

12º SIMPÓSIO
INTERNACIONAL DE

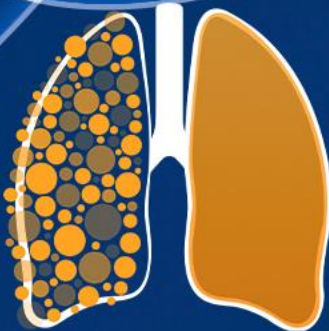
CÂNCER DE PULMÃO

2ª JORNADA ONCONNECTION MULTICARE

2024

GERENCIAMENTO E PRODUÇÃO

RV+
EVENTOS MÉDICOS



12º SIMPÓSIO
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PULMÃO

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2024

Personalizando a imunoterapia de primeira linha no câncer de pulmão - Caso Clínico: Eu faço POSEIDON

Marcelo Corassa

BP – A Beneficência Portuguesa de São Paulo

GERENCIAMENTO E PRODUÇÃO



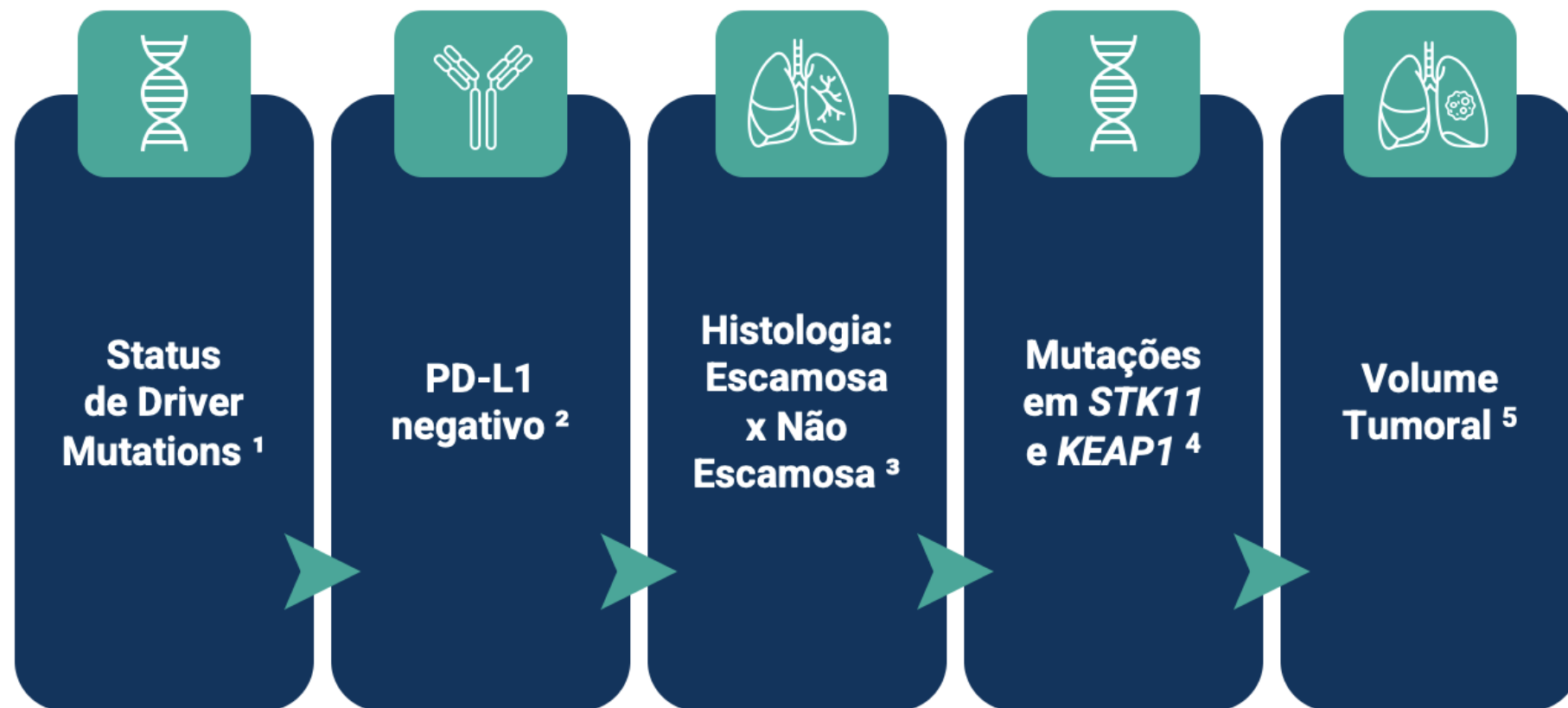
Conflitos de Interesse

- Honoraria: MSD, Roche, Pfizer, Astra Zeneca, Takeda, Lilly, Janssen, Amgen, Novartis, BMS, Sanofi, Daiichi-Sankyo.
- Travel Grants: MSD, Roche, Astra Zeneca.
- Participation in Advisory Boards: Roche, MSD, Takeda, AstraZeneca, Sanofi, Janssen.
- Participation in Clinical Trials: MSD, BMS, Roche, AstraZeneca, Boehringer, Pfizer, Abbvie, Janssen, Daiichi, Libbs, Servier.



