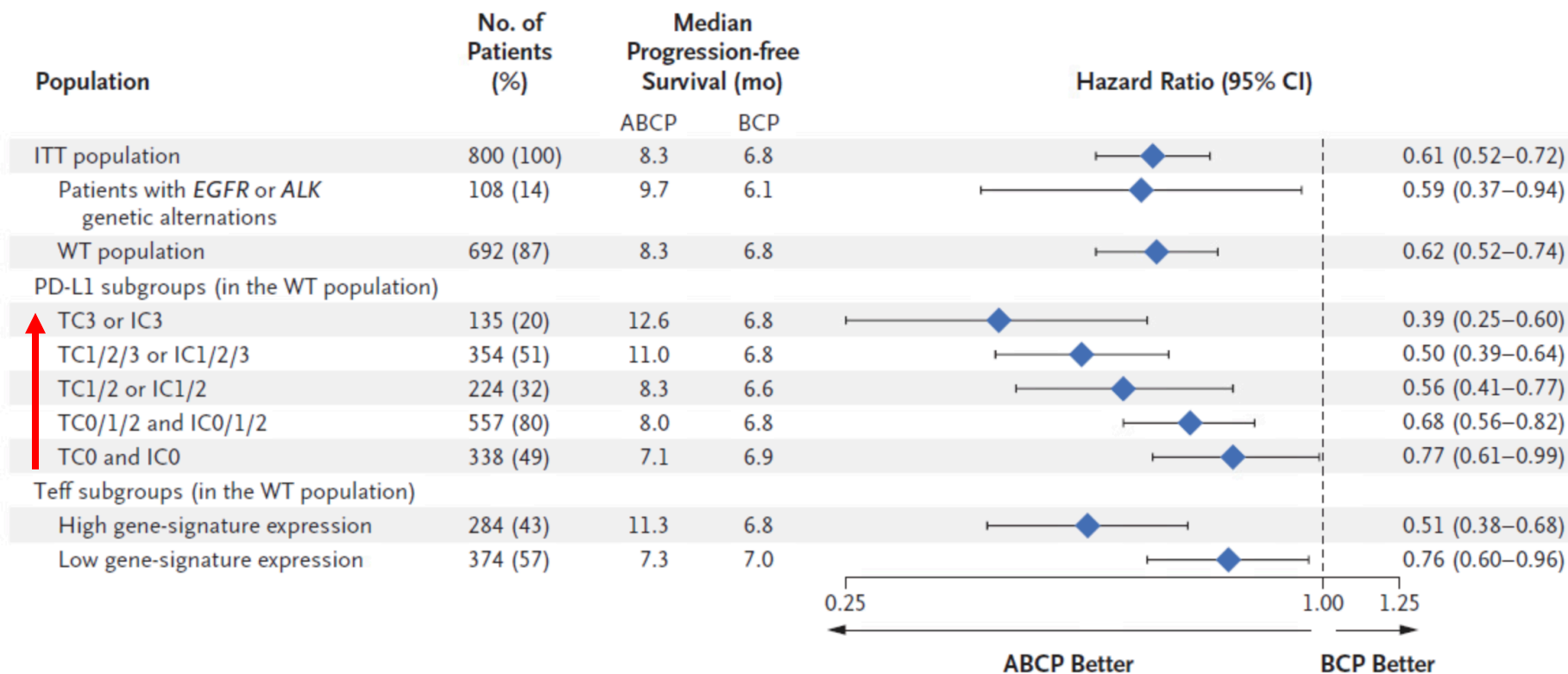


**40x
magnification**



PD-L1

Hazard Ratios for Disease Progression