

Carcinoma Espino Celular de Pele

Uma nova Era

Rafael Aron Schmerling



A Beneficência
Portuguesa
de São Paulo

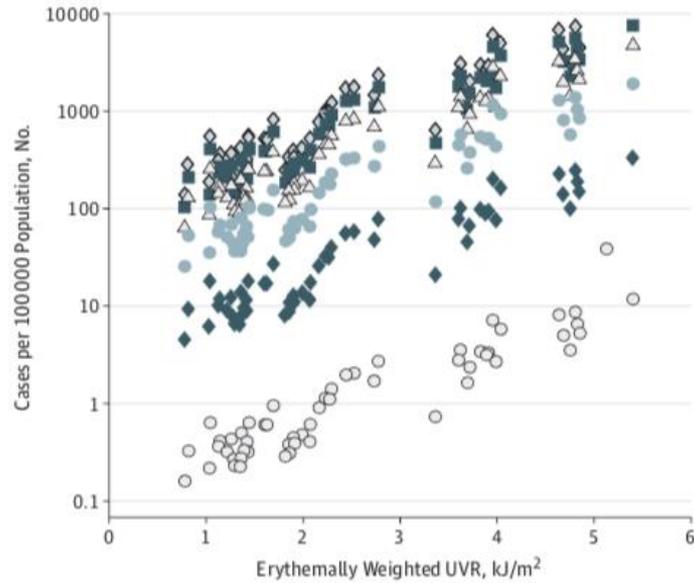
Potenciais Conflitos de Interesse

Bayer	Consultoria, honorários
Bristol-Myers Squibb	Consultoria, honorários, patrocínio
Merck Serono	Consultoria, honorários
Merck Sharp & Dome	Consultoria, honorários, pesquisa, patrocínio
Pfizer	Consultoria, honorários
Novartis	Consultoria, honorários, pesquisa
Roche	Consultoria, honorários, pesquisa, patrocínio
Sanofi Genzyme	Consultoria, honorário

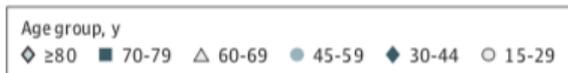
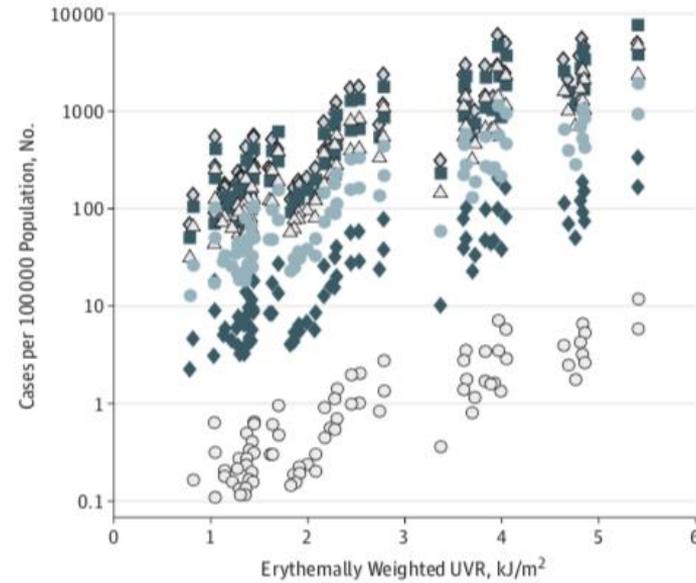
Etiologia / Fatores de Risco – Radiação UV

Estimativa de incidência de CEC de pele conforme a exposição solar ambiental

Homens



Mulheres



Etiologia / Fatores de Risco - Imunossupressão

20x mais frequente em imunossupressão para Tx renal
com ciclosporina – 2,8x adicional

90% dos tumores de pele; risco anual de 3% (tx cardíaco)

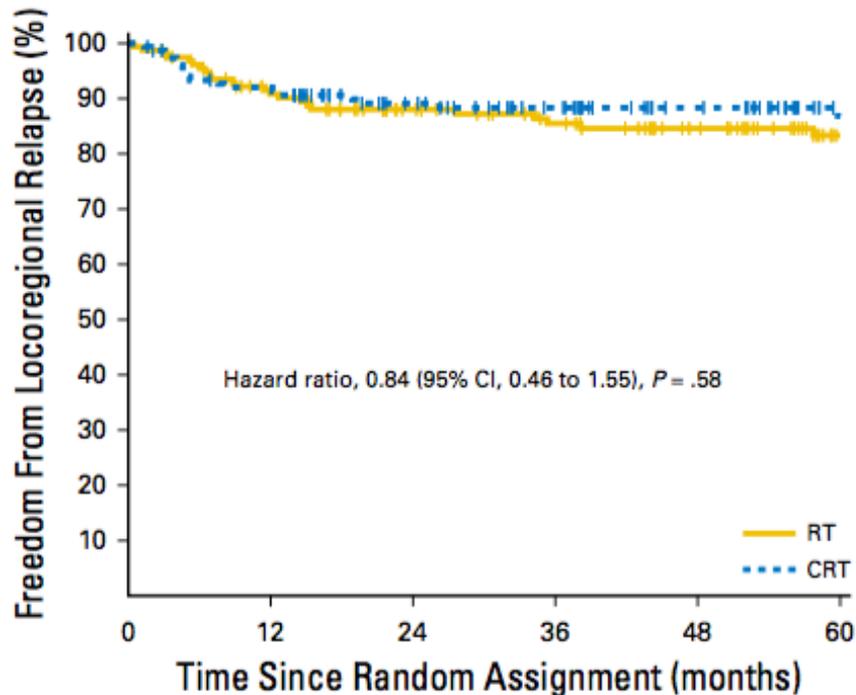
2x mais frequente em pacientes com HIV

Jensen et al. J Am Acad Dermatol. 1999 Feb;40(2 Pt 1):177-86
Lampros et al. J Heart Lung Transplant. 1998 Jun;17(6):586-91.
Silverberg et al. J Natl Cancer Inst. 2013 Mar 6;105(5):350-60



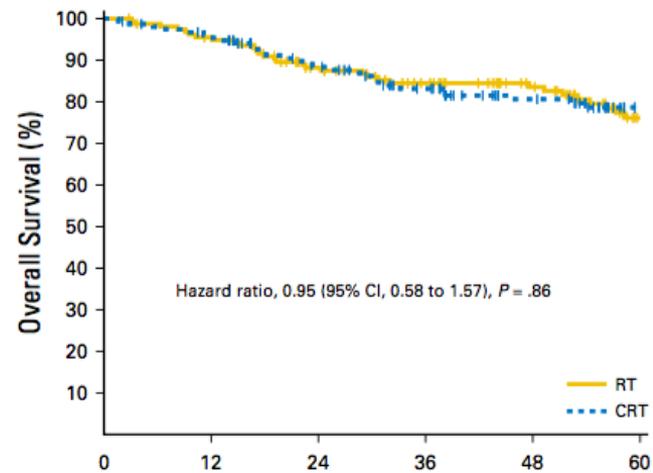
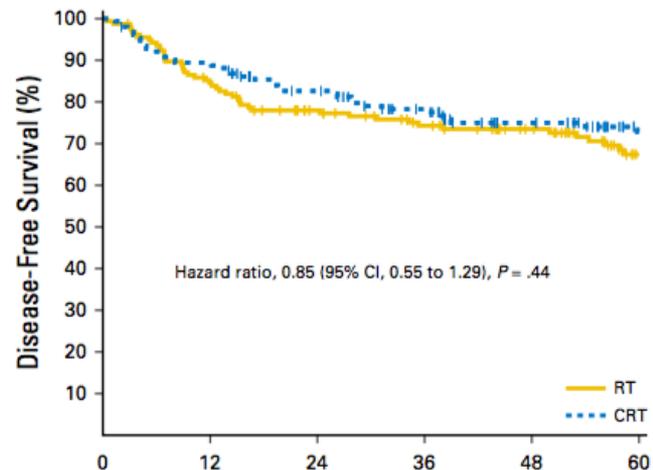
Cortesia Dr. Buzaid

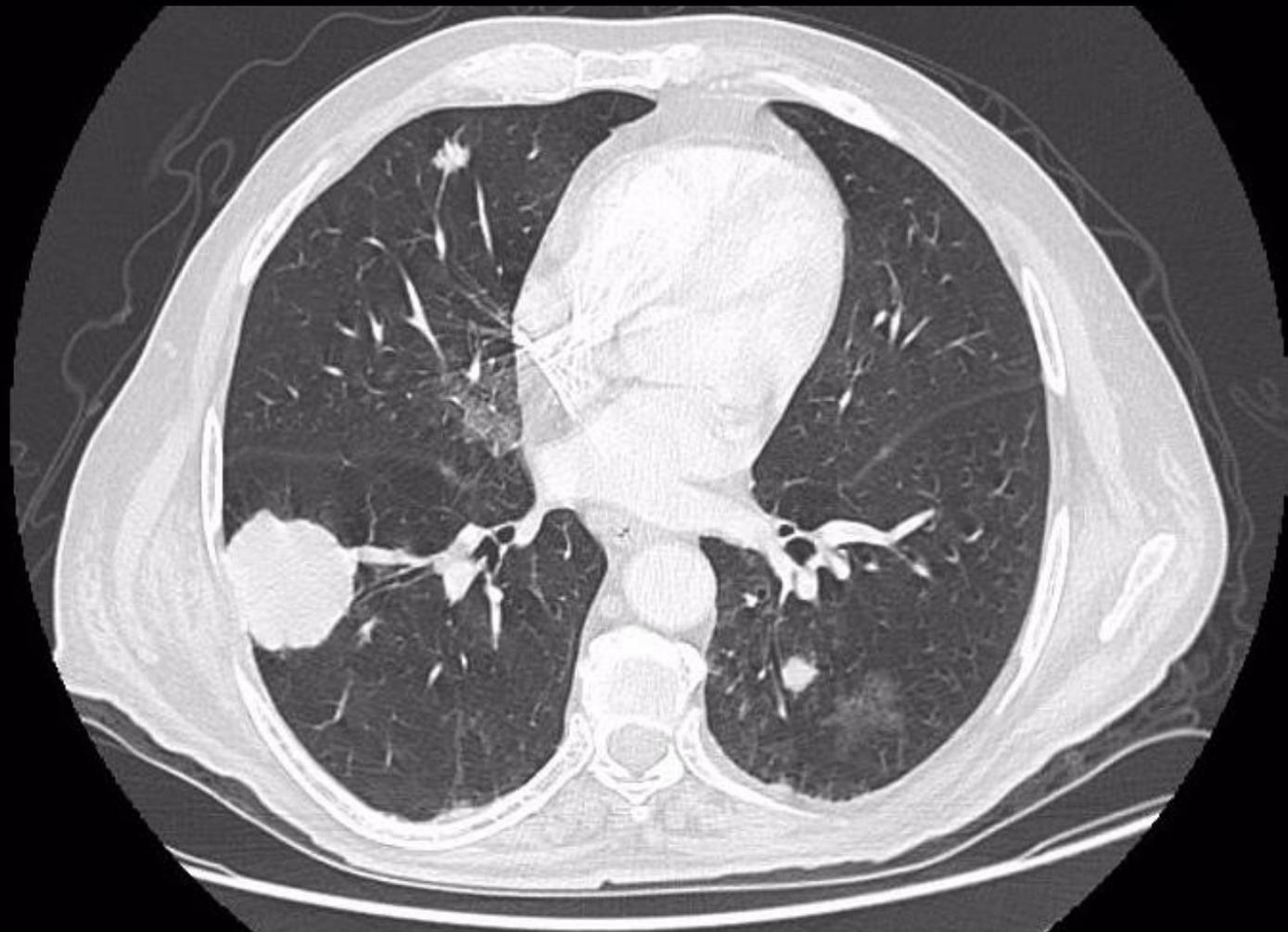
Trattamento adjuvante - TROG



No. at risk (No. of events):