PONTOS FUNDAMENTAIS

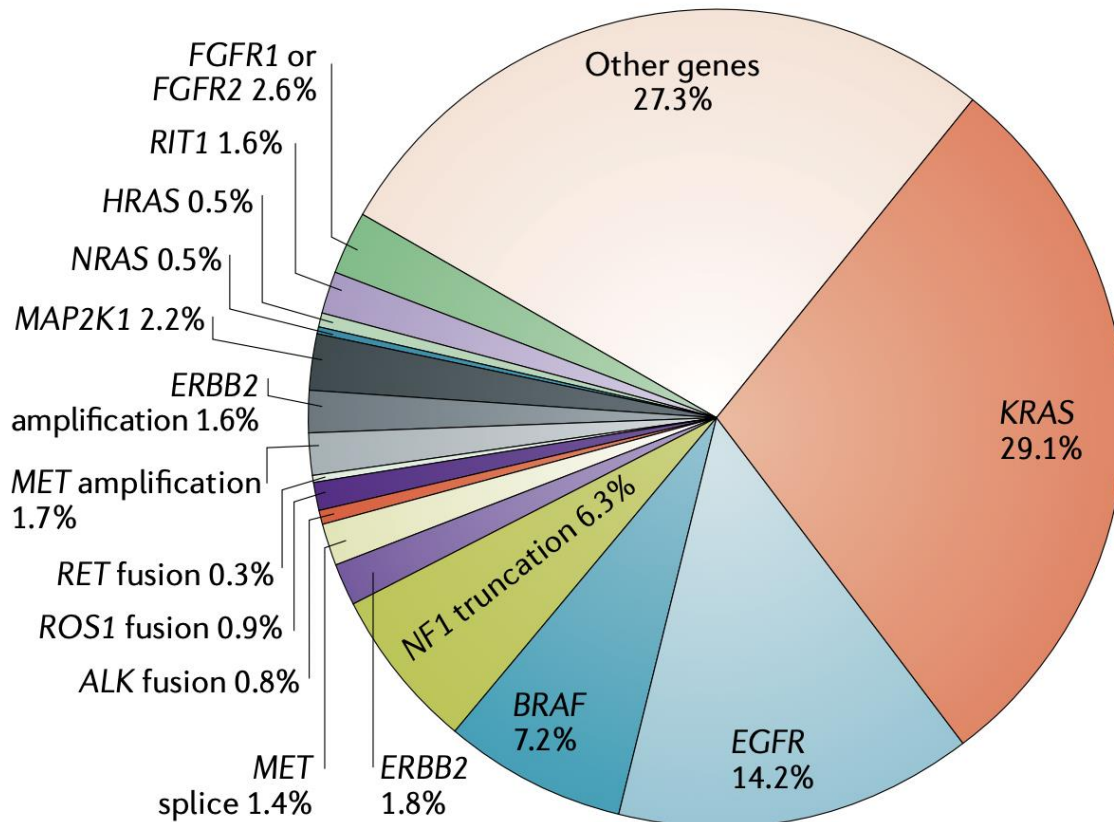
que definem
o risco do paciente



1. The Cancer Genome Atlas Research Network. Comprehensive molecular profiling of lung adenocarcinoma. Nature 511, 543–550 (2014); 2. L.H. Schmidt, et al. PD-1 and PD-L1 expression in NSCLC indicate a favorable prognosis in defined subgroups PLoS One, 10 (2015), p. e0136023; 3. Cheng TY, et al. The international epidemiology of lung cancer: latest trends, disparities, and tumor characteristics. J Thorac Oncol 2016;11:1653-1671/ Soldera SV, Leighl NB. Update on the treatment of metastatic squamous non-small cell lung cancer in new era of personalized medicine. Front Oncol 2017;7:50-50.; 4. Skoulidis F. et al. STK11/LKB1 Mutations and PD-1 Inhibitor Resistance in KRAS-Mutant Lung Adenocarcinoma. Cancer Discov (2018) 8 (7): 822–835. <https://doi.org/10.1158/2159-8290.CD-18-0099>; 5. Sakata Y, et al. Comparisons between Tumor Burden and Other Prognostic Factors that Influence Survival of Patients with Non-small Cell Lung Cancer Treated with Immune Checkpoint Inhibitors. Thorac Cancer. 2019;10:2259–66

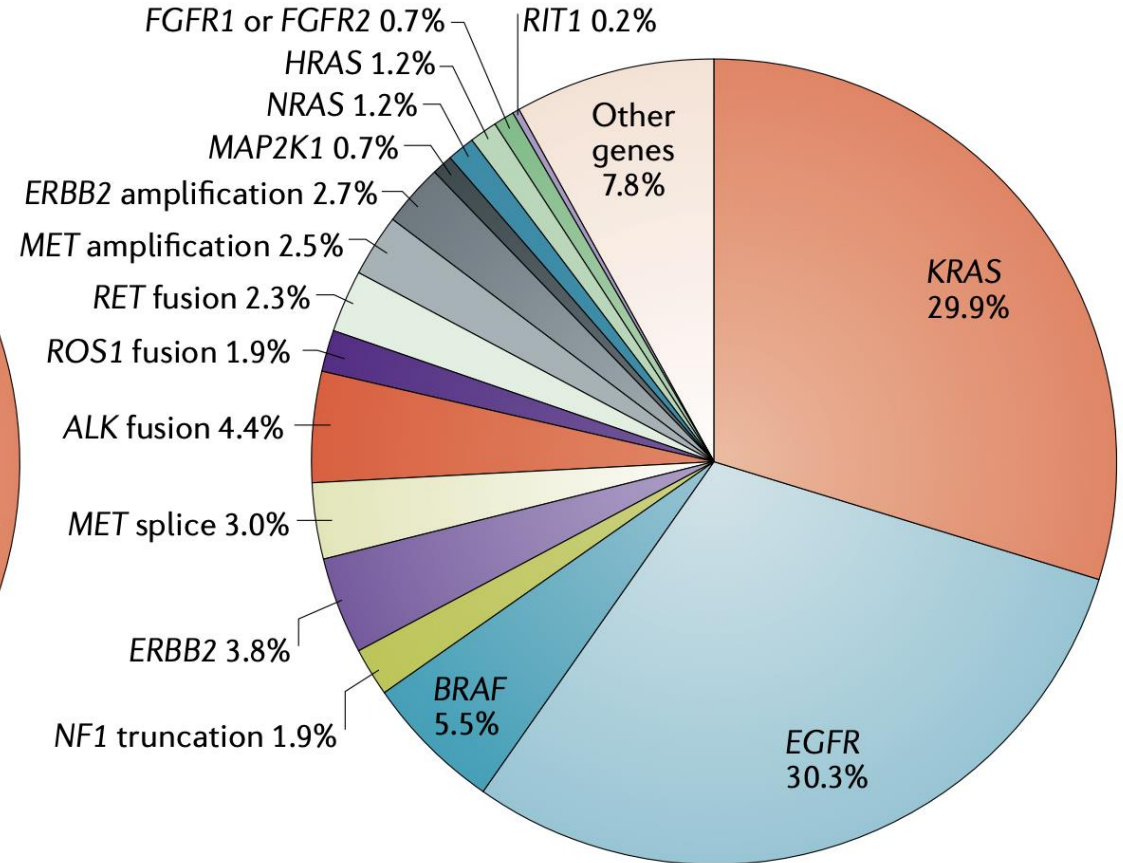
A diversidade de biomarcadores é cada vez maior, incluindo-se biomarcadores não considerados como drivers.

a Early stage

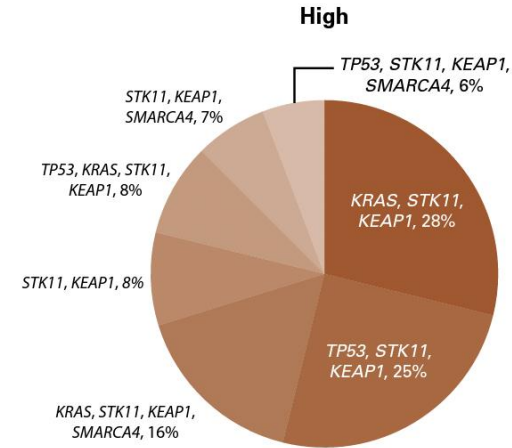
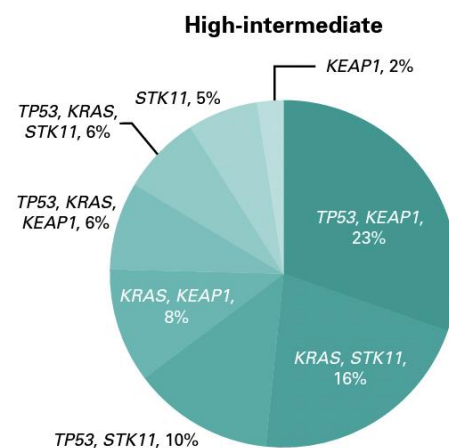
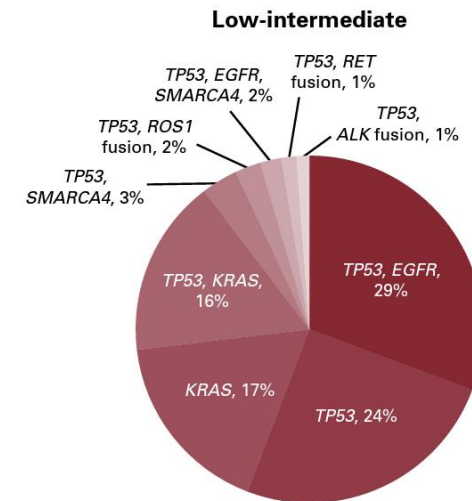
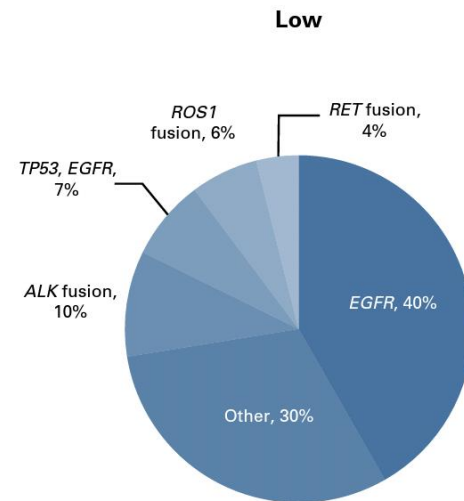
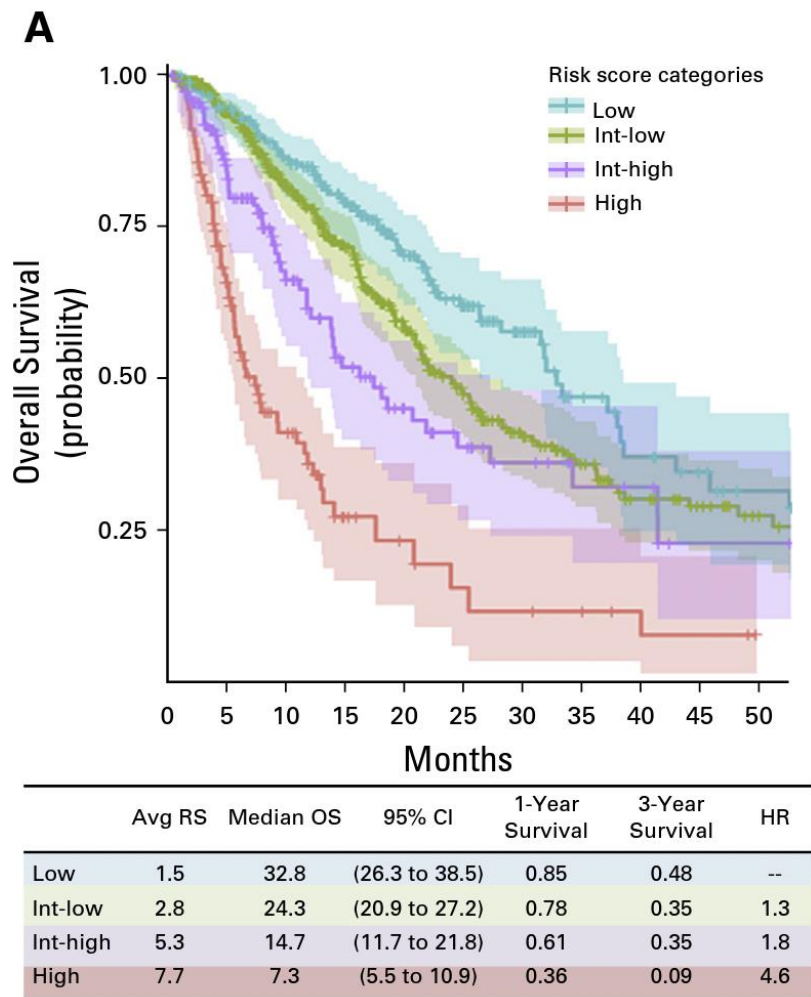