or Death in Biomarker Subgroups



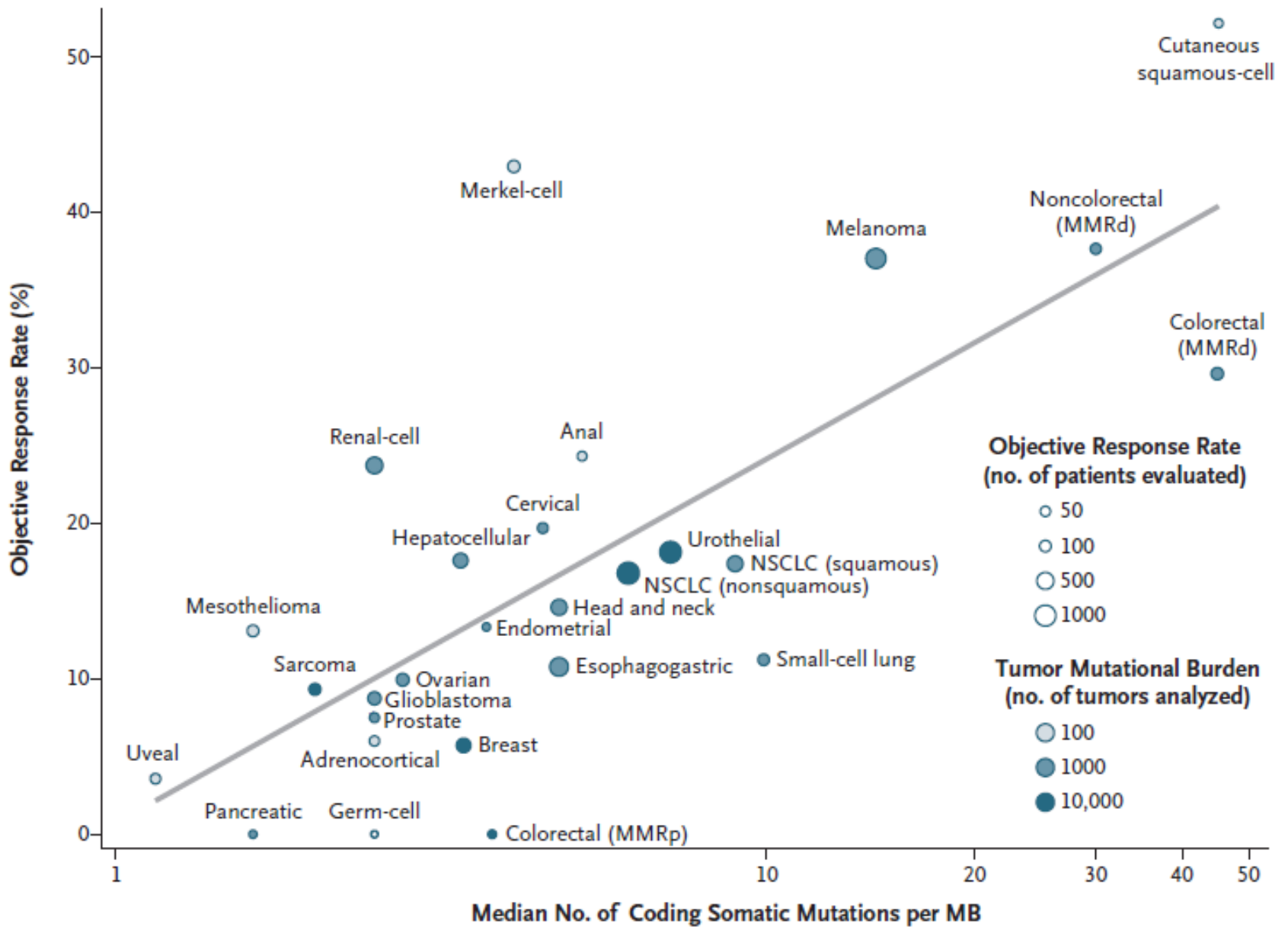
dMMR = MSI-H