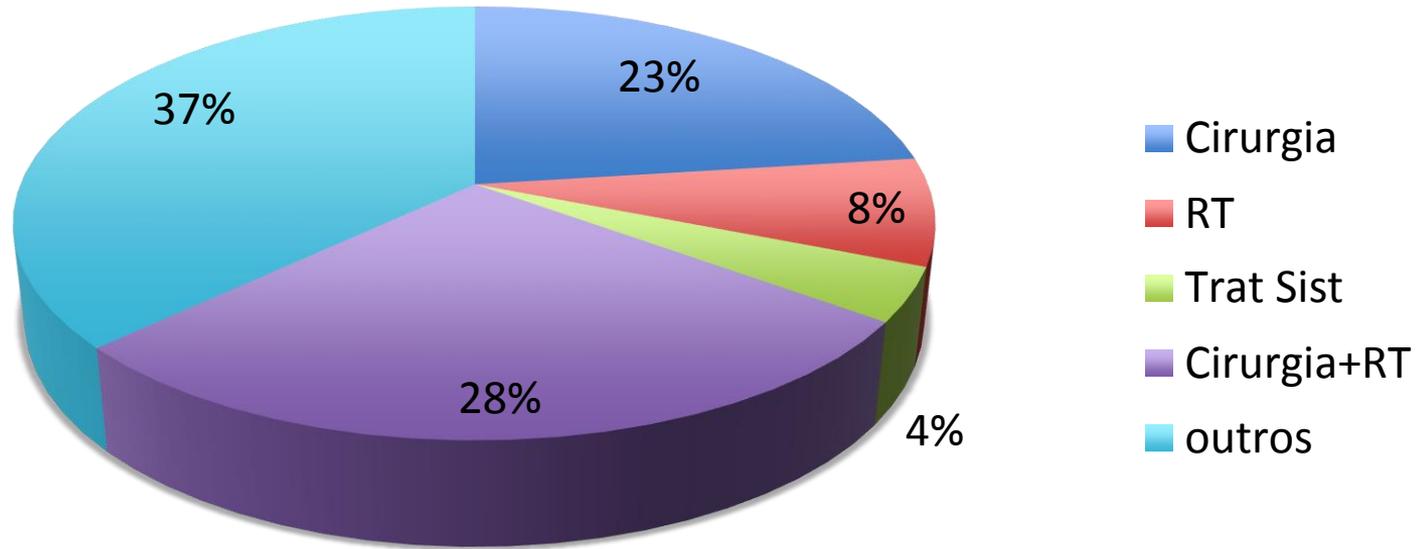
RT	157 (0)	133 (14)	112 (18)	99 (21)	83 (22)	57 (23)
CRT	153 (0)	136 (12)	115 (16)	101 (17)	83 (17)	59 (18)





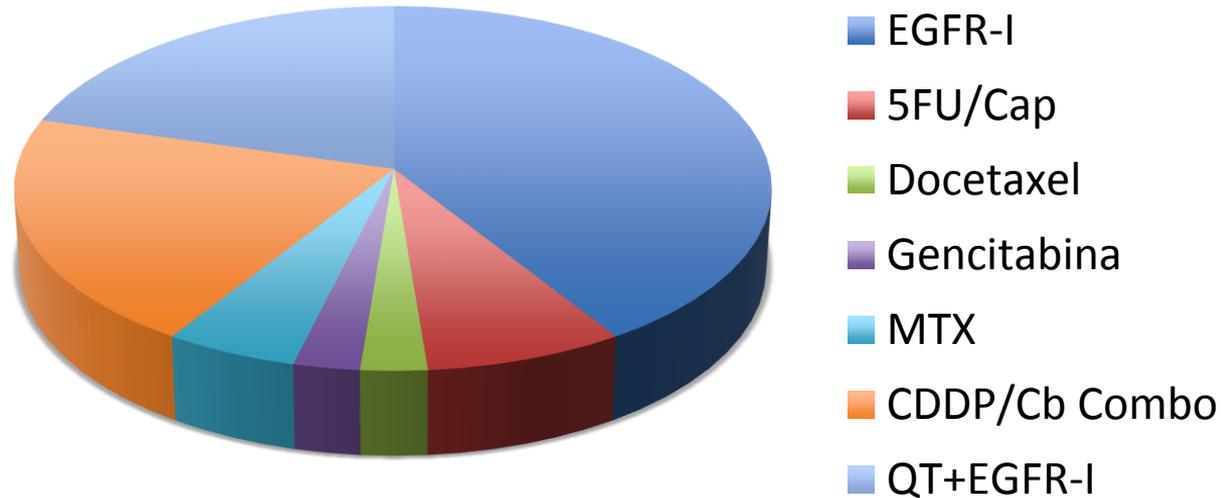
Análise retrospectiva do padrão de tratamento de CEC avançado - DECOG

N: 114

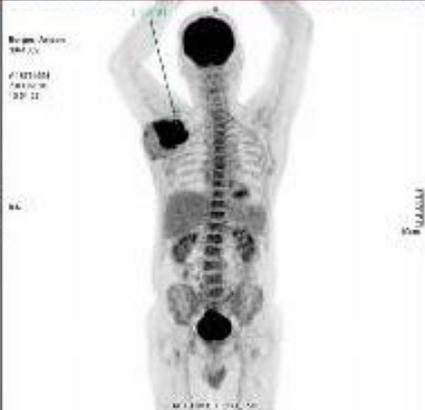
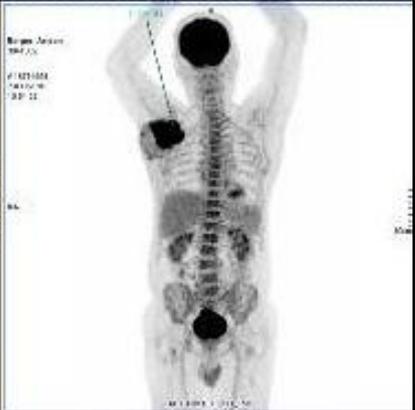
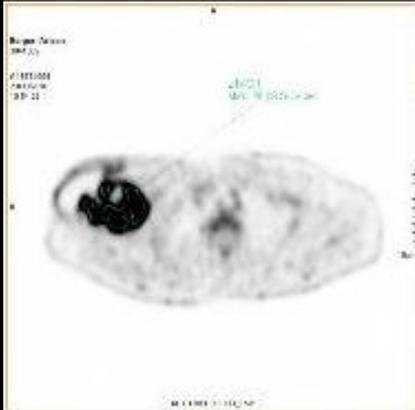
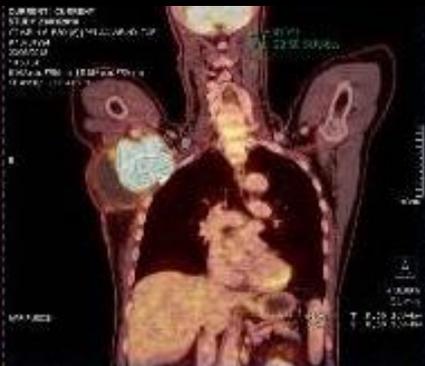
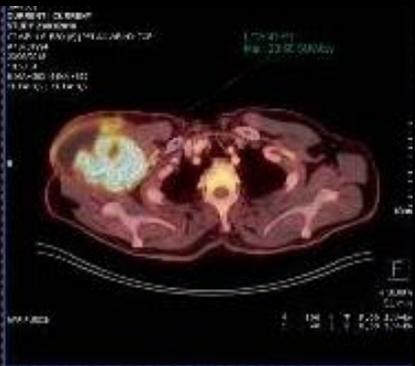


Análise retrospectiva do padrão de tratamento de CEC avançado - DECOG

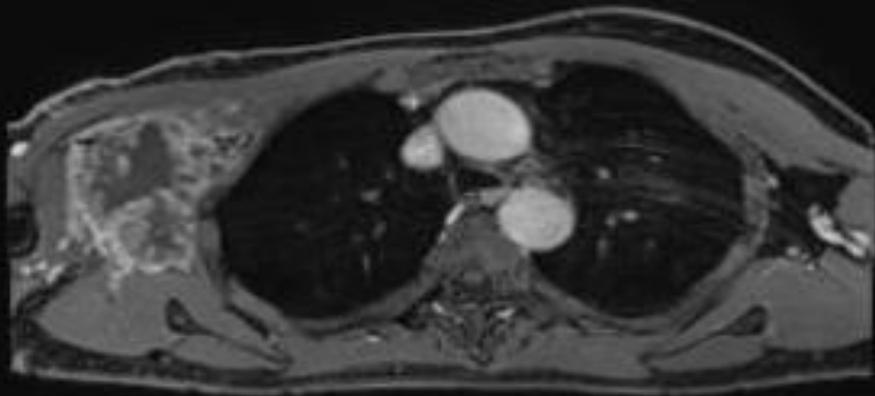
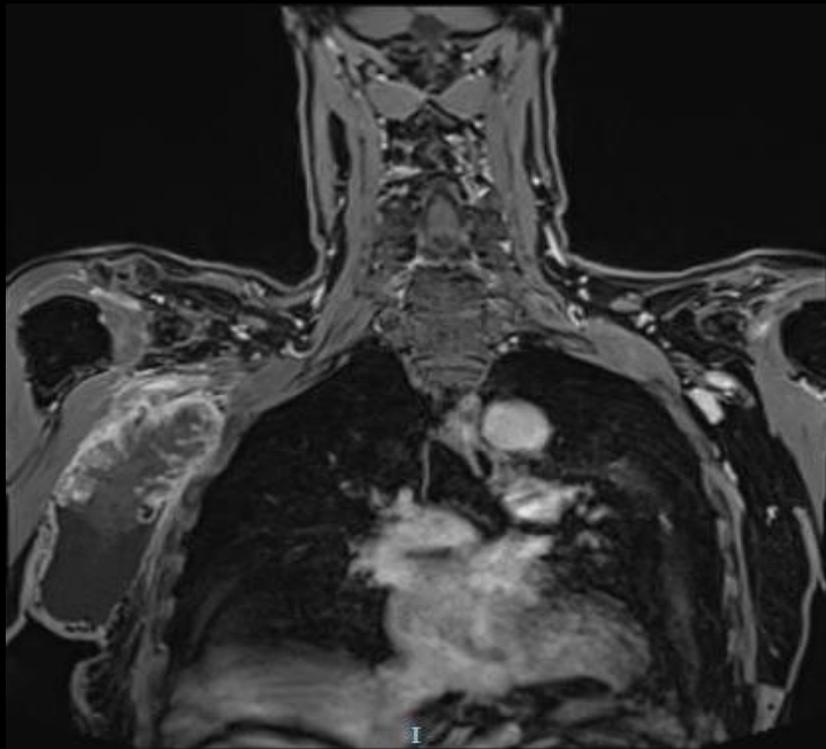
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Mar/ 2018