Data from TCGA (Sanchez-Vega et al.¹⁷⁸, Ellrott et al.¹⁷⁹ and Hoadley et al.¹⁸⁰), Imielinski et al.⁶² and Kadara et al.¹³³ (n = 741)

b Metastatic



Data from MSK-IMPACT (Jordan et al.⁵⁹) and FoundationOne (Frampton et al.¹⁵) panels (n = 5262)

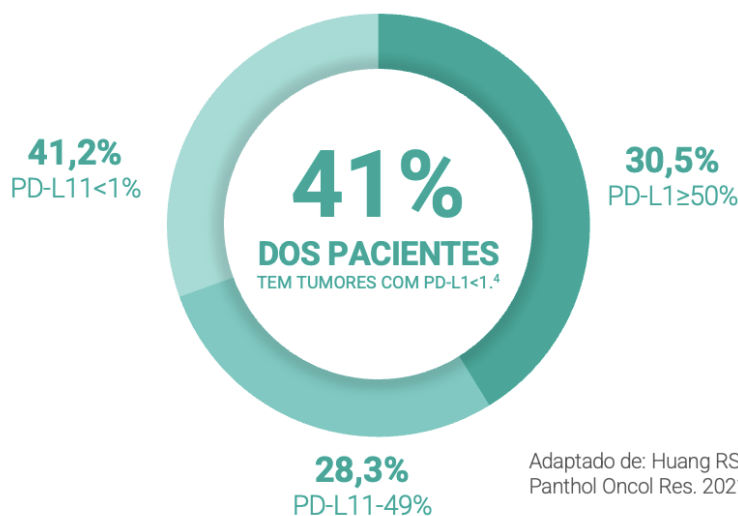


Personalizando a imunoterapia de primeira linha no câncer de pulmão - Caso Clínico: Eu faço POSEIDON

Marcadores de Pior Prognóstico

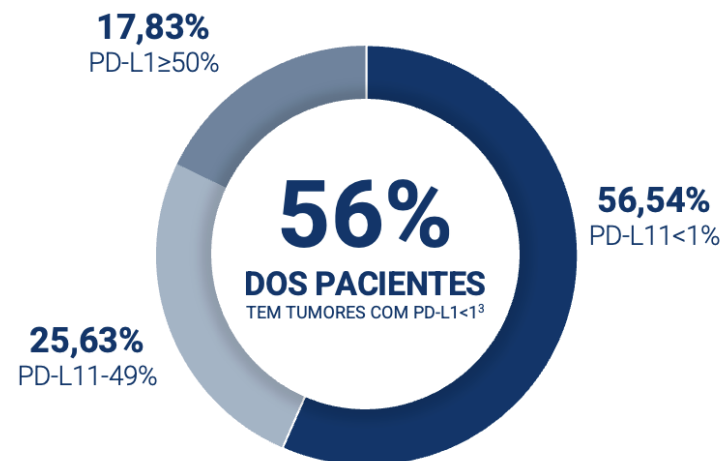
PD-L1 NEGATIVO - INCIDÊNCIA

CENÁRIO GLOBAL⁴



Adaptado de: Huang RSP, et al.
Panthol Oncol Res. 2021 Mar 11;27:592997

CENÁRIO BRASILEIRO³



Adaptado de: Gelatti ACZ, et al.
Clin Lung Cancer. 2020;21(6):e511-e515.

CARACTERÍSTICAS DA POPULAÇÃO

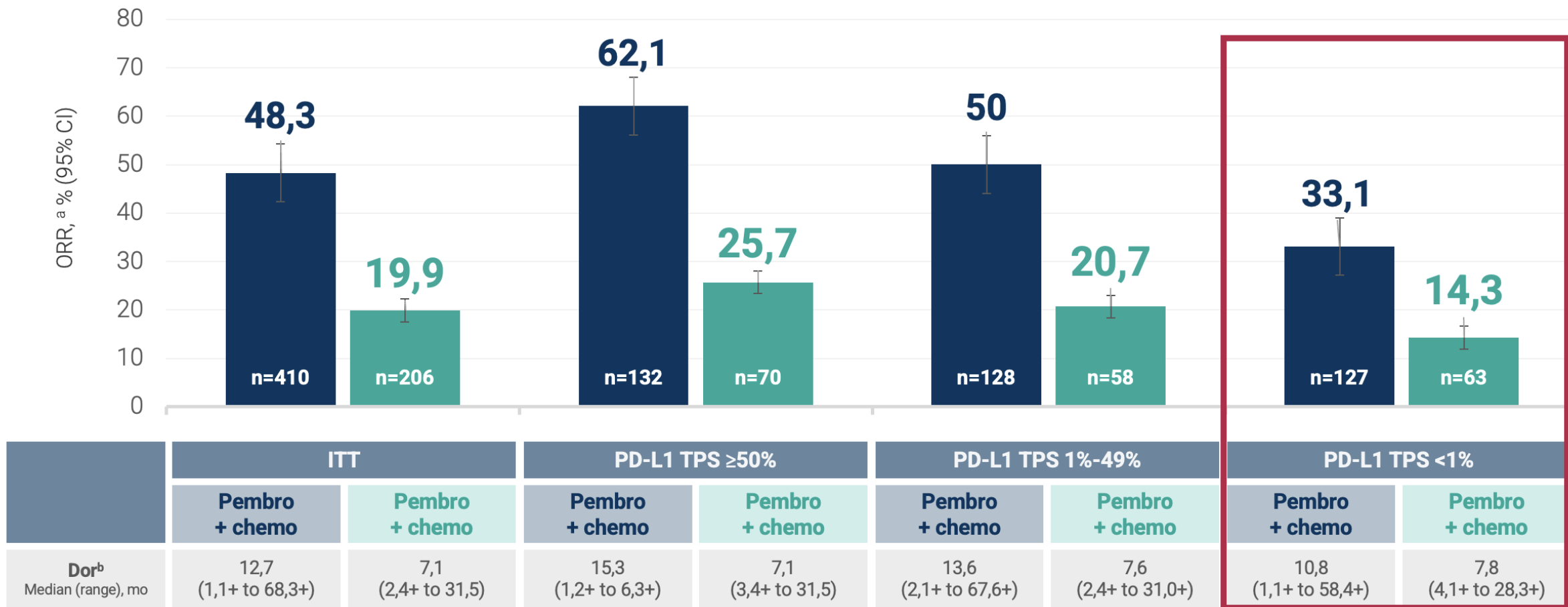
Pacientes com baixa expressão ou PD-L1 negativo têm maior probabilidade de apresentar resistência primária à terapia anti-PD-(L)1 (vs PD-L1-alto).²