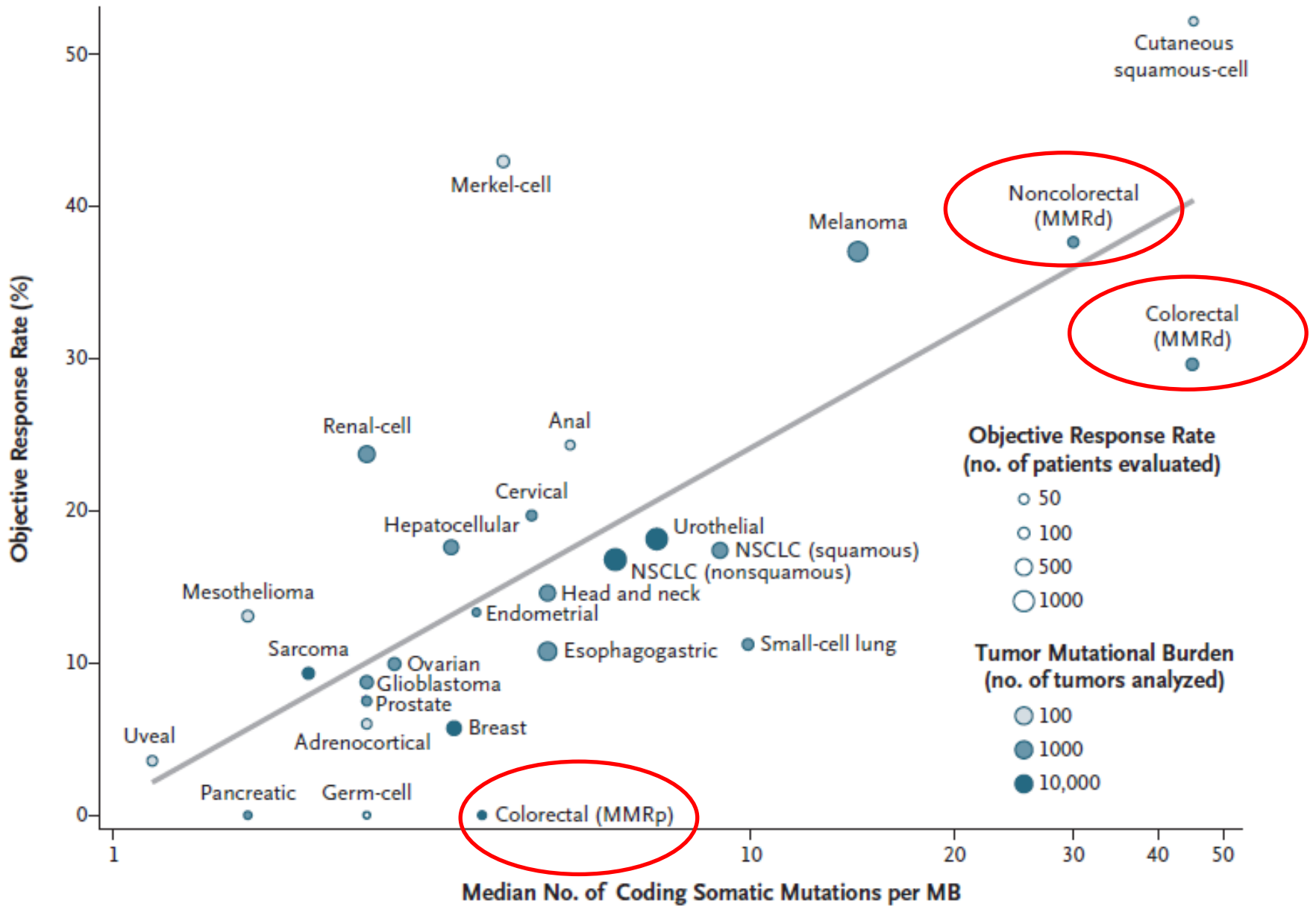
↑ mutações



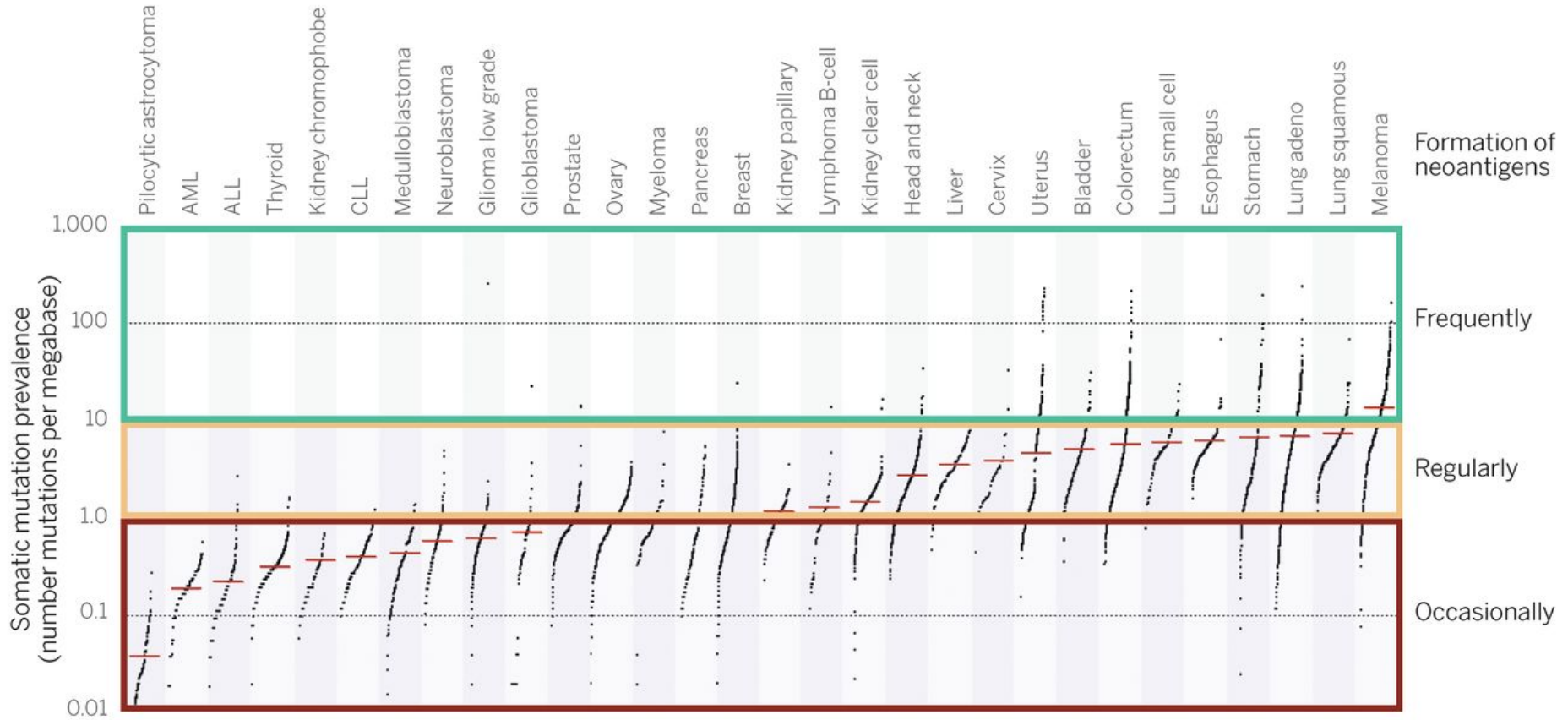
↑ TMB

(Tumor mutational burden)