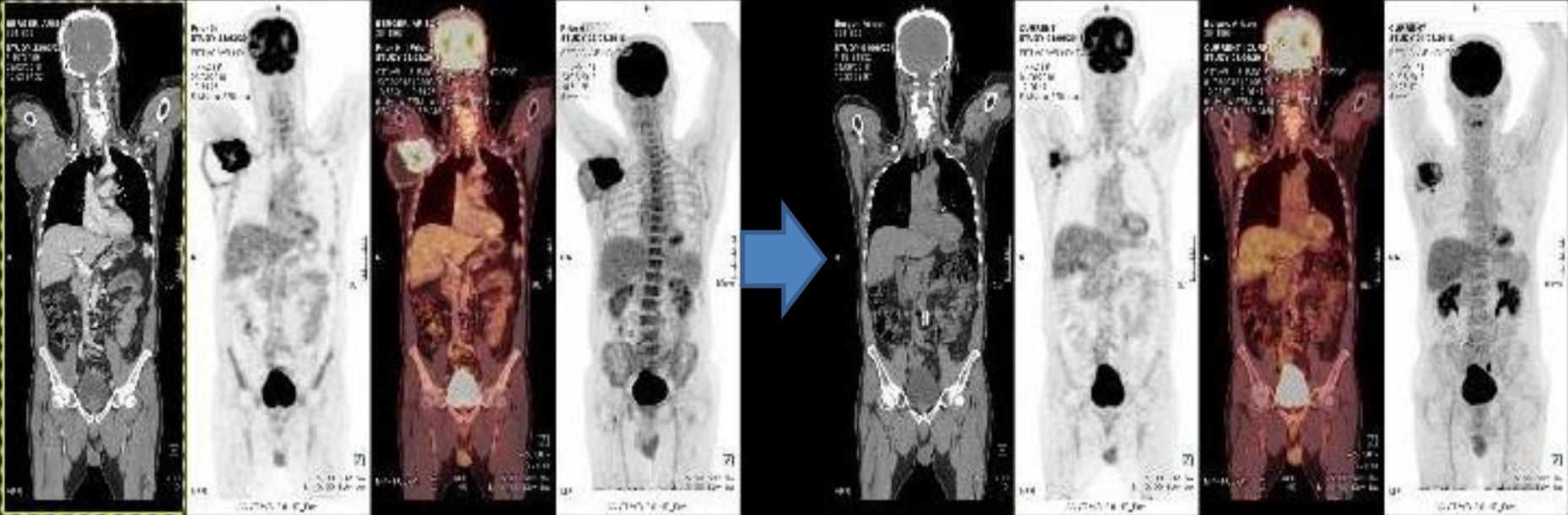
Mar/ 2018



Mar/ 2018

Jun/ 2018

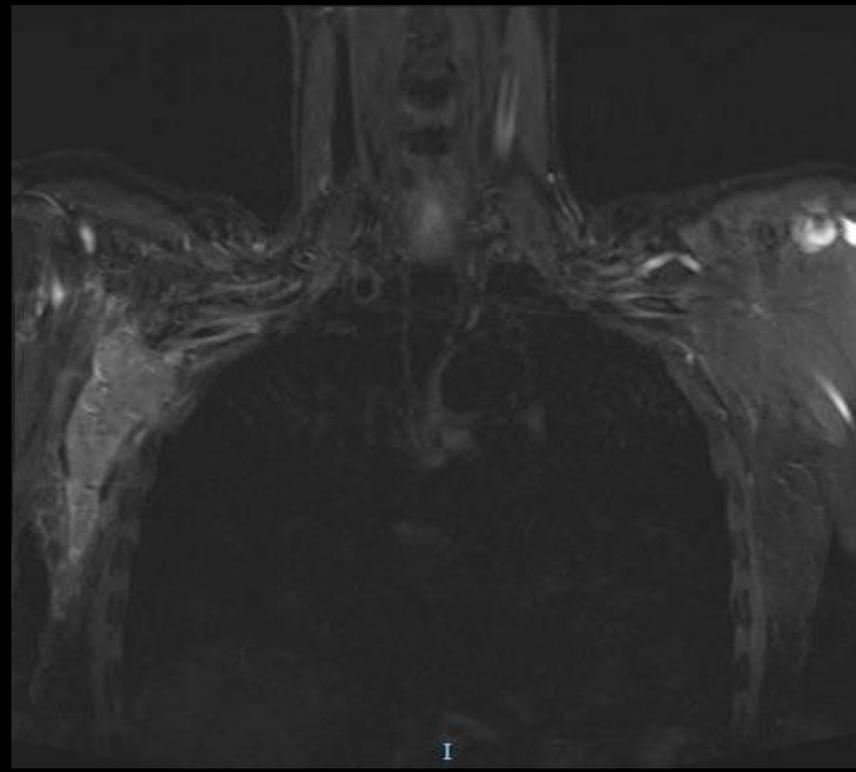
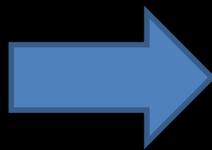
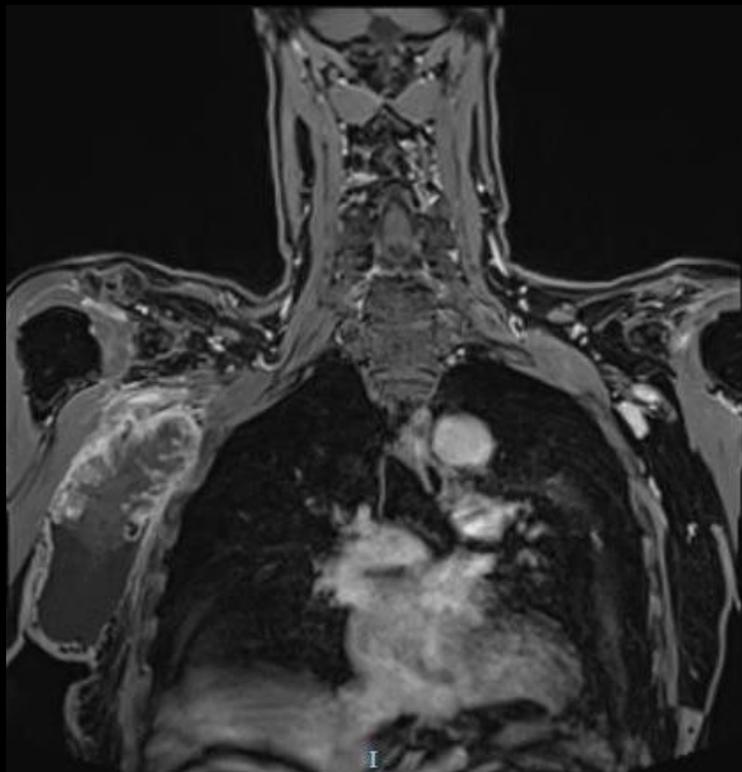
Carboplatina / Paclitaxel x4



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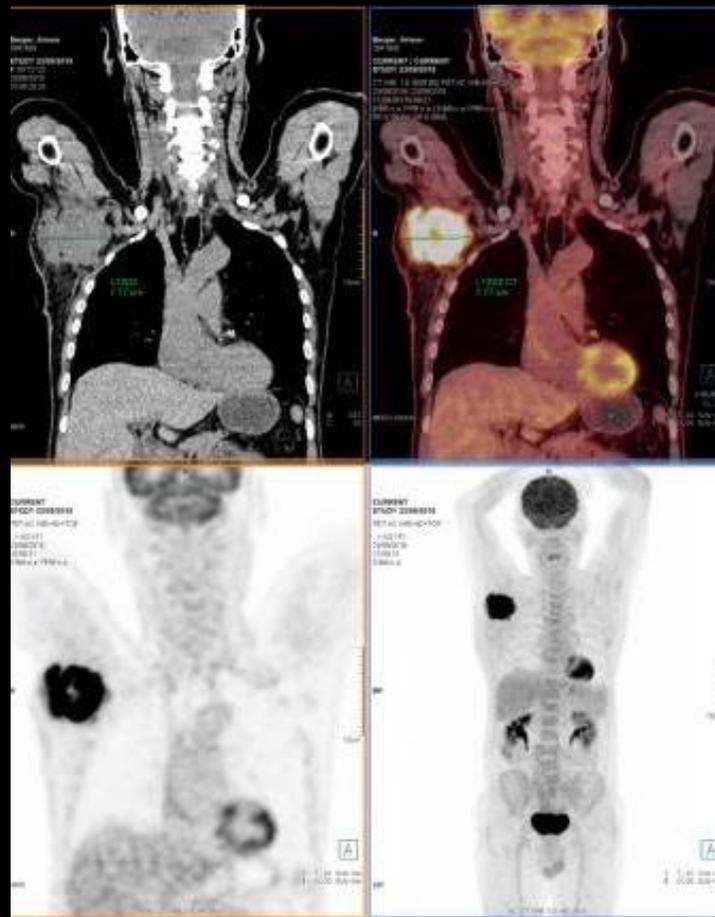
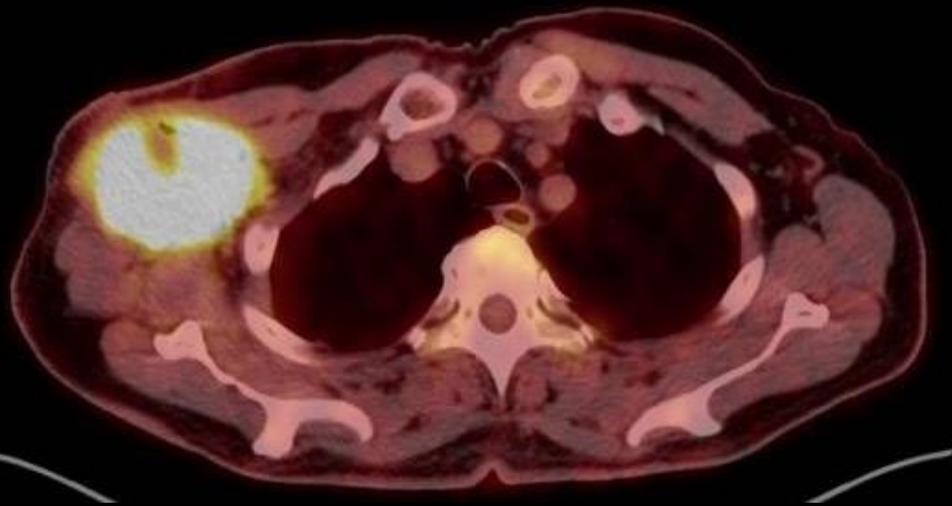
Jun/ 2018

Carboplatina / Paclitaxel x4

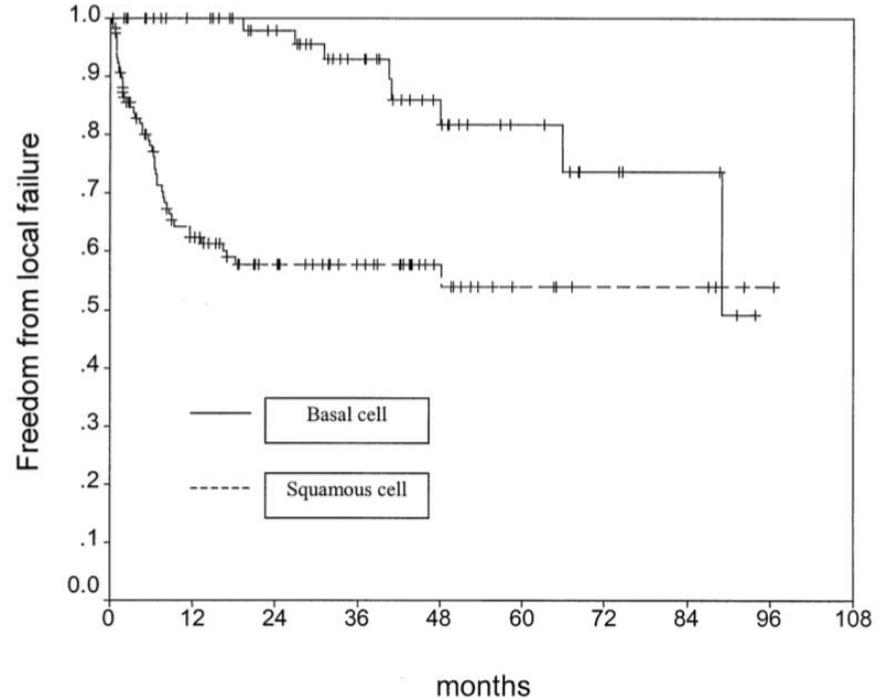
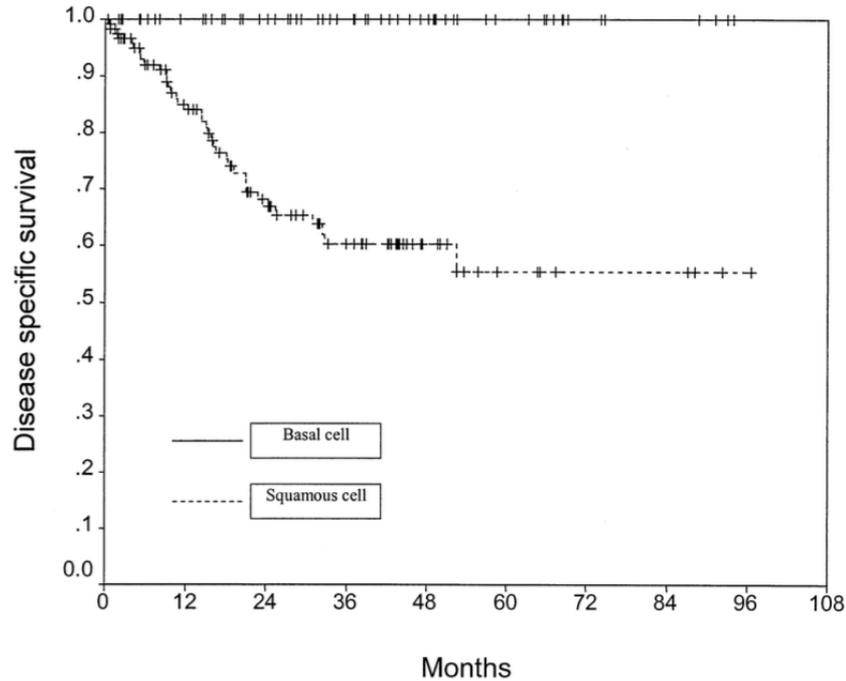


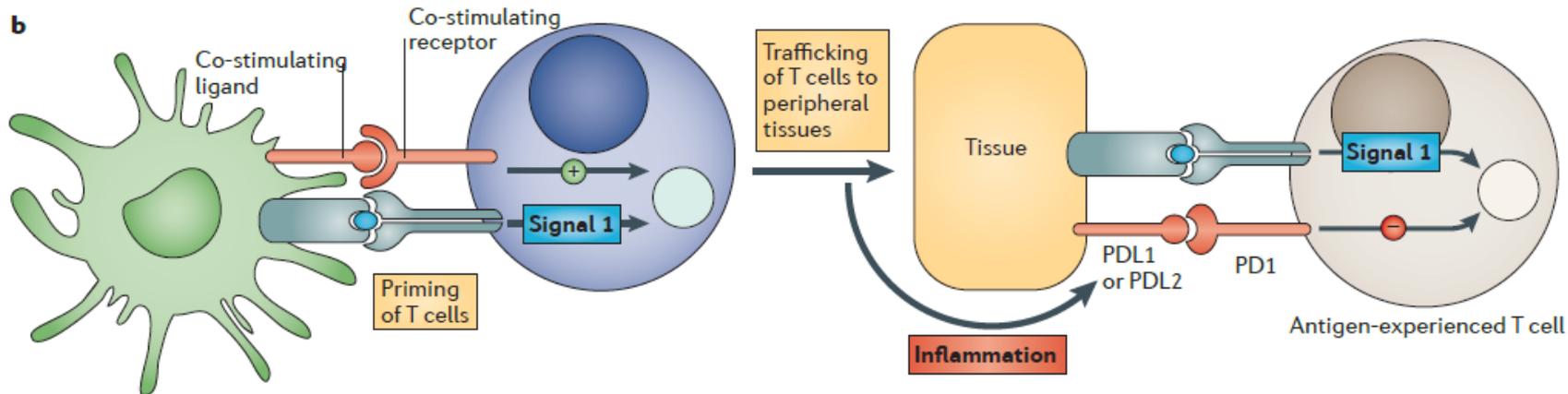
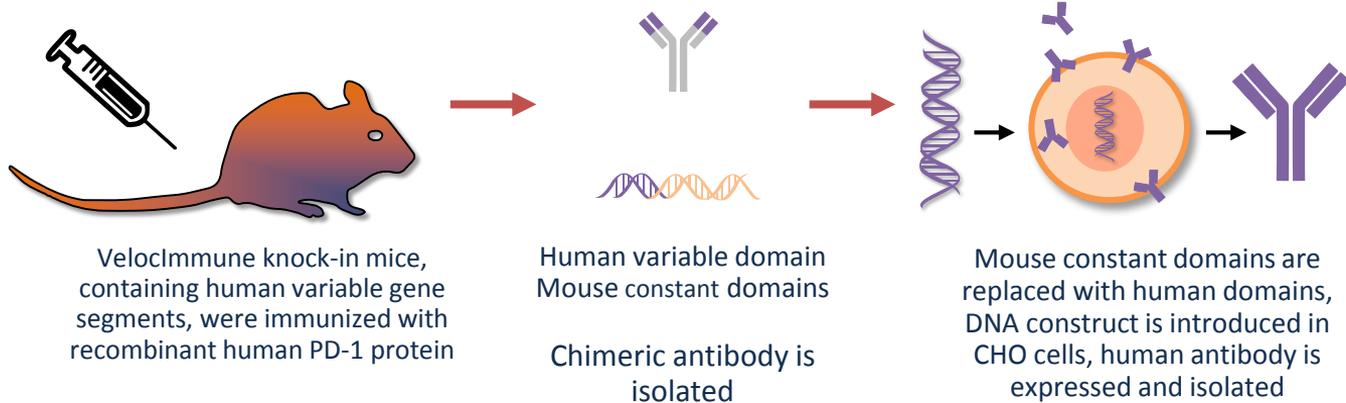
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TTP: 5meses