Dados de mundo real sugerem que ainda há **oportunidade para busca de melhores tratamentos** em pacientes baixos expressores ou com PD-L1 negativo.⁵

Tumores com PD-L1 < 1% **podem ter menor infiltração** de linfócitos T no microambiente tumoral.⁶

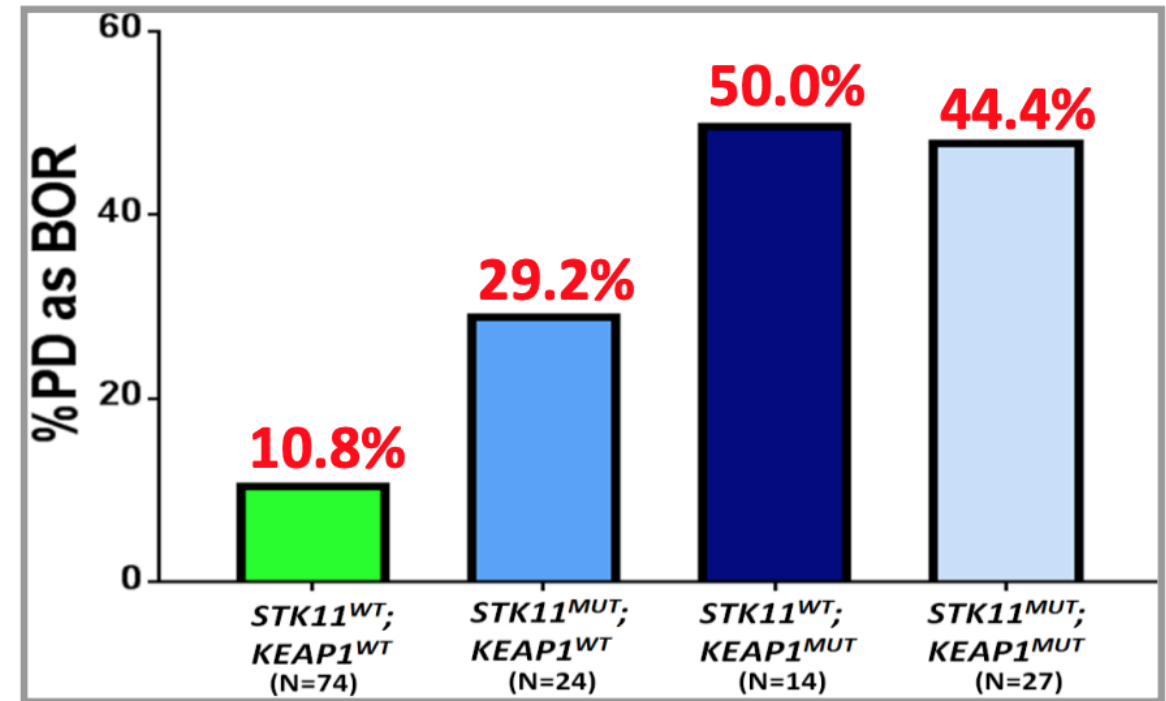
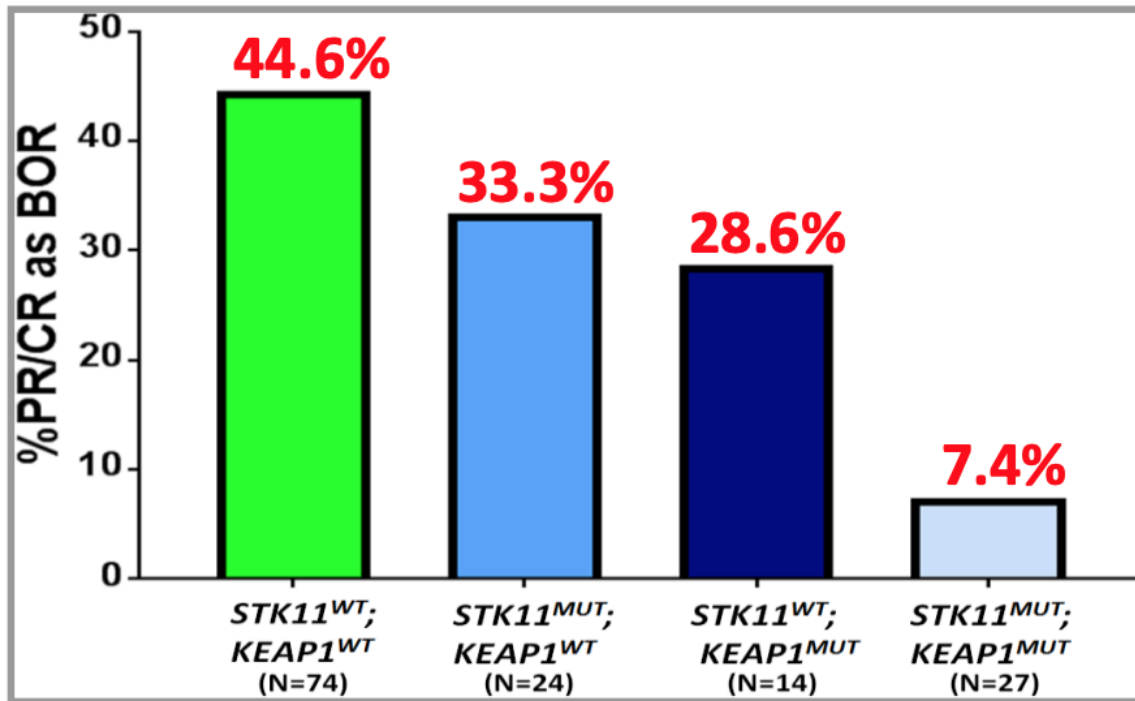
Personalizando a imunoterapia de primeira linha no câncer de pulmão - Caso Clínico: Eu faço POSEIDON

Marcadores de Pior Prognóstico



Adaptado de: Garassino et al. Annals of Oncology (2022) 33 (suppl7): S448-S554.