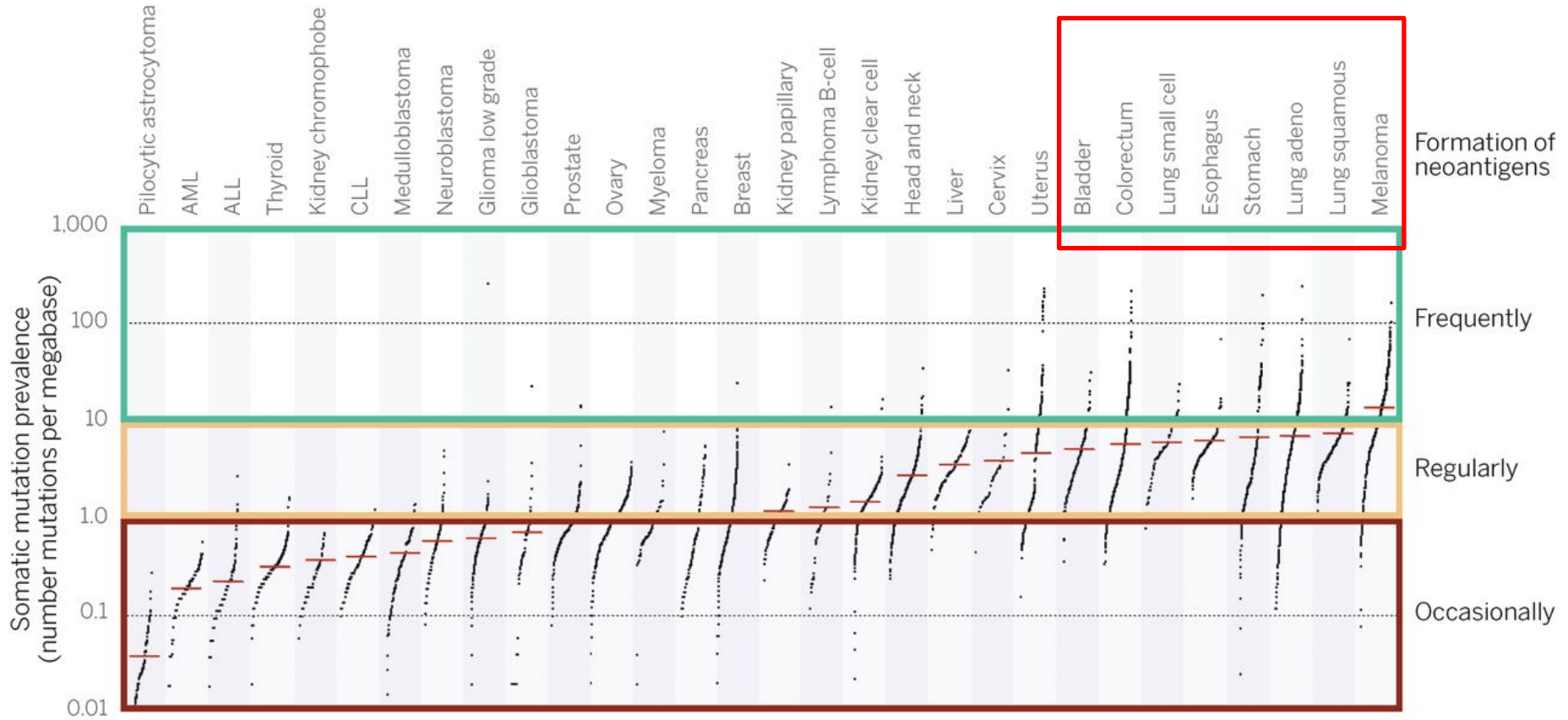




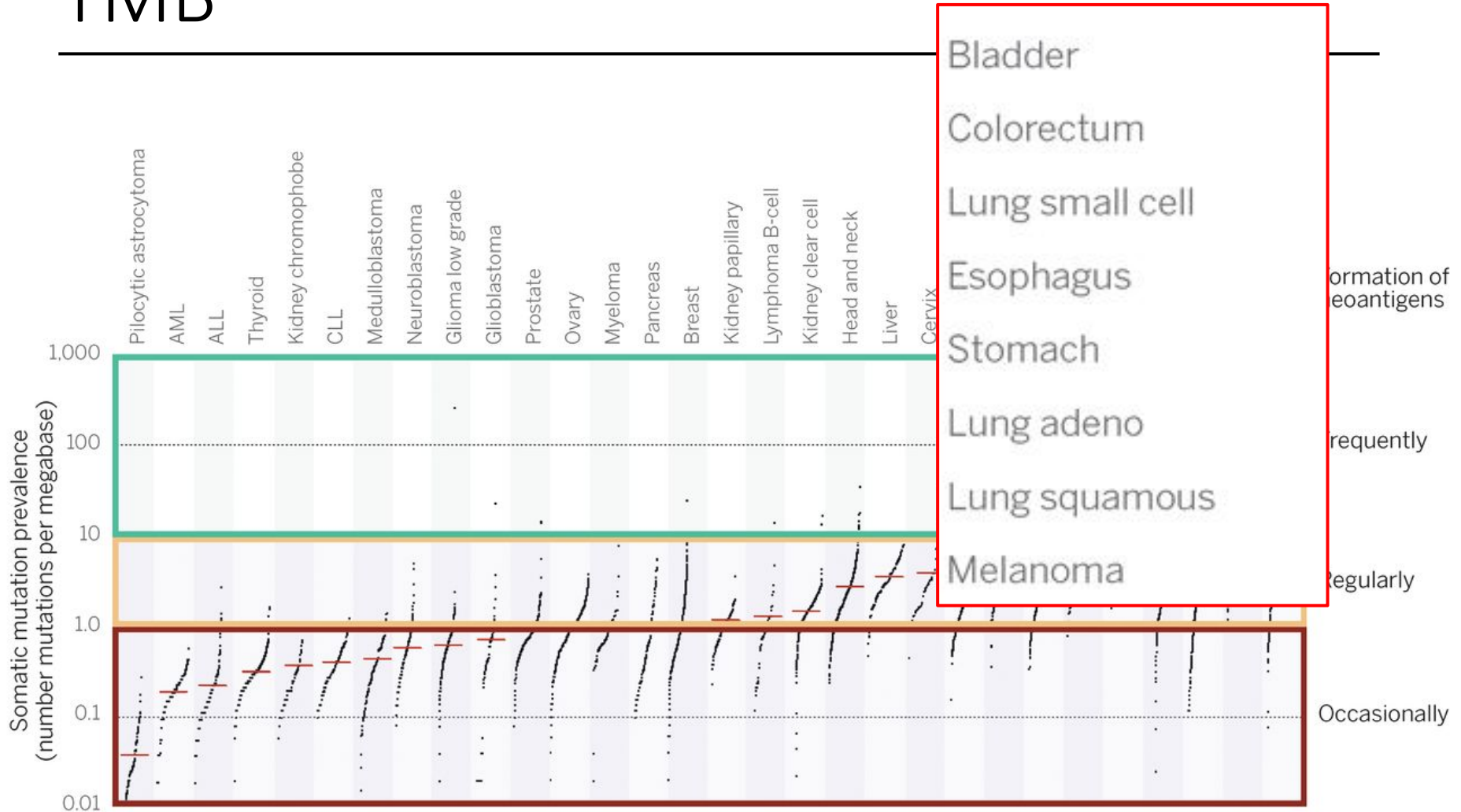
TMB



TMB



TMB



Biomarcadores predictivos

✓ PD-L1

✓ TMB

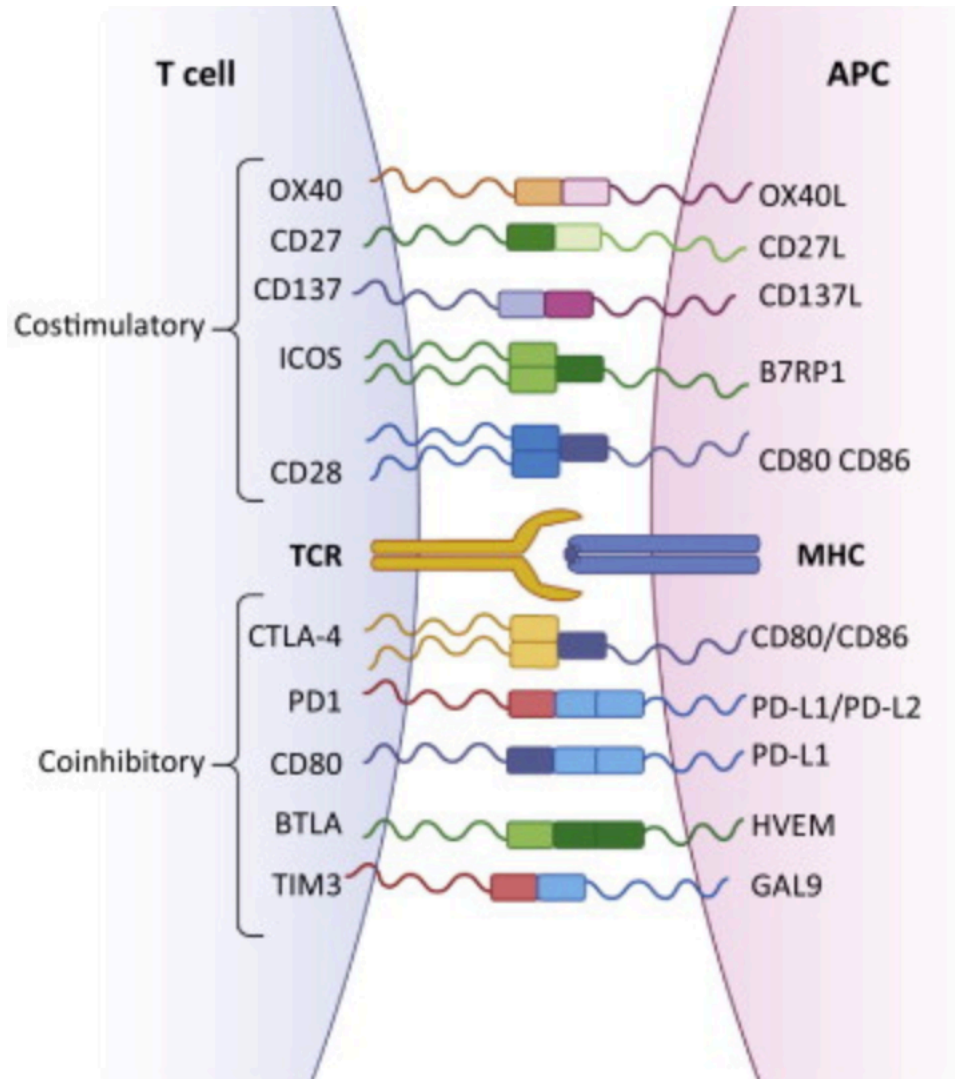
Biomarcadores preditivos

- ✓ PD-L1
- ✓ TMB
- ✓ Infiltração linfocitária
- ✓ Clonalidade dos receptores de células T
- ✓ Painel de neoantígenos
- ✓ Expressão gênica no microambiente tumoral
- ✓ Imunohistoquímica multiplex

Imunoterapia

- ✓ Mecanismos de evasão imune
- ✓ Mecanismos de ação dos inibidores de checkpoint
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- ✓ Biomarcadores preditivos
- ✓ Perspectivas