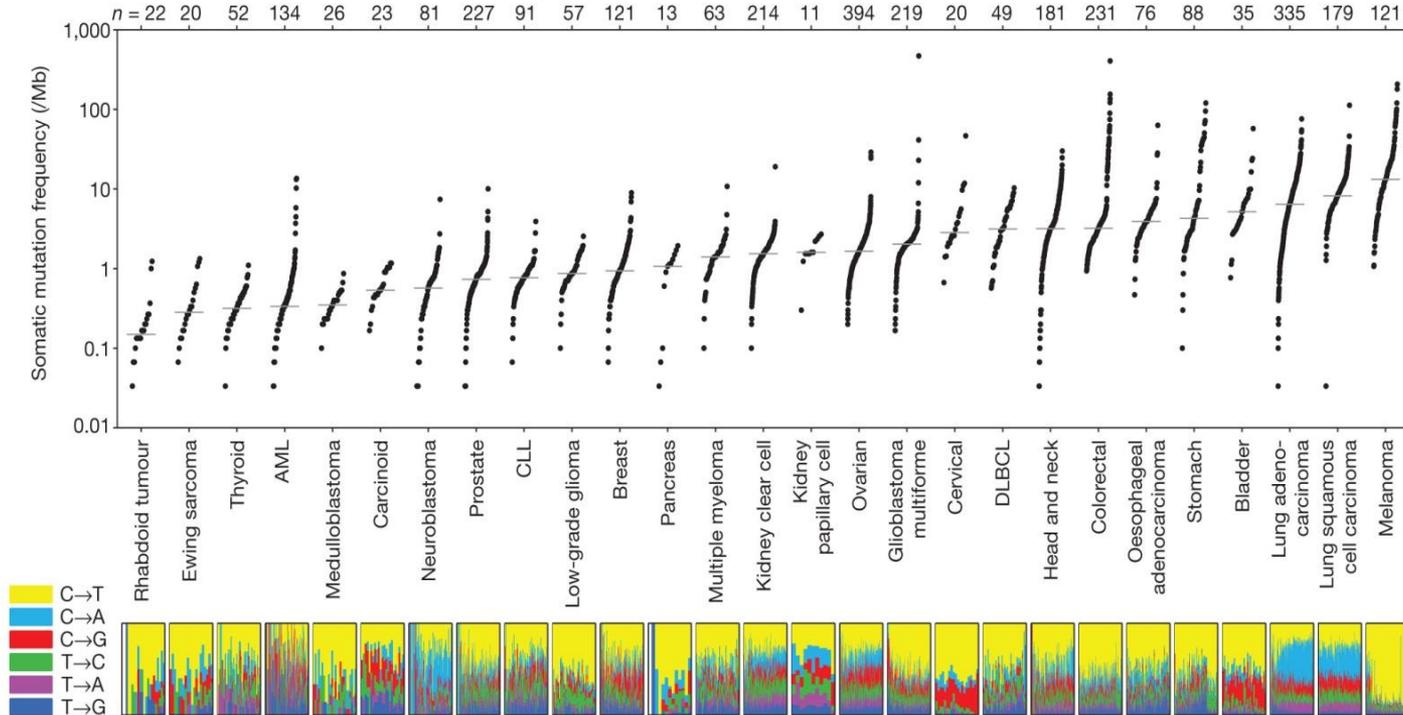


Radioterapia – em CEC/CBC localmente avançados



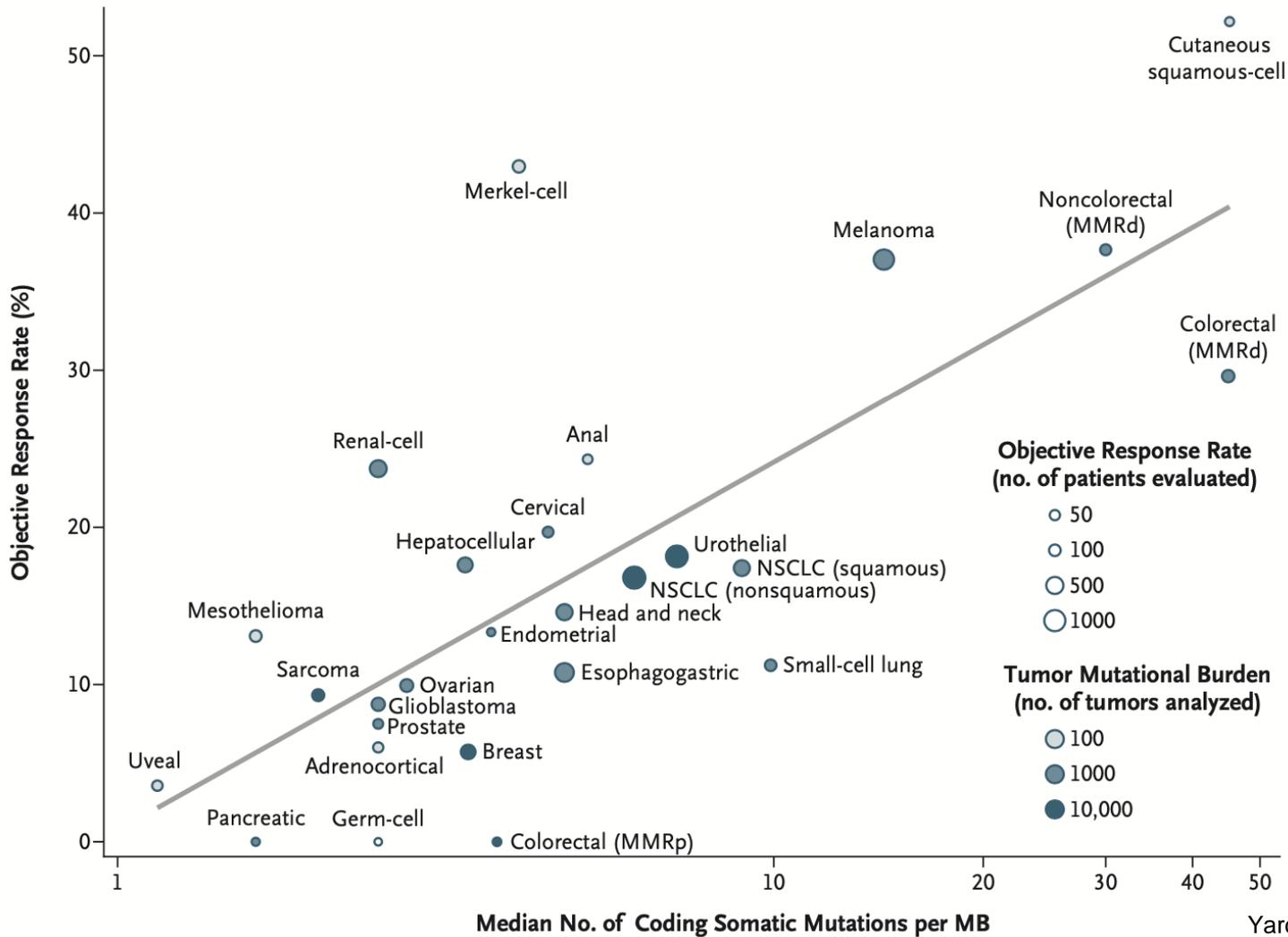


Mutações Somáticas, conforme o Tumor



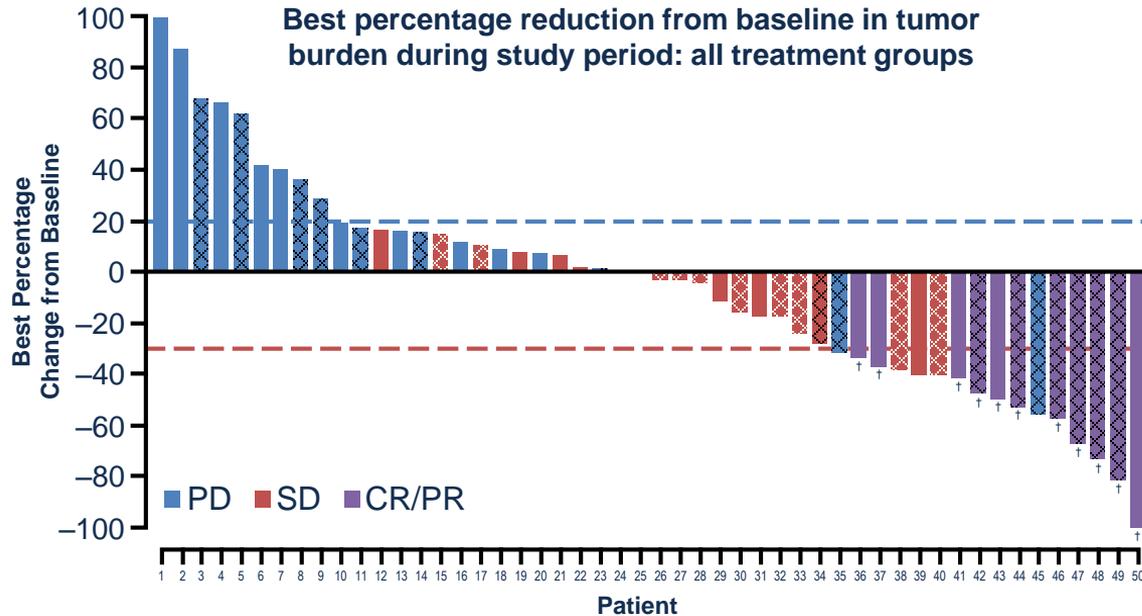
Mutational Burden:

Mutation frequencies vary more than 1000-fold between lowest and highest mutation rates across cancer and also within several tumor types.