ORR with PCP in *STK11* and *KEAP1*-defined subgroups



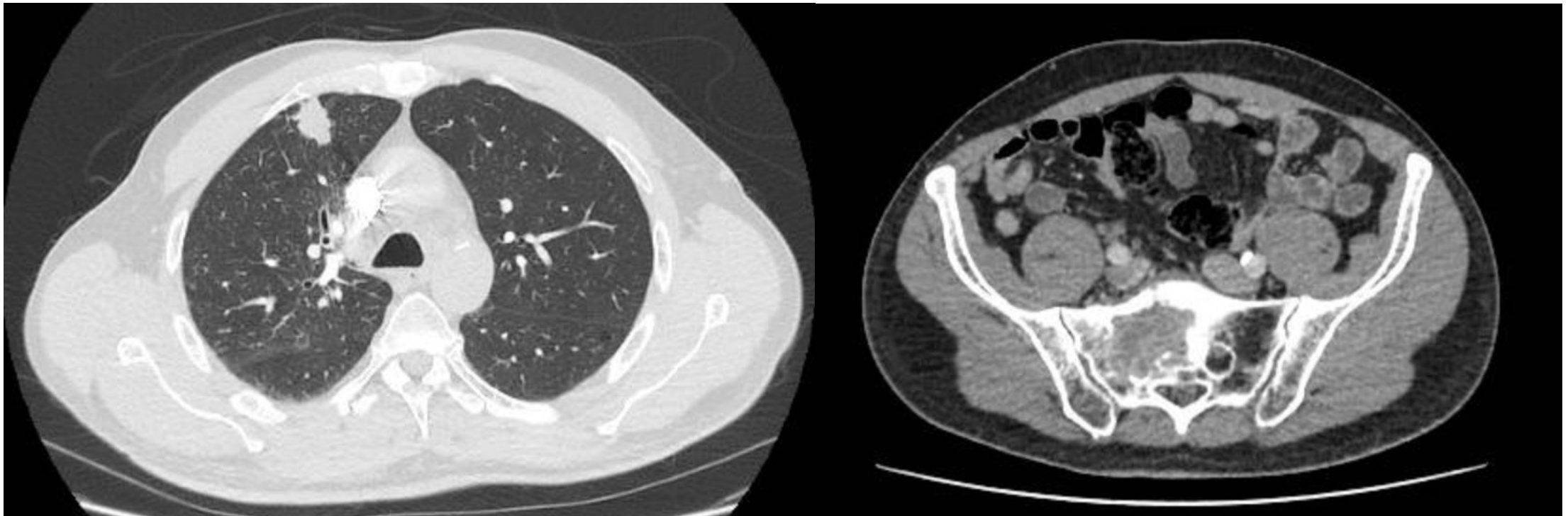
***STK11*^{MUT} and/or *KEAP1*^{MUT} PR/CR: 21.5%, SD: 38.5%, PD 40%**

26/34 (76.5%) patients with primary refractory disease had *STK11* and/or *KEAP1* mutations

- **Male, 66 years-old.**
- Previous smoker: 80 pack-years.
- ECOG 1.
- Lung adenocarcinoma metastatic to bone with high disease burden.
- Bone pain refractory to opioids.



- Male, 66 years-old. Previous smoker. Adeno. High burden of disease (bone).



PD-L1 IMMUNOHISTOCHEMISTRY (IHC) ANALYSIS (Dako 22C3 pharmDx™)

Tumor Proportion Score (TPS) (%) 0

- Male, 66 years-old. Previous smoker. Adeno. High burden of disease (bone).



Biomarker Findings

Microsatellite status - MS-Stable

Tumor Mutational Burden - 1 Muts/Mb

Genomic Findings

For a complete list of the genes assayed, please refer to the Appendix.

STK11 E223*

KEAP1 R234fs*37

KRAS G12A

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17/09/2020: C1 Carbo + Pem + Pembro q21d



15/12/2020: Pem + Pembro Maintenance.



- Male, 66 years-old. Previous smoker. Adeno. High burden of disease (bone).

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15/12/2020: Pem + Pembro Maintenance.

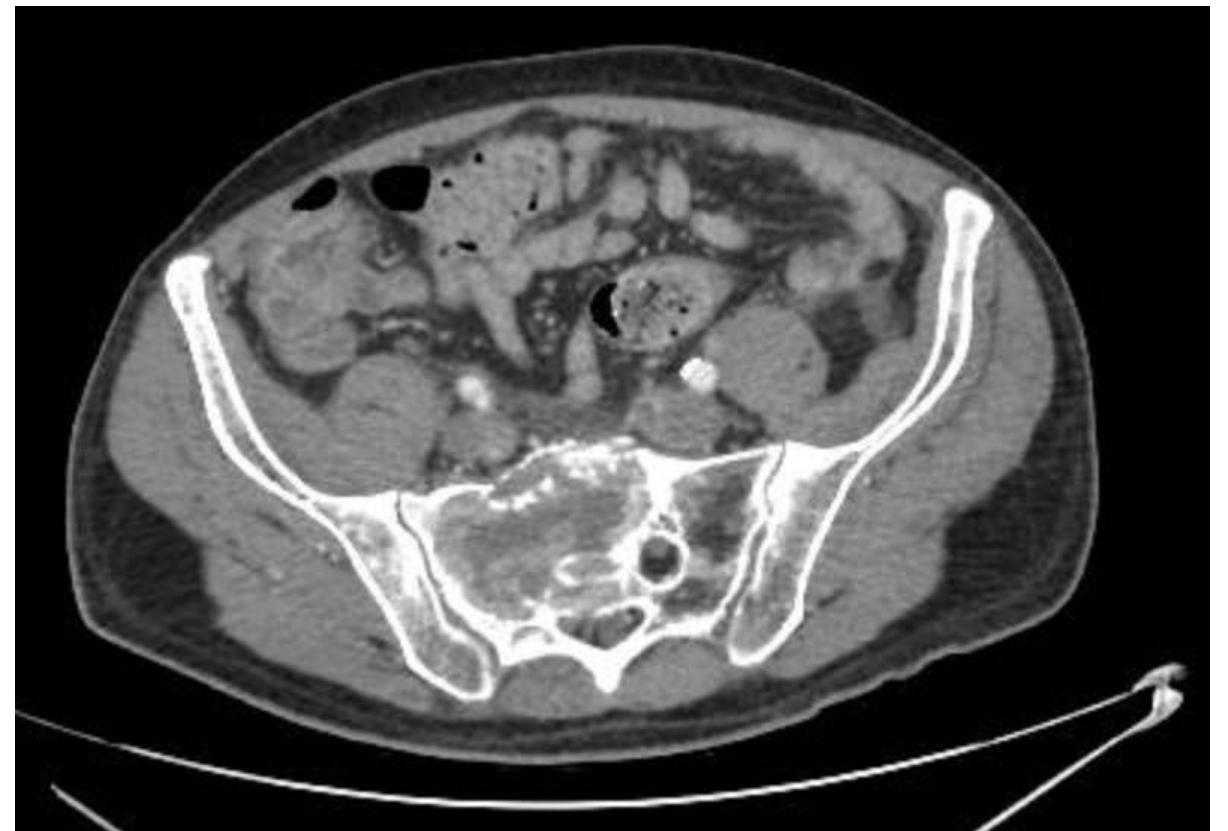


- Male, 66 years-old. Previous smoker. Adeno. High burden of disease (bone).