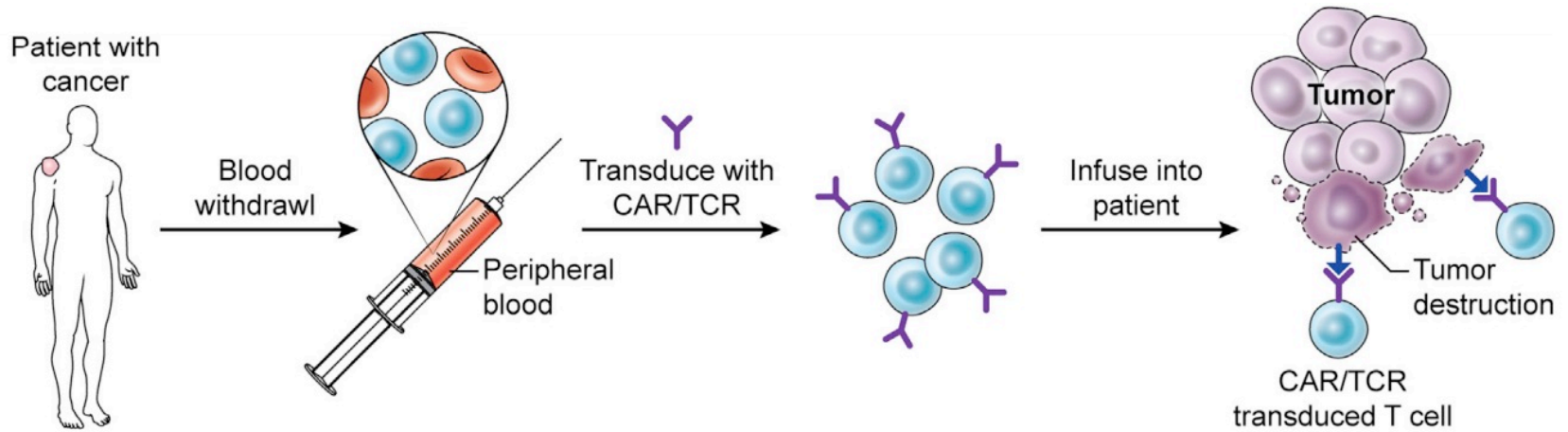
“Sinapse immune”



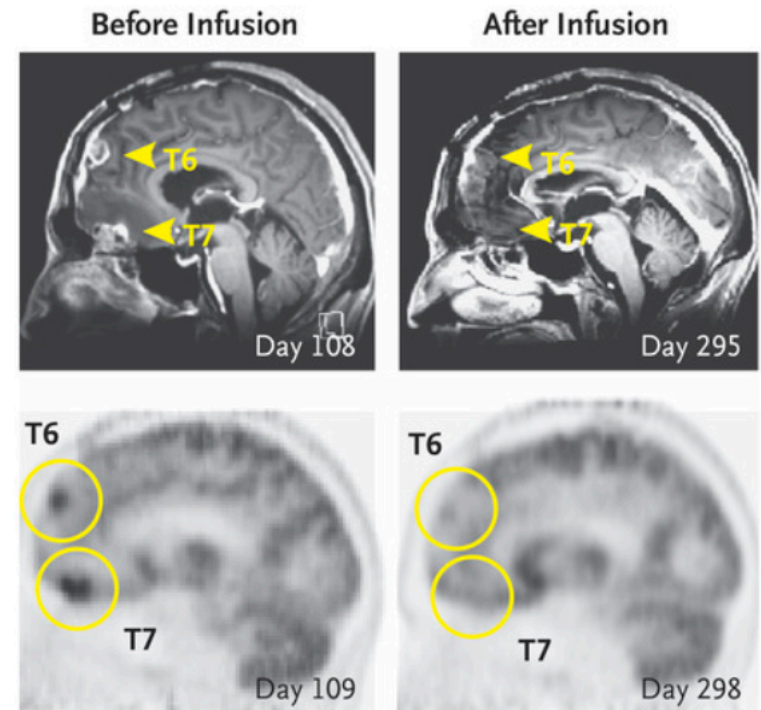
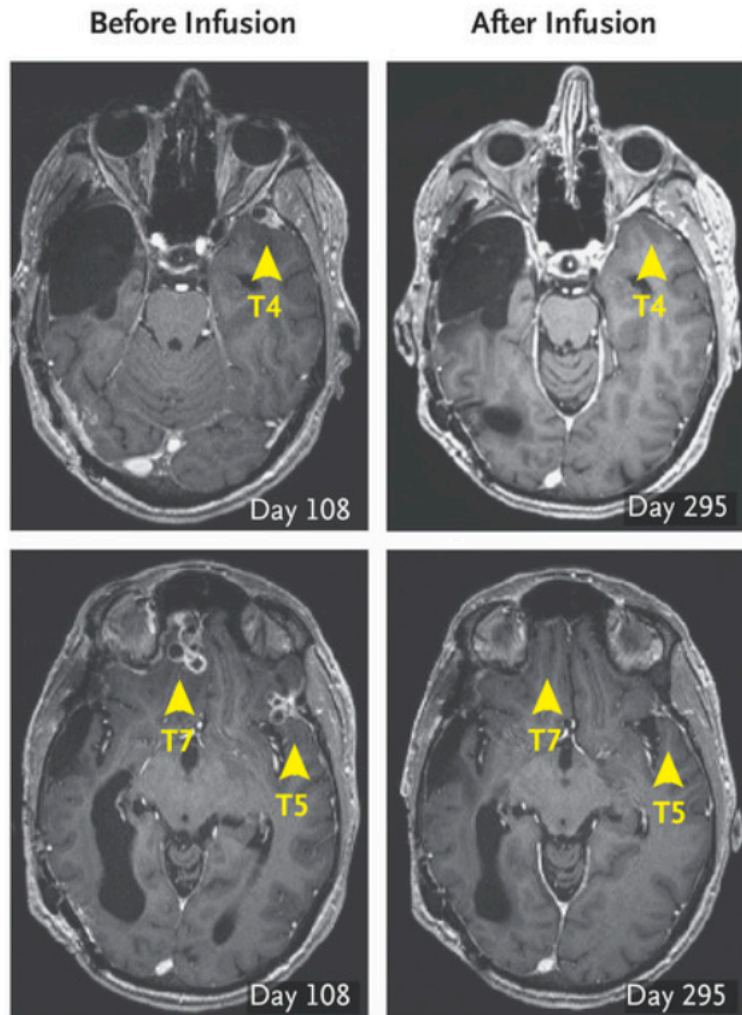
Perspectivas