Estudo de Fase 1 com Cemiplimabe :

Taxa de Resposta Objetiva de 18.3% em todos os tumores



ORR (CR + PR) = 18.3% (11 [1 CR + 10 PR] / 60 patients)
DCR (ORR + SD) = 51.7% (31 [1 CR + 10 PR + 20 SD] / 60 patients)

†Patients with confirmed CR or PR. Unhatched boxes represent patients who did not receive hfRT. Hatched boxes represent patients who received hfRT

Resposta completa com cemiplimab em um paciente com CEC de pele metastático (Phase I Open-Label Study)

Homem, 52 anos, diagnosticado com CEC de pele IV

Submetido a 10 cirurgias de Mohs
(9 por recorrência)

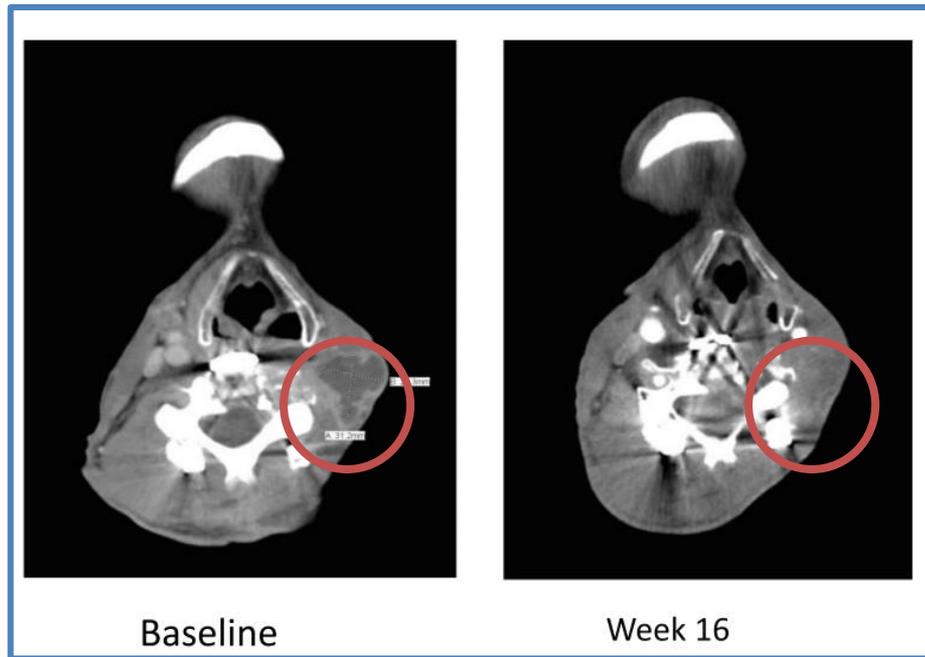
Tratado com ET e QT

Recebeu cemiplimab 1 mg/kg IV cemiplimab q2w for
48 weeks

Resposta completa na 40ª semana

Toxicidade

Rash	G1
Sintomas gripais,	G1
Calafrios	G2
Linfopenia	G2

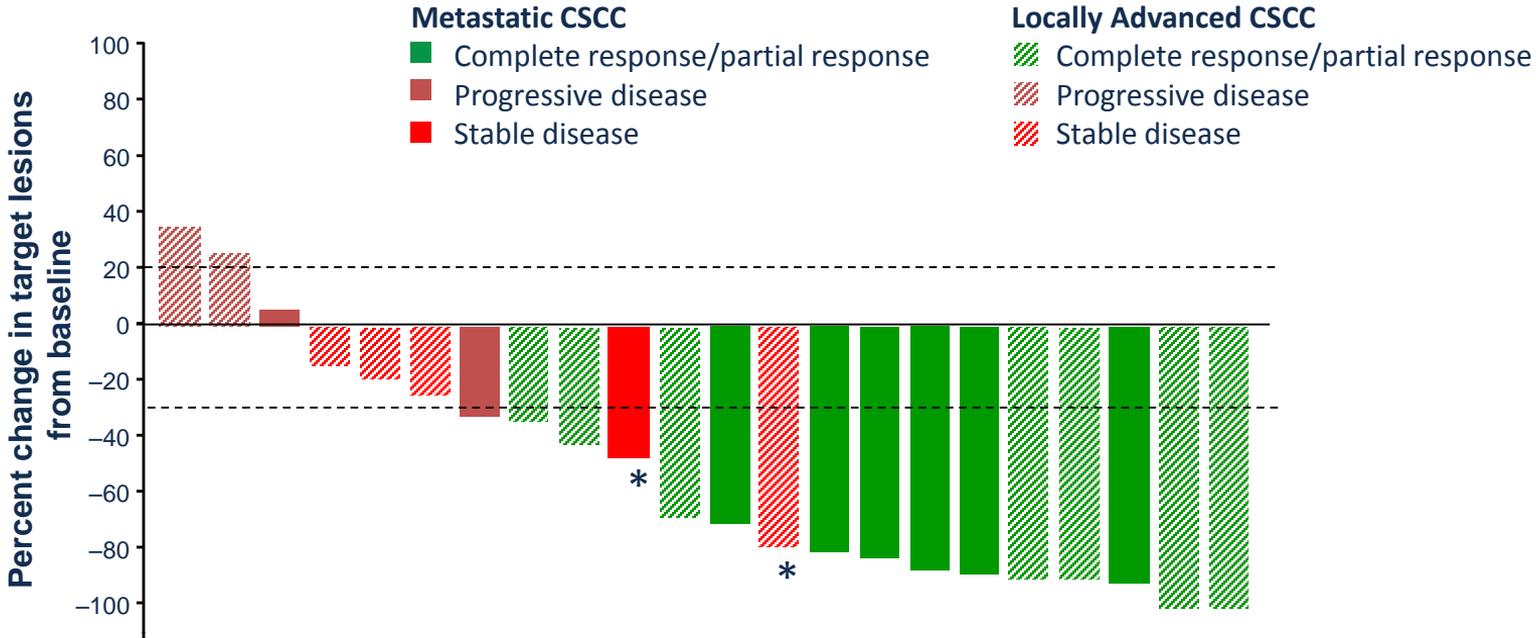


Neck mass in CSCC patient at baseline (3.1 cm) and at week 16 (1.6 cm).

CSCC, cutaneous squamous cell carcinoma.

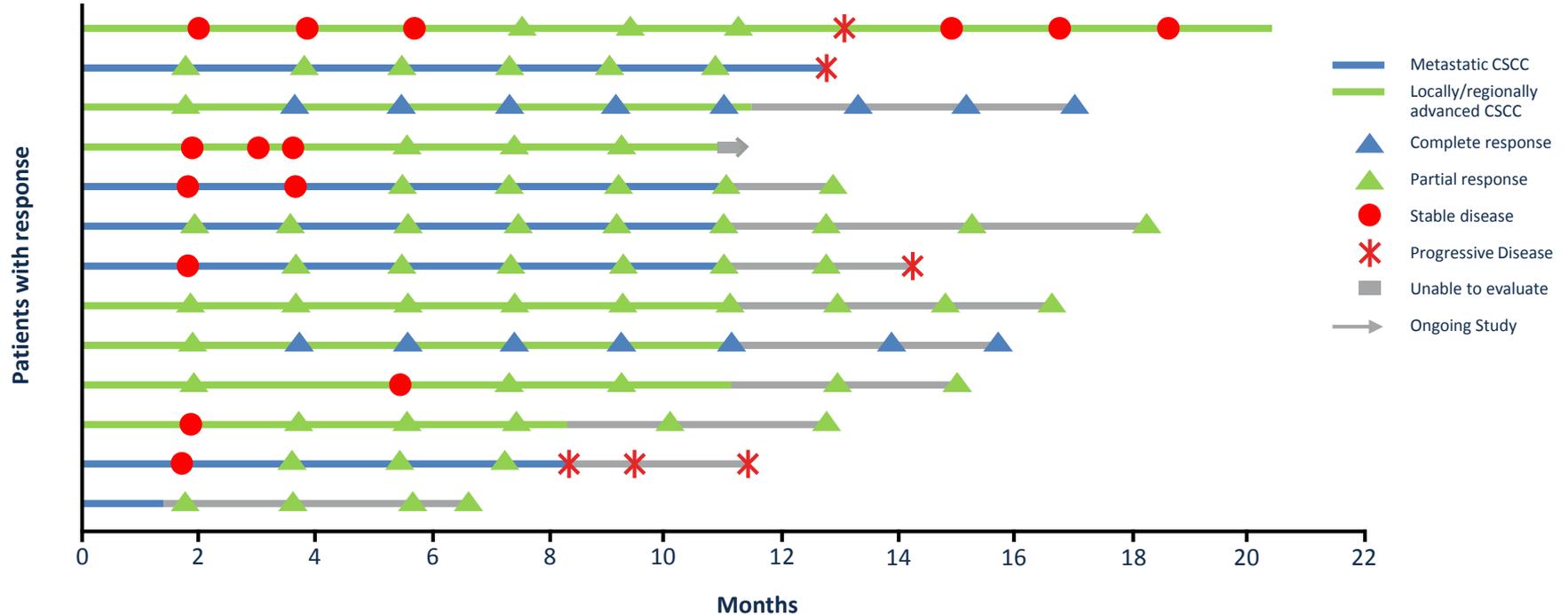
Falchook GS, et al. J Immunother Cancer. 2016;4,70.

Proporção de mudança de tamanho do tumor com Cemiplimab em pacientes com CEC de pele avançado, conforme a avaliação do investigador (CSCC Expansion Cohorts)



Bars show the best percentage change in the sum of target lesion diameters from baseline for 22 patients from both CSCC expansion cohorts who underwent radiologic evaluation per investigator assessment. Lesion measurements after progression were excluded. Patients may have progressed after achieving best overall response. The horizontal dashed lines indicate criteria for partial response (≥30% decrease in the sum of target lesion diameters) and progressive disease (≥20% increase in the target lesion diameters), respectively. Two patients (with asterisks under bar) had tumour lesion reduction >30% from baseline; however, best overall response was stable disease as the tumor lesion reduction had not been confirmed. The following four patients do not appear in the figure (but are included in the ORR analysis [slide 23], per intention-to-treat): one patient with locally advanced CSCC who had missing target lesion measurements and three patients (one with metastatic, and two with locally advanced, CSCC) with no evaluable post-treatment tumor assessment.

Tempo até resposta e duração de resposta em 13 pacientes com CEC de pele, que tiveram resposta a Cemiplimabe

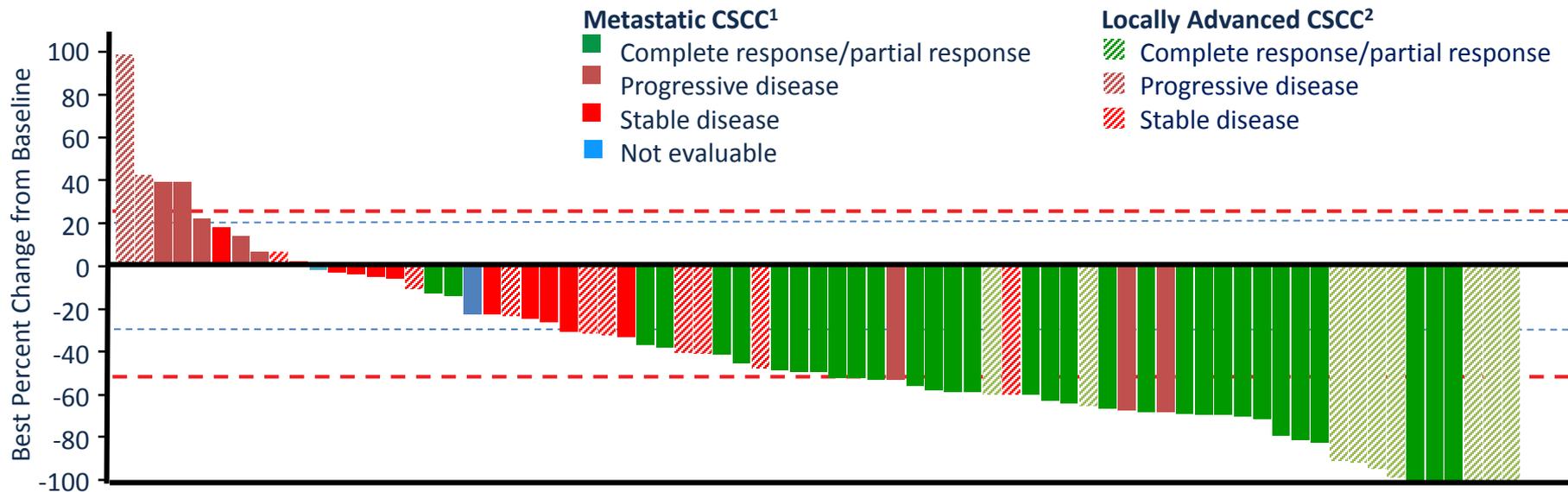


Plot shows time to response and duration of response in the 13 patients with complete or partial response at the time of data cut-off. Each horizontal bar represents one patient.