17/09/2020: C1 Carbo + Pem + Pembro q21d

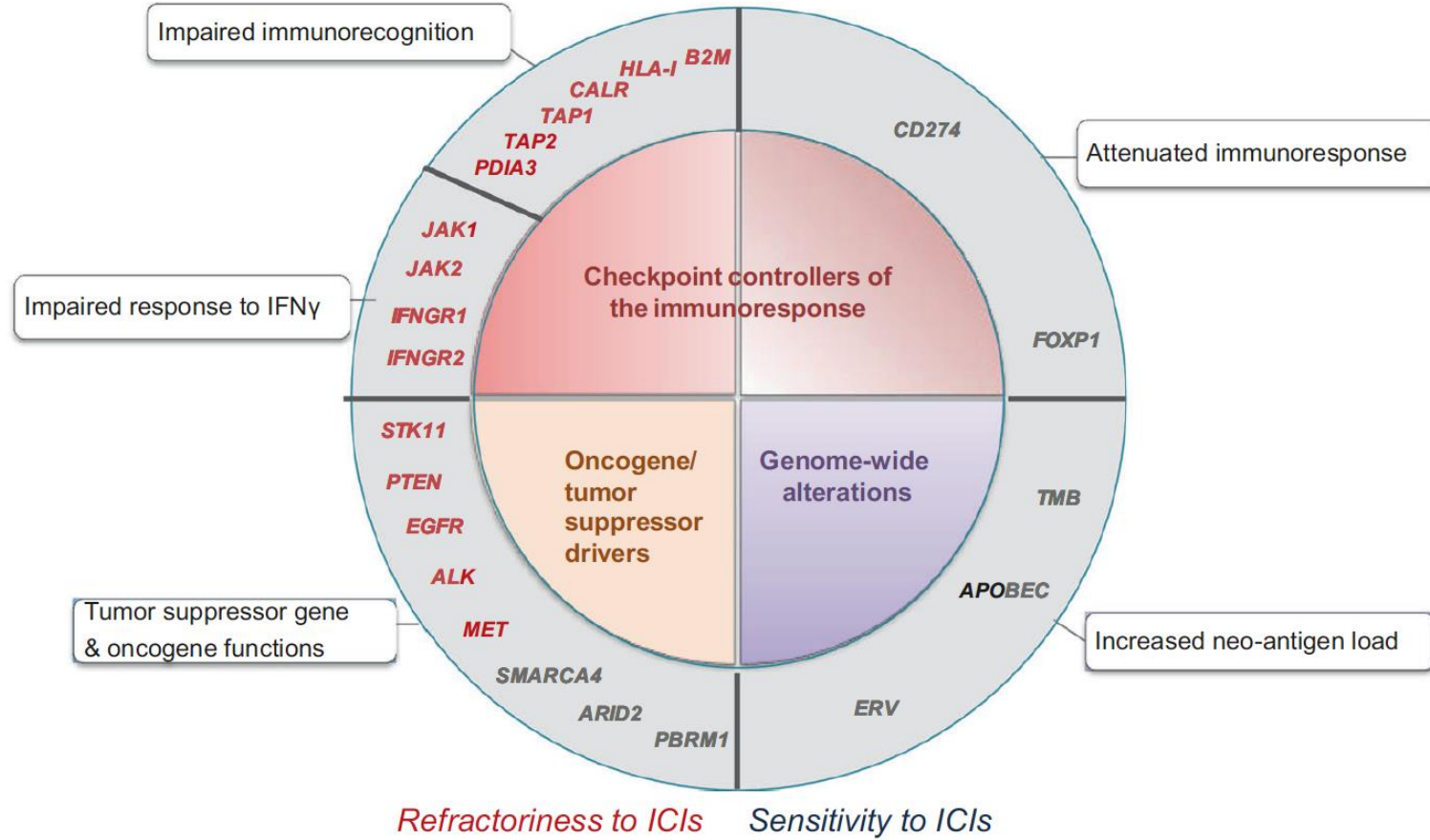


15/12/2020: Pem + Pembro Maintenance.



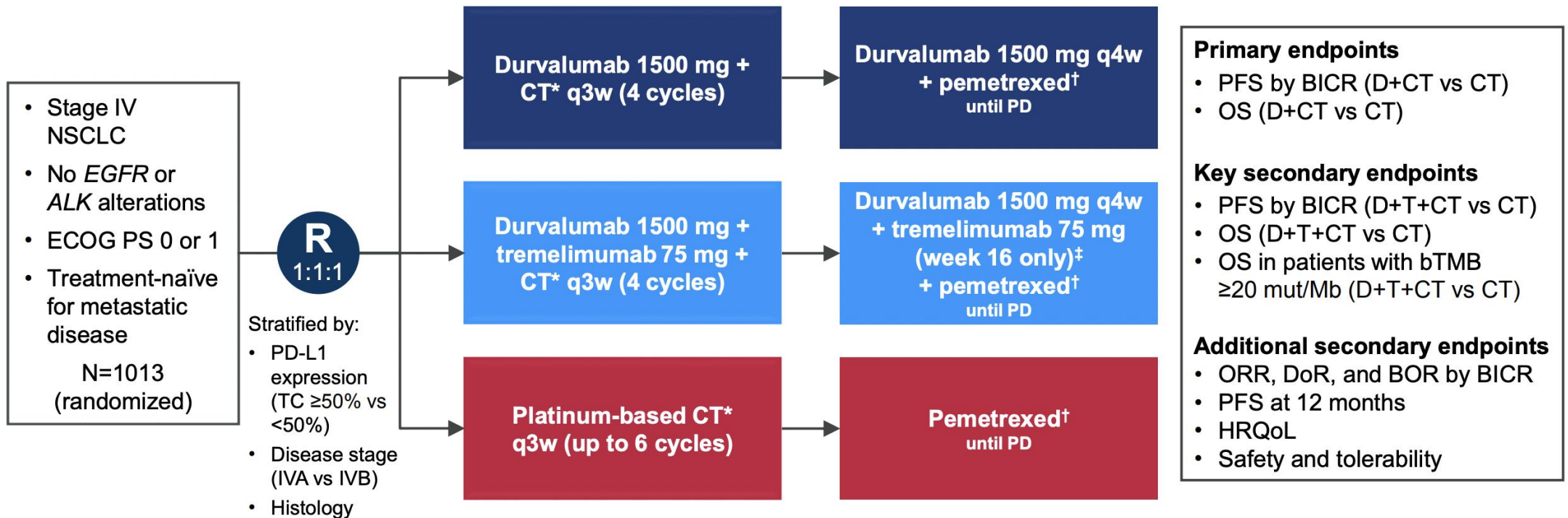
Personalizando a imunoterapia de primeira linha no câncer de pulmão - Caso Clínico: Eu faço POSEIDON

Por Que POSEIDON?



POSEIDON Study Design

Phase 3, global, randomized, open-label, multicenter study



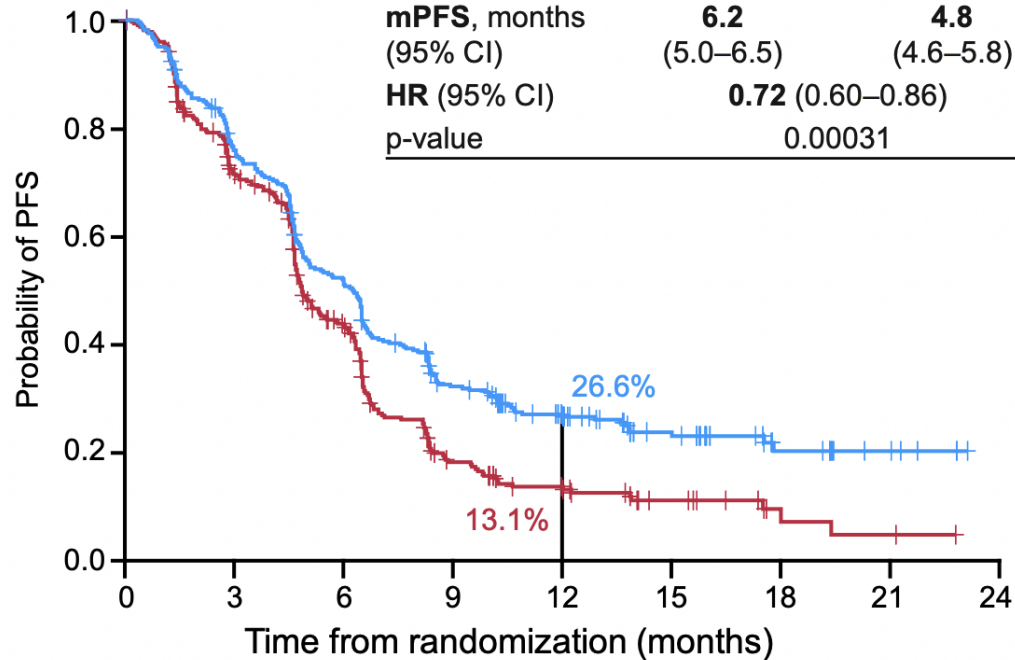
*CT options: gemcitabine + carboplatin/cisplatin (squamous), pemetrexed + carboplatin/cisplatin (non-squamous), or nab-paclitaxel + carboplatin (either histology);