- ✓ Adoptive T cell therapies
 - ✓ CAR-T cell
 - ✓ Tumor infiltrating lymphocytes (TILs)
 - ✓ TCR-T cell

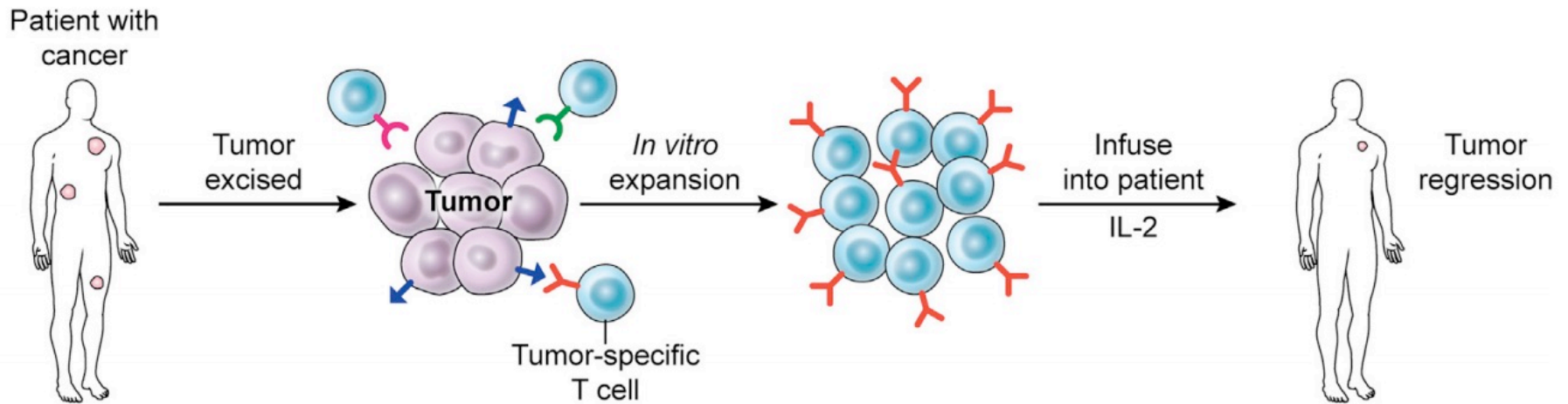
CAR T cell therapy




CAR T cell therapy



Tumor infiltrating lymphocytes (TILs)



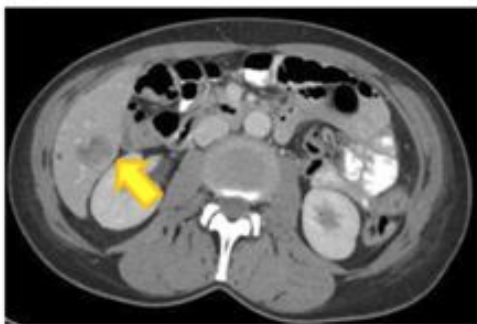
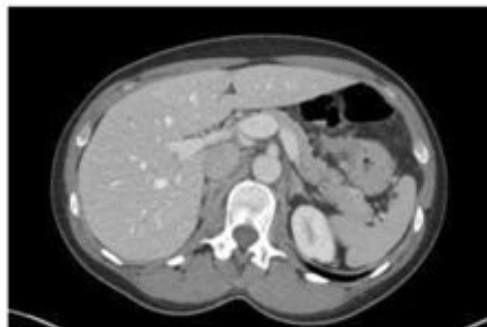
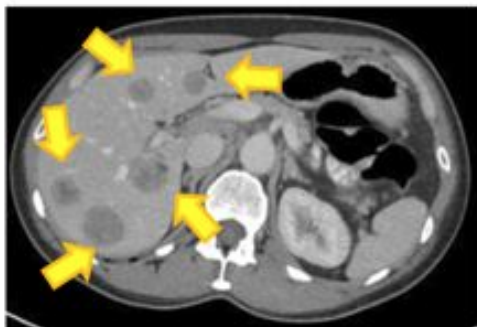
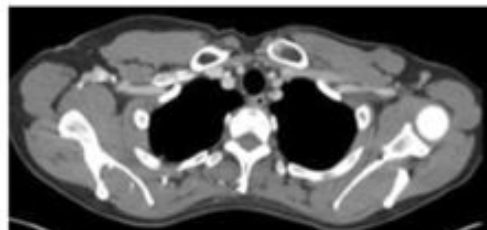
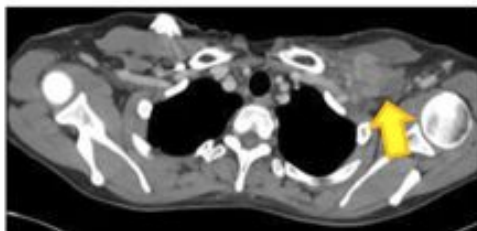
Immune recognition of somatic mutations leading to complete durable regression in metastatic breast cancer