Proporção de mudança de tamanho do tumor com Cemiplimab em pacientes com CEC de pele avançado, conforma a avaliação do investigador (CSCC Expansion Cohorts)

	Metastatic CSCC (N = 10)	Locally/regionally advanced CSCC (N = 16)	Total (N = 26)
Best overall response, n (%)			
Complete response	0	2 (12.5)	2 (7.7)
Partial response	6 (60.0)	5 (31.3)	11 (42.3)
Stable disease	1 (10.0)	4 (25.0)	5 (19.2)
Progressive disease	2 (20.0)	4 (25.0)	6 (23.1)
Not evaluable [‡]	1 (10.0)	1 (6.3)	2 (7.7)
Overall response rate, % (95% CI)	60.0 (26.2–87.8)	43.8 (19.8–70.1)	50.0 (29.9–70.1)
Durable disease control rate, % (95% CI)[§]	60.0 (26.2–87.8)	56.3 (29.9–80.2)	57.7 (36.9–76.6)
Median observed time to response, months (range) [¶]	2.1 (1.7–5.5)	1.9 (1.7–7.5)	1.9 (1.7–7.5)

EMPOWER 1: Proporção de mudança de tamanho do tumor em pacientes com CEC de pele avançado, conforme a avaliação do independente



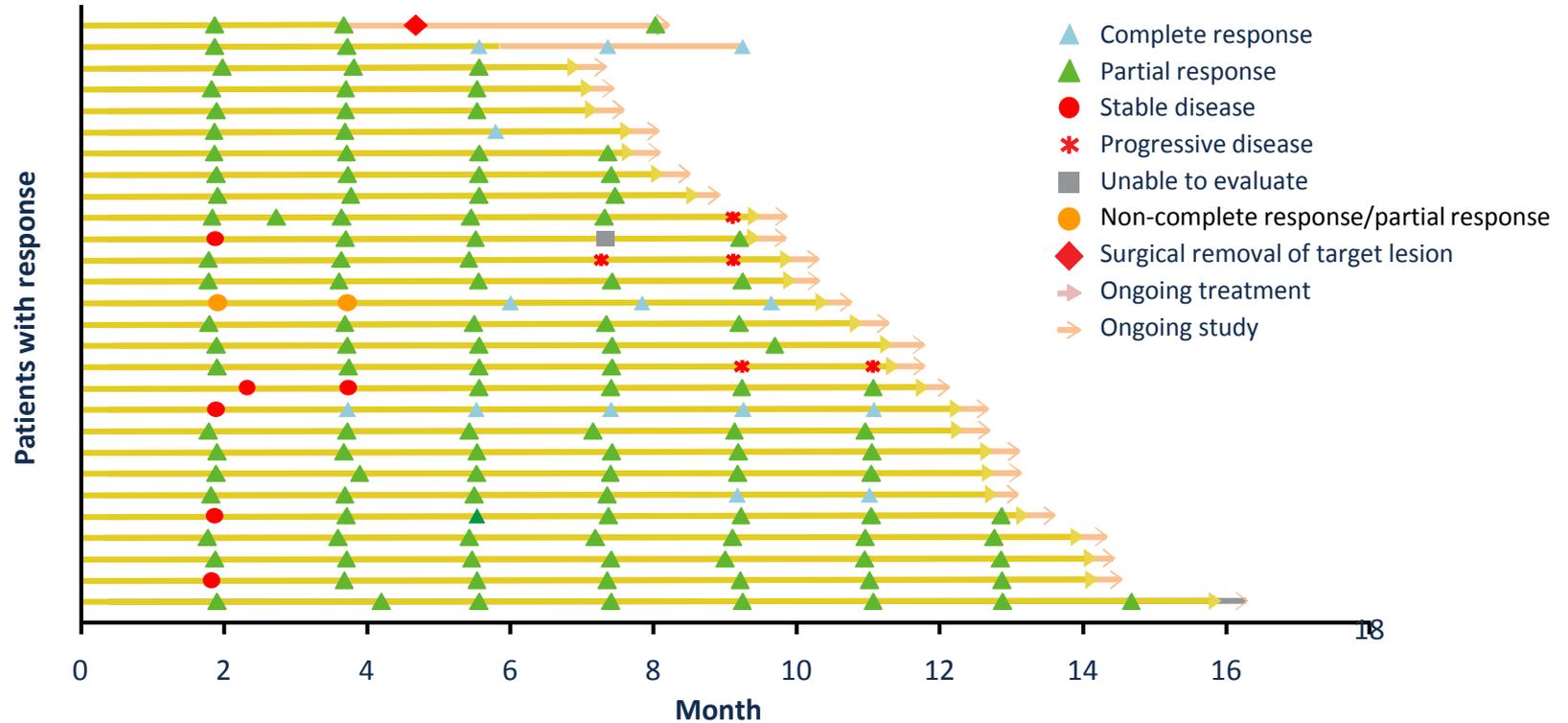
1. Rischin et al. *J Clin Oncol*. 2018;36(suppl; abstr 9519). 2. Migden et al. EADV; 2018. e-Poster P0668.

Eficácia de Cemiplimab em pacientes com CEC de pele avançado, conforma a avaliação do investigador (CSCC Expansion Cohorts)

	Group 1 (mCSCC) ^{a,1}	Group 2 (laCSCC) ^{b,2}
Median PFS	NR	NR
Estimated PFS at 12 months	52.5% (95% CI: 37.0 – 65.8)	65.6% (95% CI: 37.6 – 83.4)
Median OS	NR	NR
Estimated OS at 12 months	80.6% (95% CI: 67.7 – 88.8)	91.1% (95% CI: 68.6 – 97.7)
Median DOR	NR	NR
Objective Response - CR/PR	6,8% / 40,7%	0 / 43,5%
SD	15,3%	39,1%
PD	18,6%	8,7%

1. Rischin et al. *J Clin Oncol*. 2018;36(suppl; abstr 9519). 2. Migden et al. EADV; 2018. e-Poster P0668.

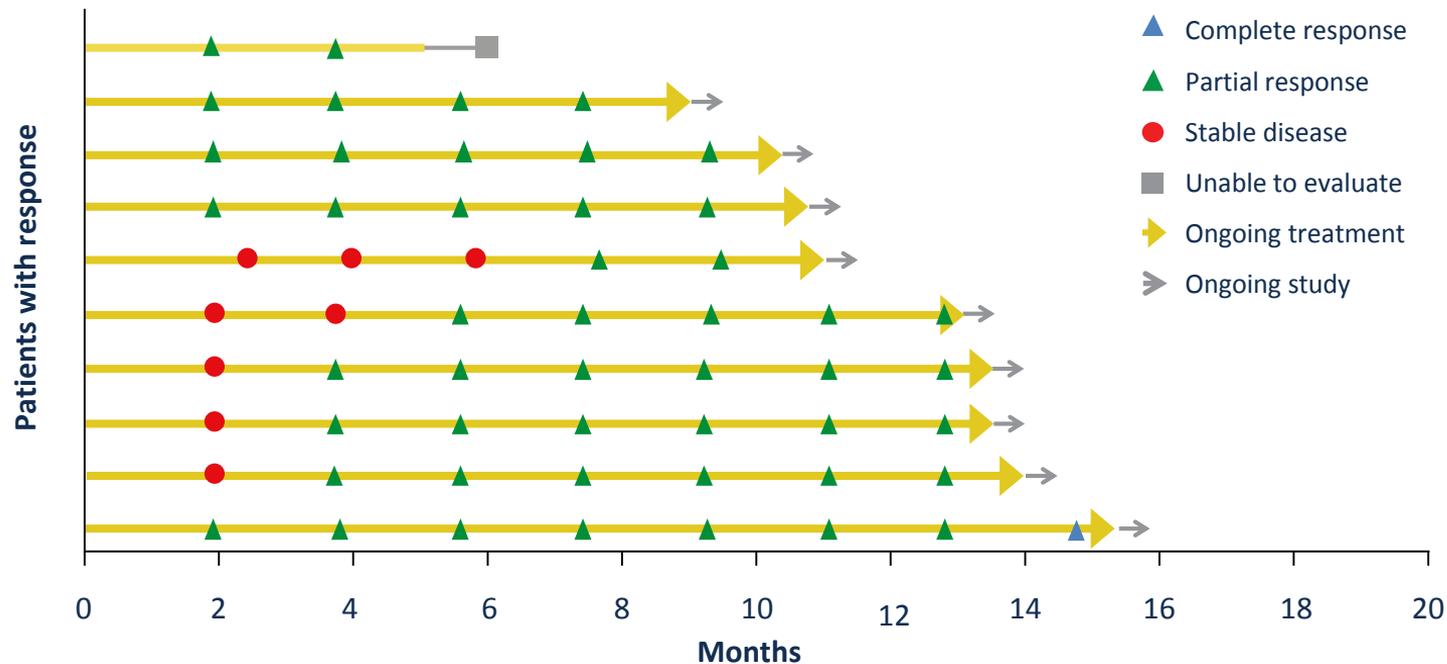
Tempo até resposta e duração de resposta em 28 pacientes com CEC de pele metastático, que tiveram resposta a Cemiplimabe



Each horizontal line represents one patient. Twenty-three of the 28 patients remain in response and on study at time of data cut-off. Three patients had disease progression (red asterisks); one patient was censored after surgical resection of responding target lesion (top line); and one was lost to follow-up after experiencing complete response (second-from-top line).

Data cut-off date: October 27, 2017

Tempo até resposta e duração de resposta em 28 pacientes com CEC de pele localmente avançado, que tiveram resposta a Cemiplimabe



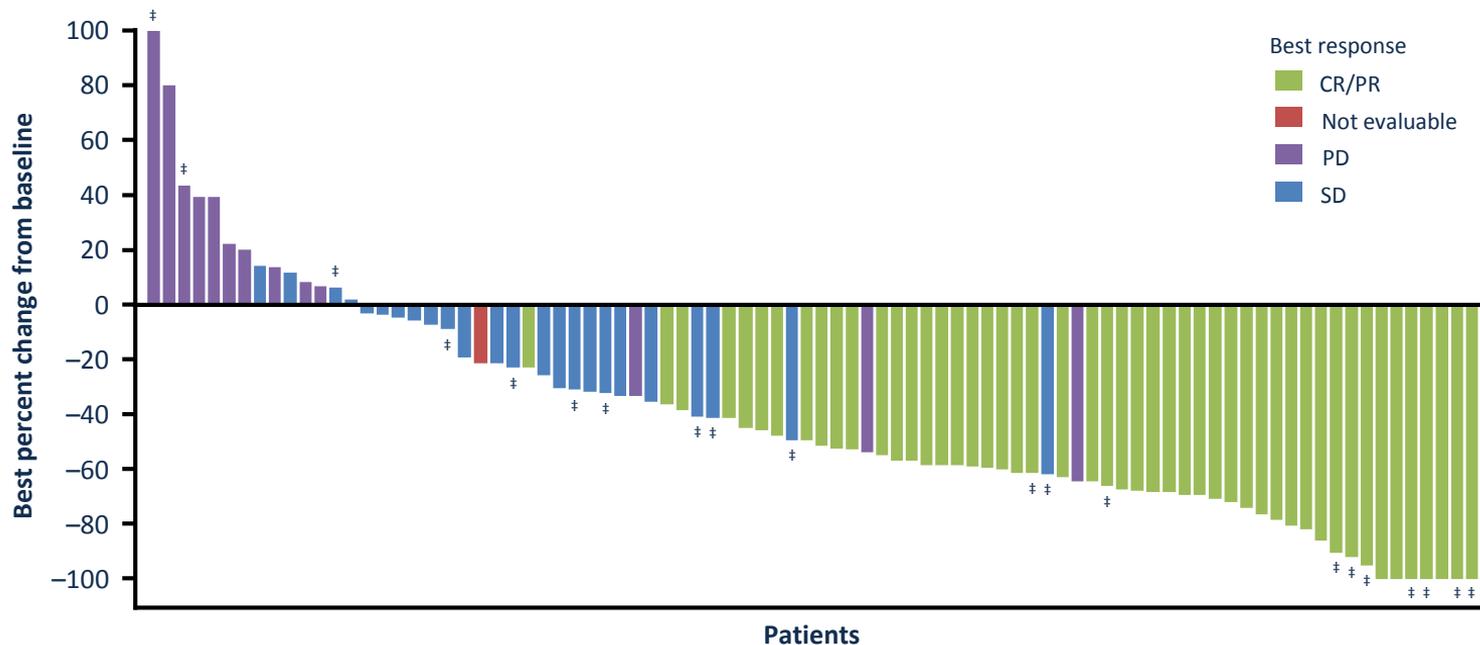
Plot shows time to response and duration of response in the 10 responding patients. Each horizontal line represents one patient. Nine of the 10 patients remain in response and on study at time of data cut-off. One patient was censored (top line) after missing treatments due to co-morbidities and withdrawing consent from study; therefore, they no longer met the dual criteria of ongoing response per independent central review and ongoing study treatment.

Migden MR, et al. EADV 2018. e-Poster P0668.

Data cut-off date: October 27, 2017

Proporção de redução do tumor em pacientes com CEC de pele localmente avançado

Análise combinada: Fase 1 e Fase 2



[†]Figure shows best percent change in the sum of target lesion diameters from baseline. Lesion measurements after progression are excluded. Bars without double cross symbols are based on lesion measurements per RECIST 1.1; bars with double cross symbols are based on lesions measurements per WHO criteria.