†Patients with non-squamous histology who initially received pemetrexed during first-line treatment only (if eligible); ‡Patients received an additional dose of tremelimumab post CT (5th dose)

Durvalumab + Tremelimumab + CT vs CT: PFS and OS

PFS

	D+T+CT	CT
Events, n/N (%)	238/338 (70.4)	258/337 (76.6)
mPFS, months	6.2	4.8
(95% CI)	(5.0–6.5)	(4.6–5.8)
HR (95% CI)	0.72 (0.60–0.86)	
p-value	0.00031	

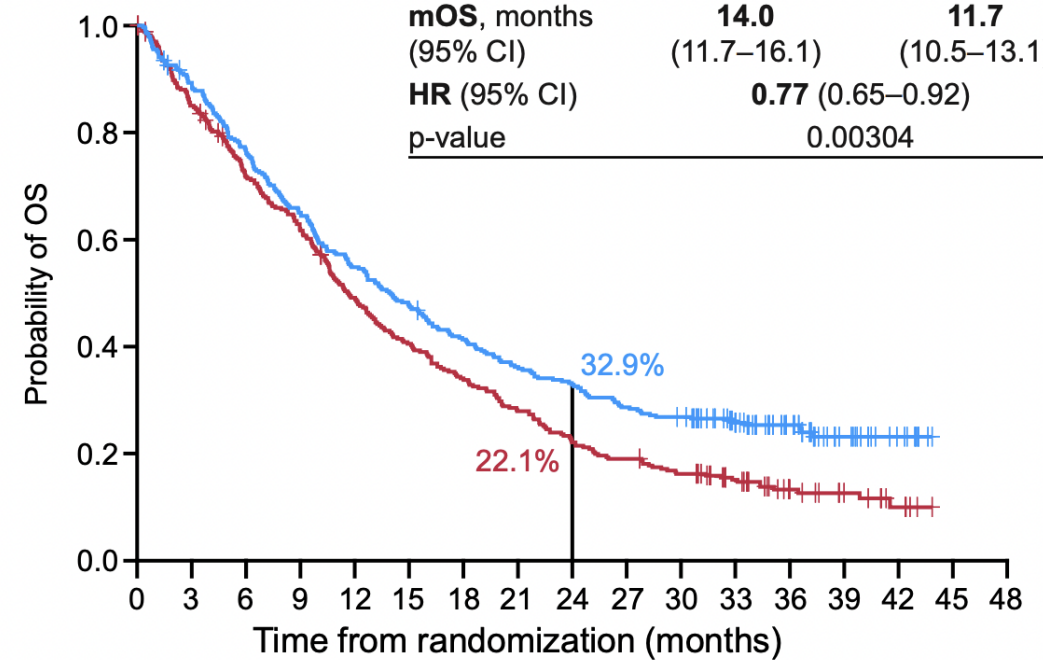


No. at risk	0	3	6	9	12	15	18	21	24
D+T+CT	338	243	161	94	56	32	13	5	0
CT	337	219	121	43	23	12	3	2	0

- Median follow-up in censored patients at DCO: 10.3 months (range 0–23.1)

OS

	D+T+CT	CT
Events, n/N (%)	251/338 (74.3)	285/337 (84.6)
mOS, months	14.0	11.7
(95% CI)	(11.7–16.1)	(10.5–13.1)
HR (95% CI)	0.77 (0.65–0.92)	
p-value	0.00304	



No. at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48
D+T+CT	338	298	256	217	183	159	137	120	109	95	88	64	41	20	9	0	0
CT	337	284	236	204	160	132	111	91	72	62	52	38	21	13	6	0	0

- Median follow-up in censored patients at DCO: 34.9 months (range 0–44.5)

Outcomes in Patients with Non-Squamous Histology

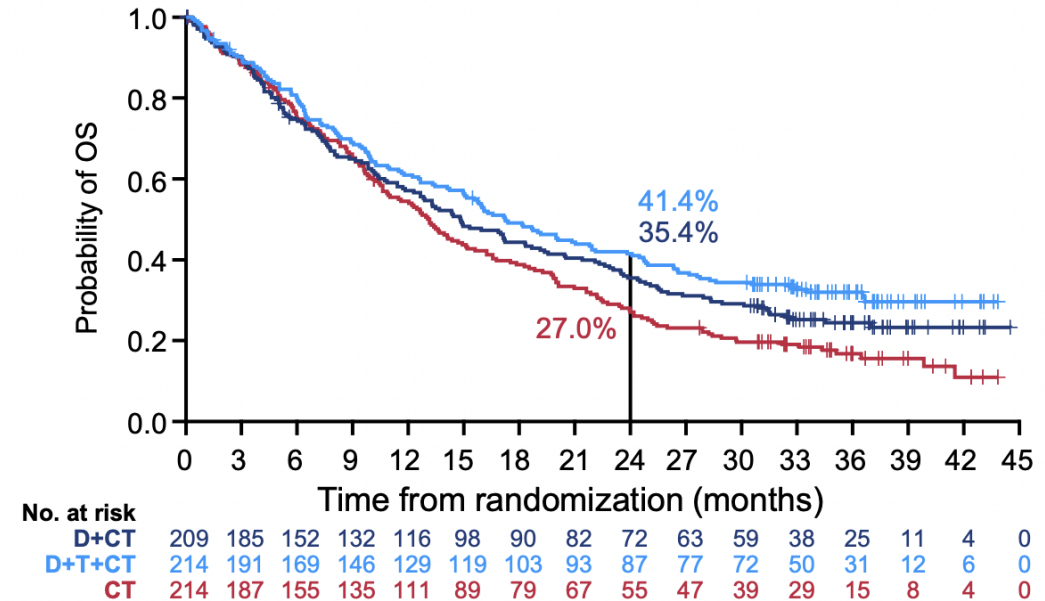
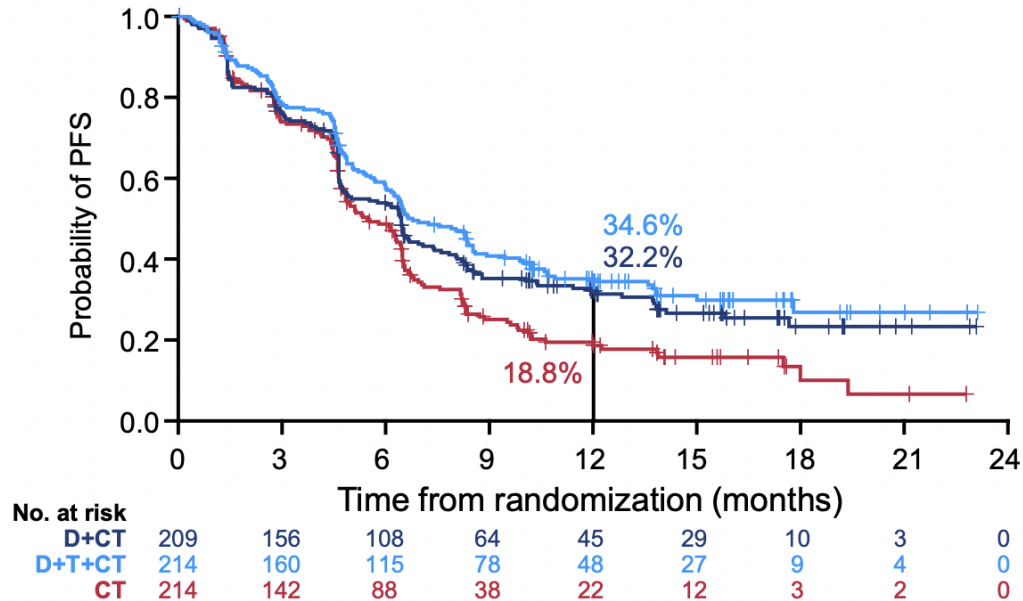
95.5% of patients with non-squamous histology receiving CT had pemetrexed + platinum