Nikolaos Zacharakis¹, Harshini Chinnasamy¹, Mary Black¹, Hui Xu¹, Yong-Chen Lu ¹, Zhili Zheng¹, Anna Pasetto¹, Michelle Langan¹, Thomas Shelton¹, Todd Prickett¹, Jared Gartner¹, Li Jia¹, Katarzyna Trebska-McGowan², Robert P. Somerville¹, Paul F. Robbins¹, Steven A. Rosenberg^{1*}, Stephanie L. Goff¹ and Steven A. Feldman¹

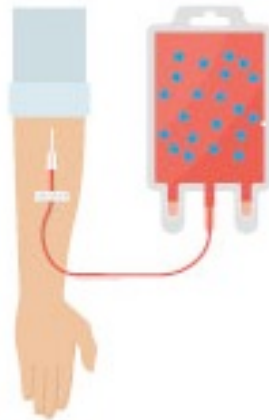
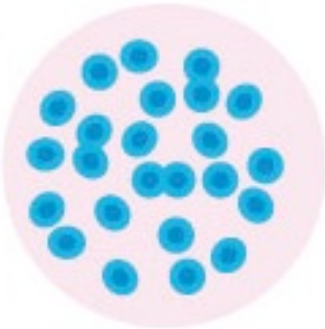
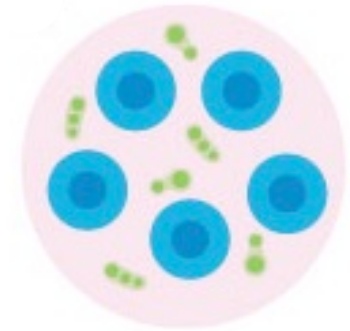
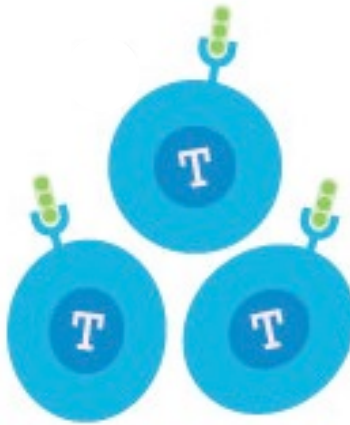
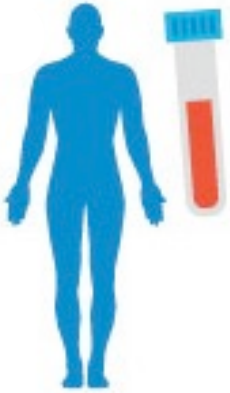
5

Pre-treatment

22 months
post-treatment



TCR T cell therapy





A photograph of the Golden Gate Bridge in San Francisco at sunset. The sky is a vibrant mix of orange, red, and purple, reflecting on the water. The bridge's towers and suspension cables are silhouetted against the bright sky. Three white circles are overlaid on the image, containing the text 'Cirurgia', 'Radiação', and 'Quimioterapia'.

Cirurgia

Radiação

Quimioterapia

A photograph of the Golden Gate Bridge in San Francisco at sunset. The sky is a mix of orange, red, and purple. The bridge's towers and cables are silhouetted against the bright sky. The water below is calm, reflecting the colors of the sky. In the foreground, there is a grassy hillside. Overlaid on the image are five white circles containing text: 'Cirurgia' (top left), 'Radiação' (top right), 'mAbs' (middle left), 'Quimioterapia' (bottom center), and 'TKI' (bottom right).

Cirurgia

Radiação

mAbs

Quimioterapia

TKI

A photograph of the Golden Gate Bridge in San Francisco at sunset. The sky is a vibrant mix of orange, red, and purple. The bridge's towers and suspension cables are silhouetted against the bright sky. The water below reflects the colors of the sunset. Three white circles are overlaid on the image, each containing a different type of medical treatment name in Portuguese. The circle on the left is positioned over the lower part of the bridge, the one on the right is over the upper part, and the one at the bottom is over the foreground.

Cirurgia

Radiação

Terapia
sistêmica

A photograph of the Golden Gate Bridge in San Francisco at sunset. The sky is a mix of orange, red, and purple. The bridge's towers and suspension cables are silhouetted against the bright sky. The water below reflects the colors of the sunset. Four white circles are overlaid on the image, each containing a medical treatment name in Portuguese. The circles are arranged in a diamond pattern: top-left, top-right, bottom-left, and bottom-right.

Cirurgia

Radiação

Terapia
sistêmica

Imunoterapia

AAndrade4@mdanderson.org