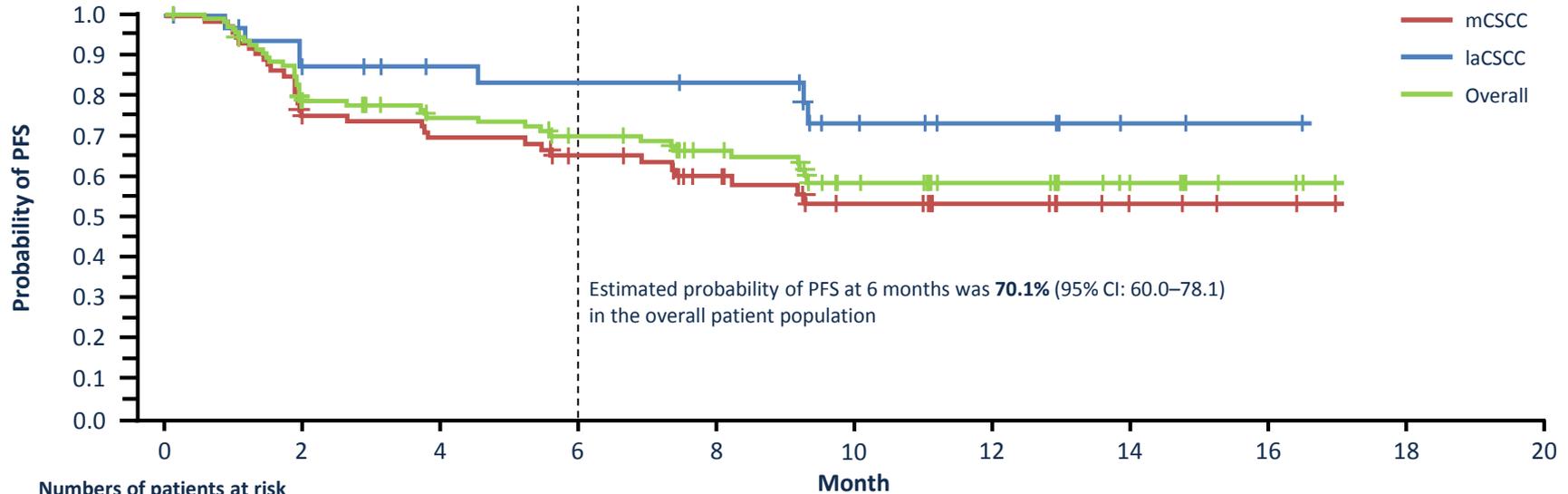
CR, complete response; CSCC, cutaneous squamous cell carcinoma; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria In Solid Tumors version; SD, stable disease; WHO, World Health Organization.

Migden et al. American Academy of Dermatology 2019. Poster Number 8554. March 2019

Sobrevida Livre de Progressão

avaliação independente

Análise combinada: Fase 1 e Fase 2



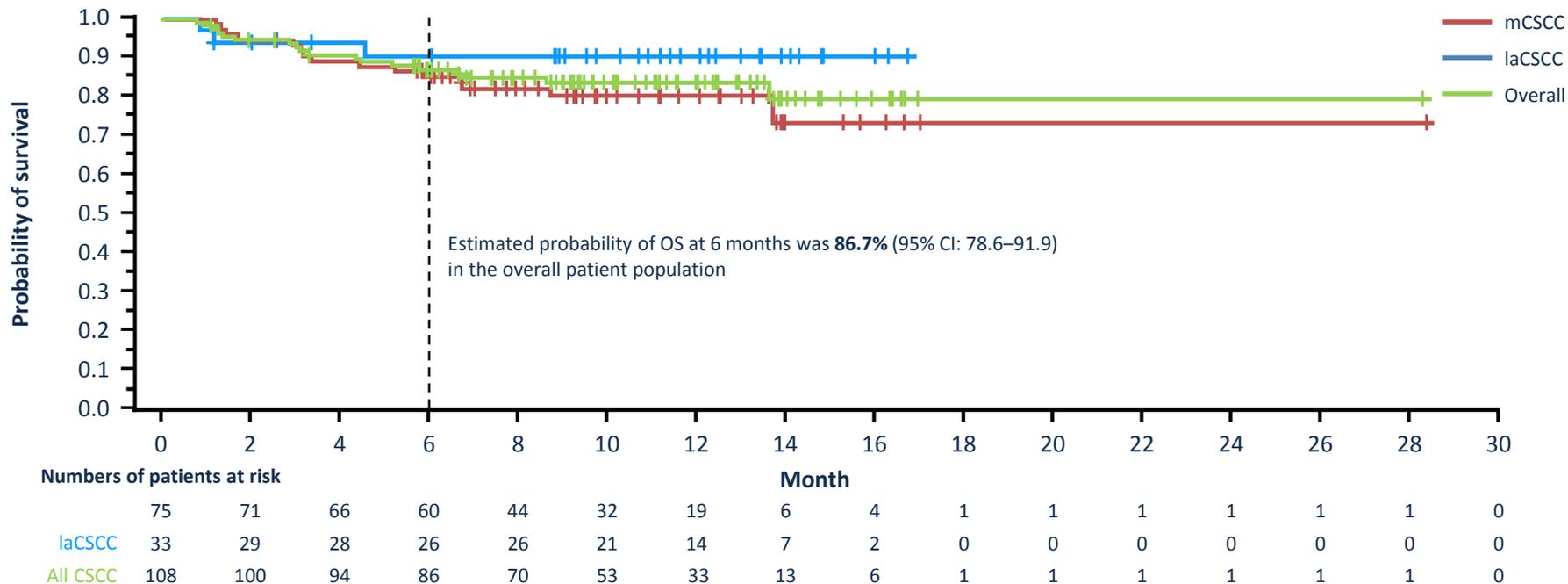
Numbers of patients at risk

	0	2	4	6	8	10	12	14	16	18	20
	75	52	48	39	29	18	12	5	2	0	0
laCSCC	33	26	21	20	18	11	8	2	1	0	0
All CSCC	108	78	69	59	47	29	20	7	3	0	0

CI, confidence interval; CSCC, cutaneous squamous cell carcinoma; laCSCC, locally advanced CSCC; mCSCC, metastatic CSCC; PFS, progression-free survival.

Sobrevida Global

Análise combinada: Fase 1 e Fase 2



CI, confidence interval; CSCC, cutaneous squamous cell carcinoma; laCSCC, locally advanced CSCC; mCSCC, metastatic CSCC; OS, overall survival.

Eventos Adversos

Events	mCSCC (n=75)		laCSCC (n=33)		Overall (N=108)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any	75 (100.0)	32 (42.7)	33 (100.0)	13 (39.4)	108 (100.0)	45 (41.7)
Serious	24 (32.0)	19 (25.3)	9 (27.3)	8 (24.2)	33 (30.6)	27 (25.0)
Led to discontinuation	6 (8.0)	3 (4.0)	1 (3.0)	1 (3.0)	7 (6.5)	4 (3.7)
With an outcome of death [†]	3 (4.0)	3 (4.0)	3 (9.1)	3 (9.1)	6 (5.6)	6 (5.6)
Occurred in ≥10% of overall patient group						
Fatigue	17 (22.7)	1 (1.3)	13 (39.4)	1 (3.0)	30 (27.8)	2 (1.9)
Diarrhea	20 (26.7)	1 (1.3)	8 (24.2)	0	28 (25.9)	1 (0.9)
Nausea	13 (17.3)	0	8 (24.2)	0	21 (19.4)	0
Constipation	12 (16.0)	1 (1.3)	14 (12.1)	0	16 (14.8)	1 (0.9)
Decreased appetite	11 (14.7)	0	5 (15.2)	0	16 (14.8)	0
Pruritus	9 (12.0)	0	7 (21.2)	0	16 (14.8)	0
Cough	11 (14.7)	0	3 (9.1)	0	14 (13.0)	0
Rash [‡]	11 (14.7)	0	3 (9.1)	0	14 (13.0)	0
Dry skin	8 (10.7)	0	4 (12.1)	0	12 (11.1)	0
Headache	9 (12.0)	0	3 (9.1)	0	12 (11.1)	0
Hypothyroidism	6 (8.0)	0	6 (18.2)	0	12 (11.1)	0
Maculopapular rash [‡]	9 (12.0)	1 (1.3)	2 (6.1)	0	11 (10.2)	1 (0.9)

[†]One death was considered related to study treatment (see next slide). [‡]Although rash and maculopapular rash may reflect the same condition, they were listed as two distinct events for the safety report of the studies.

Migden et al. American Academy of Dermatology 2019. Poster Number 8554. March 2019

Data cut-off date: October 2017

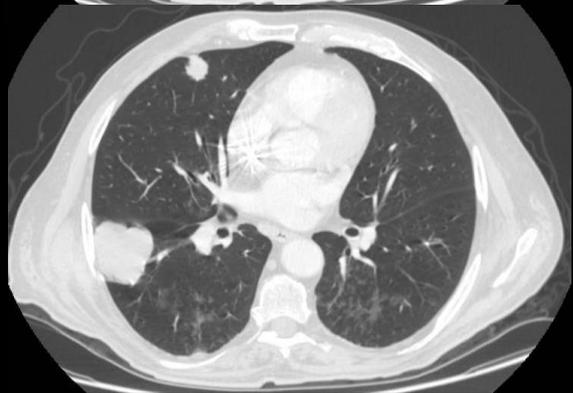
Resposta precoce em hoem de 62 anos com CEC de pele localmente avançado

Screening

Resposta em 6 semanas com cemiplimabe



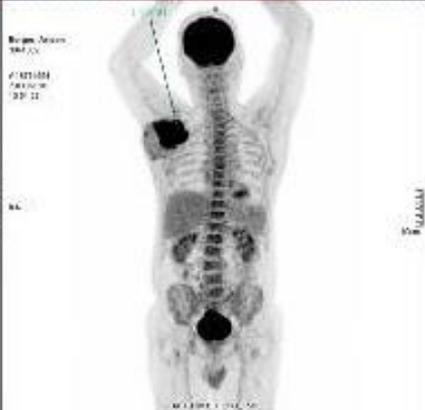
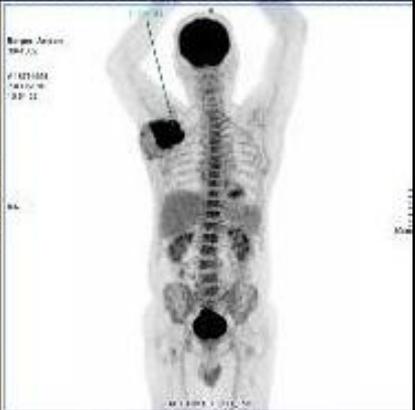
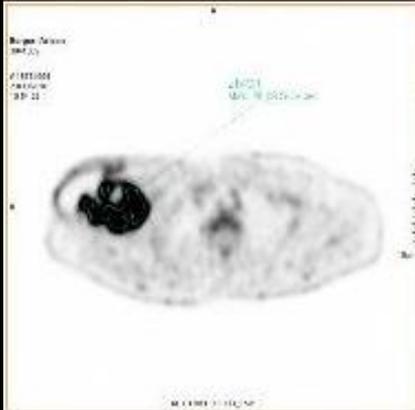
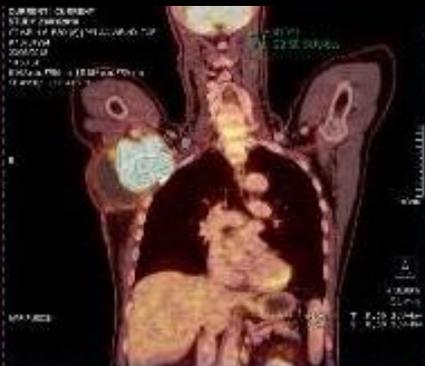
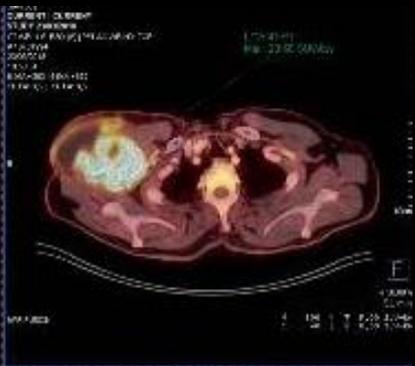
Pré
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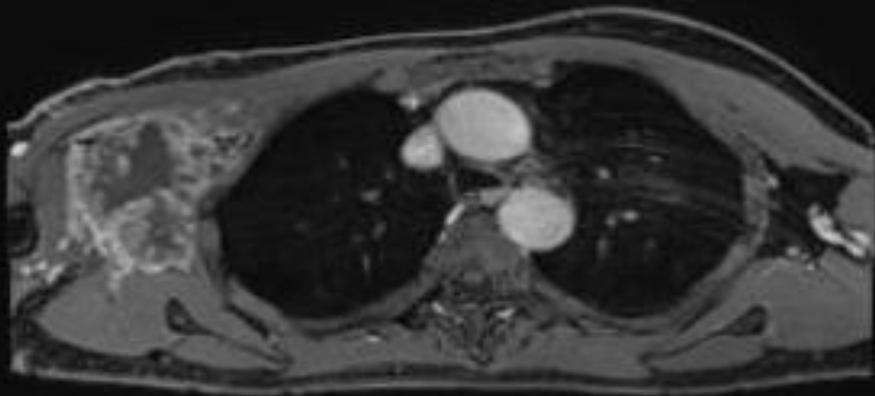
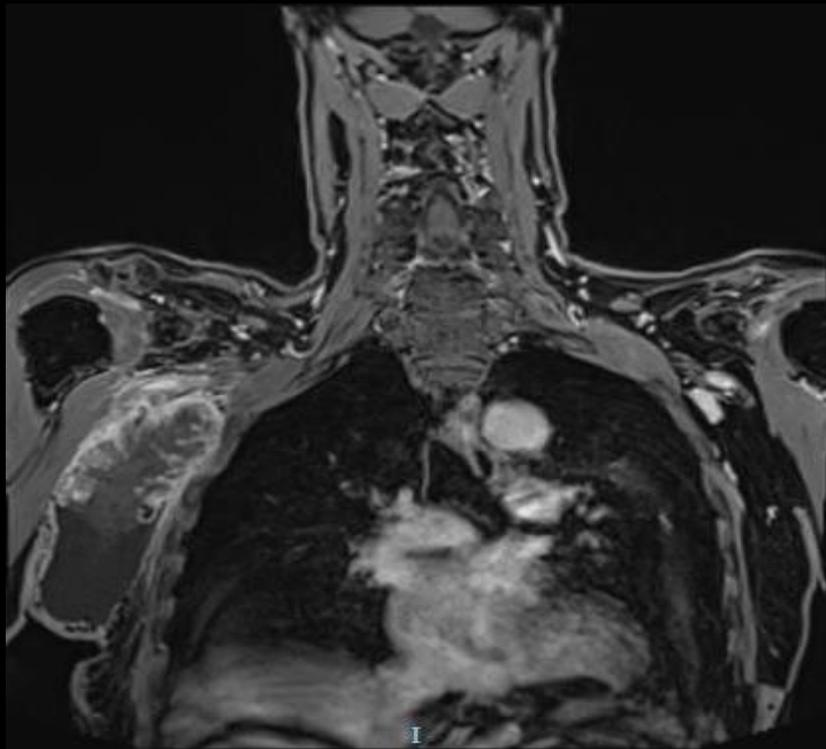
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Mar/ 2018



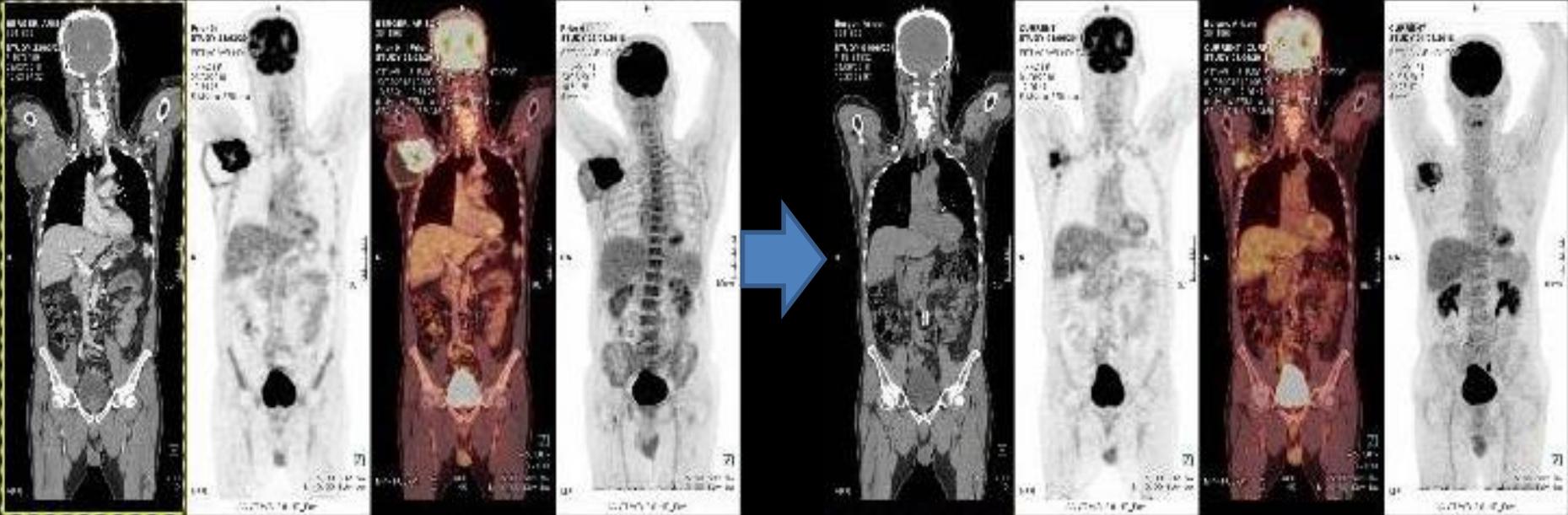
Mar/ 2018



Mar/ 2018

Jun/ 2018

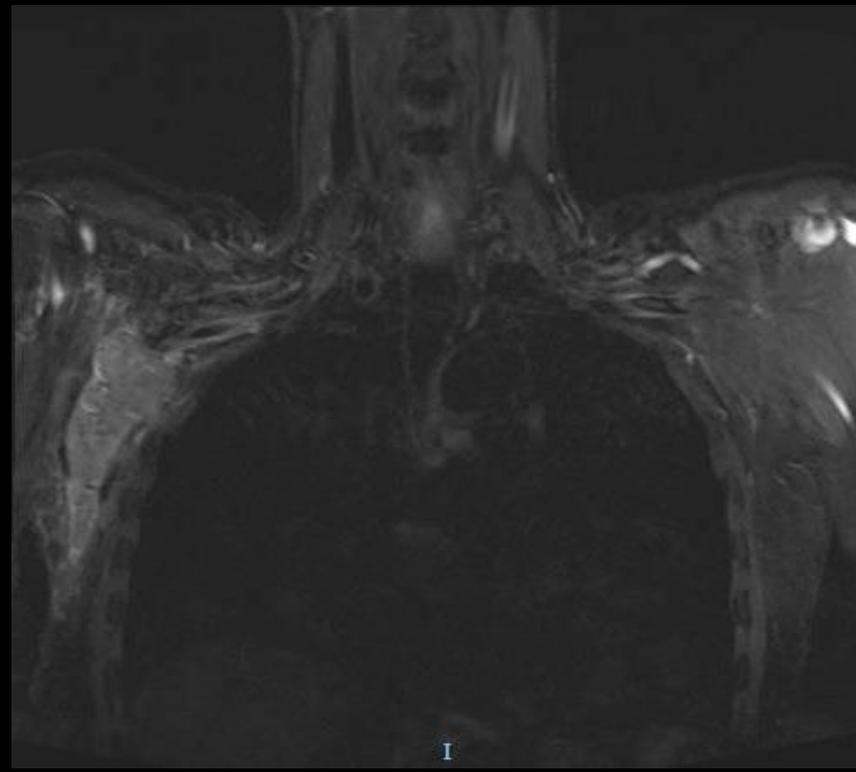
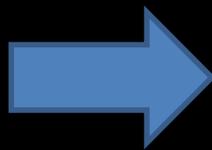
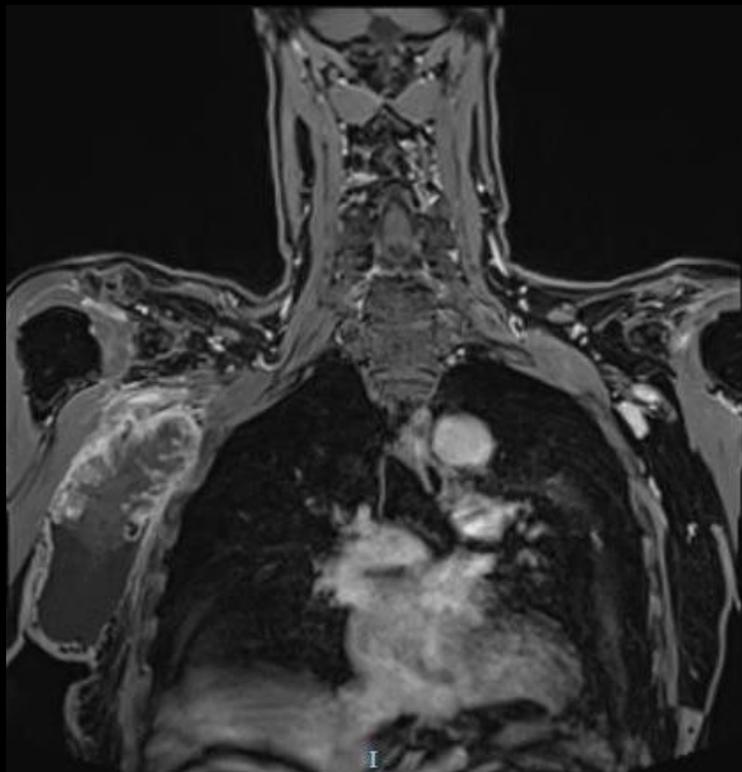
Carboplatina / Paclitaxel x4



Mar/ 2018

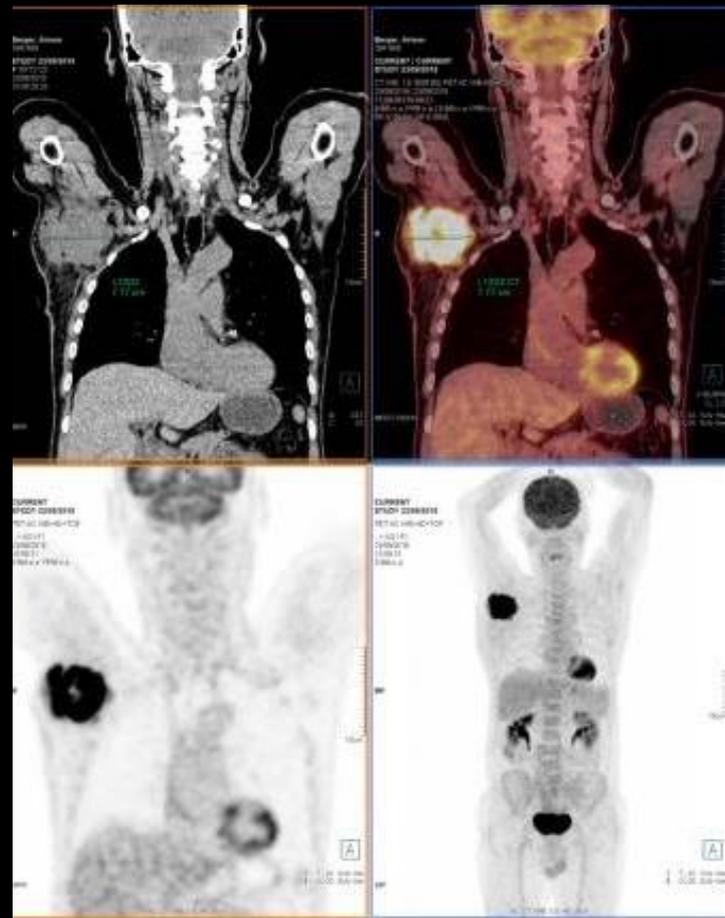
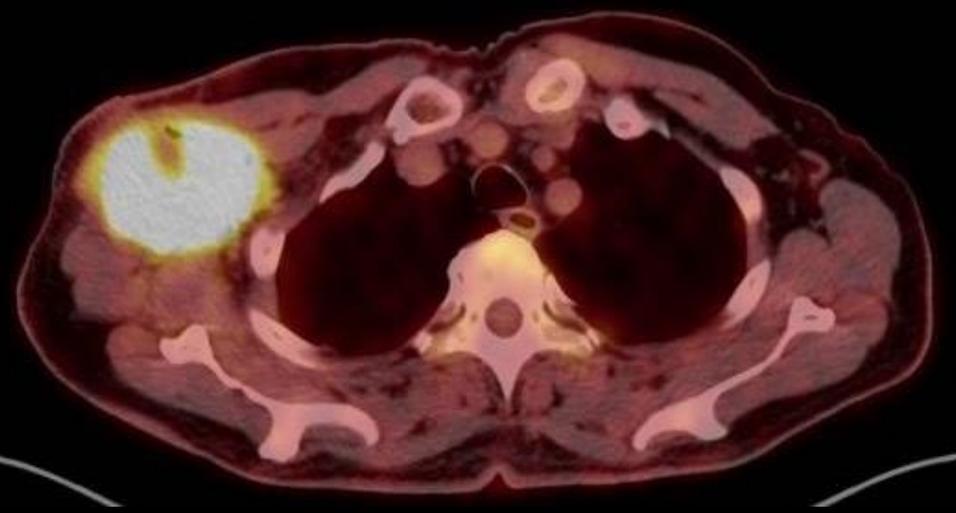
Jun/ 2018

Carboplatina / Paclitaxel x4



Ago/ 2018

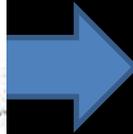
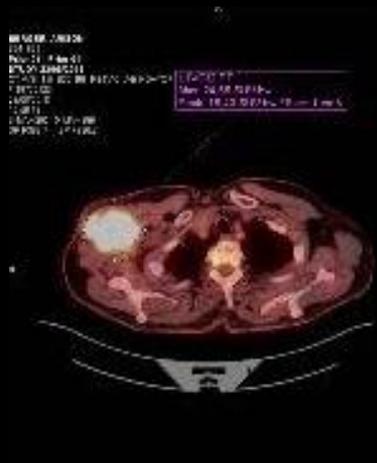
TTP: 5meses



Ago/ 2018

Out/ 2019

Pembrolizumab x2



Em resumo...

Imunoterapia tem um excelente racional para CEC

Taxas de resposta na ordem de 50%, mas redução em SD

Sobrevida Livre de Progressão em 6 meses de 70%

Sobrevida Global em 6 meses de 86,7%

Cemiplimabe em Carcinoma Espino Celular de Pele

Obrigado!



A Beneficência
Portuguesa
de São Paulo