PFS and ORR

	D+CT	D+T+CT	CT
Events, n/N (%)	144/209 (68.9)	136/214 (63.6)	154/214 (72.0)
mPFS, months (95% CI)	6.4 (4.7–7.4)	6.8 (6.1–8.5)	5.5 (4.8–6.4)
HR* (95% CI)	0.77 (0.61–0.96)	0.66 (0.52–0.84)	–
Confirmed ORR†, % (n/N)	44.3 (90/203)	45.5 (96/211)	23.7 (50/211)
mDoR†, months (95% CI)	10.6 (6.6–NE)	16.4 (9.3–NE)	6.0 (4.4–8.7)

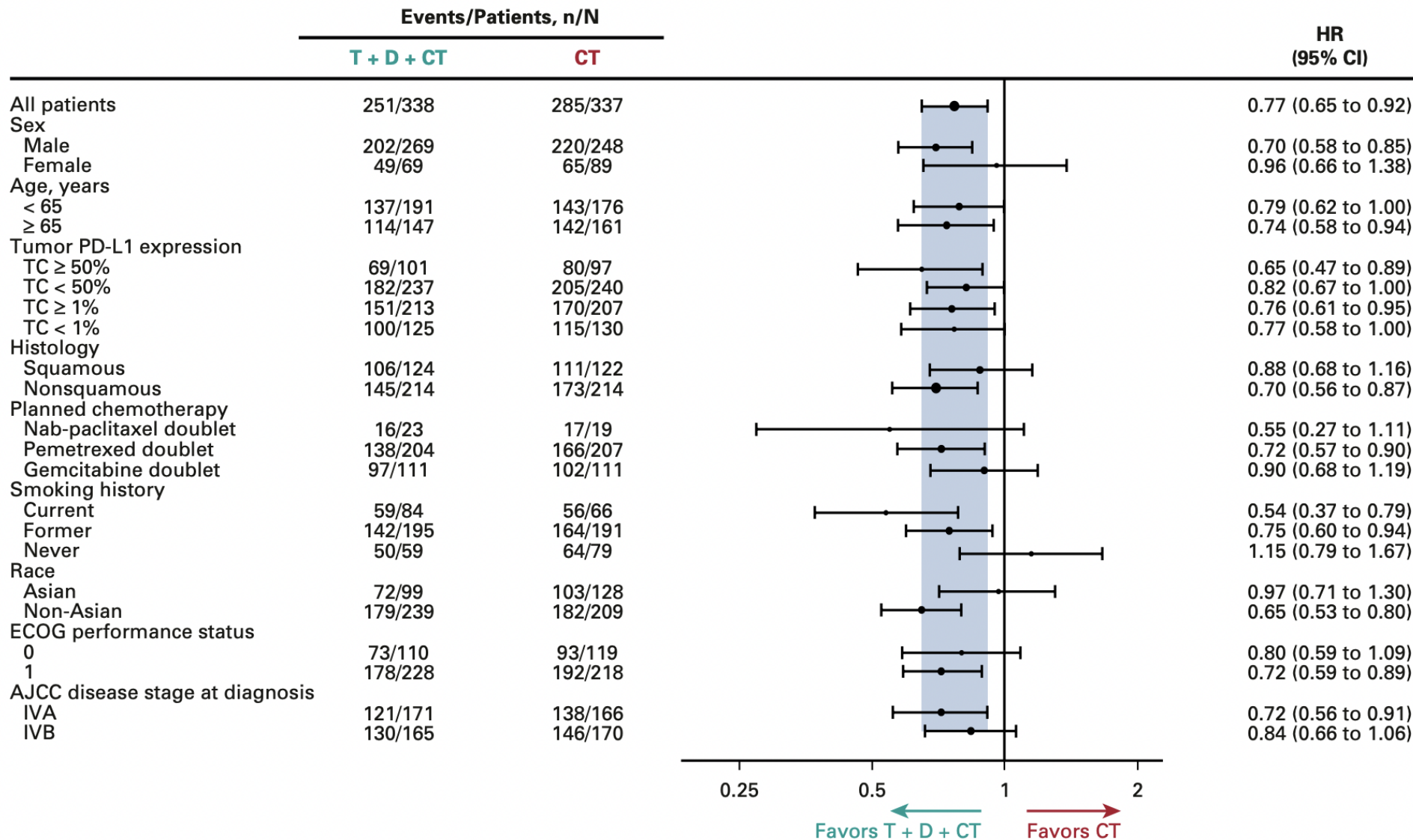
OS

	D+CT	D+T+CT	CT
Events, n/N (%)	154/209 (73.7)	145/214 (67.8)	173/214 (80.8)
mOS, months (95% CI)	14.8 (11.8–18.3)	17.2 (14.9–21.8)	13.1 (10.6–15.1)
HR* (95% CI)	0.82 (0.66–1.03)	0.70 (0.56–0.87)	–



Personalizando a imunoterapia de primeira linha no câncer de pulmão - Caso Clínico: Eu faço POSEIDON

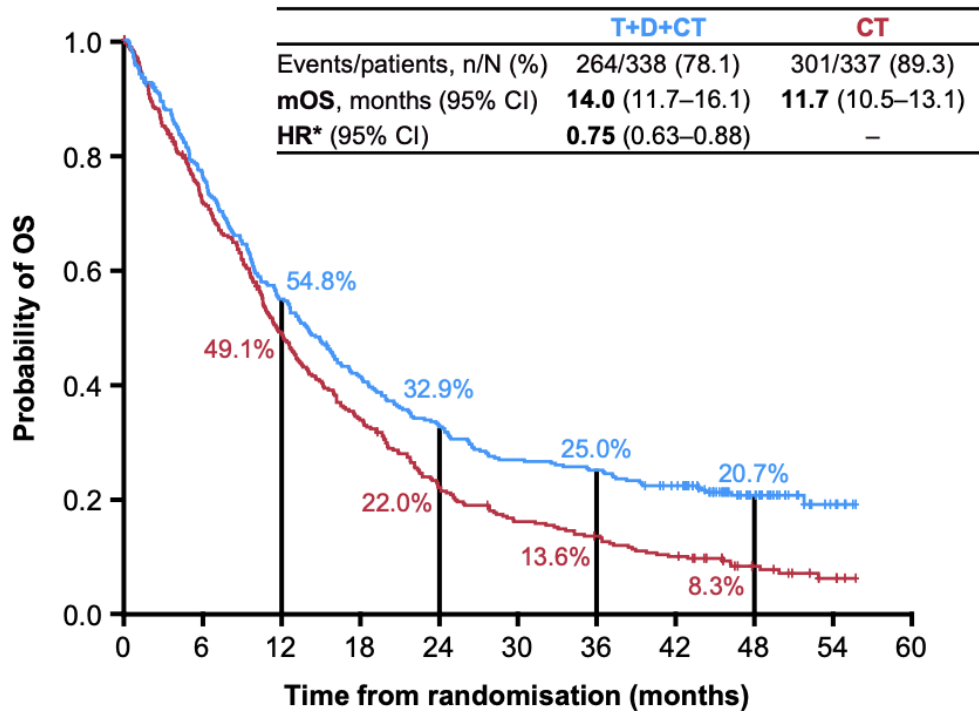
Por Que POSEIDON?



OS Update

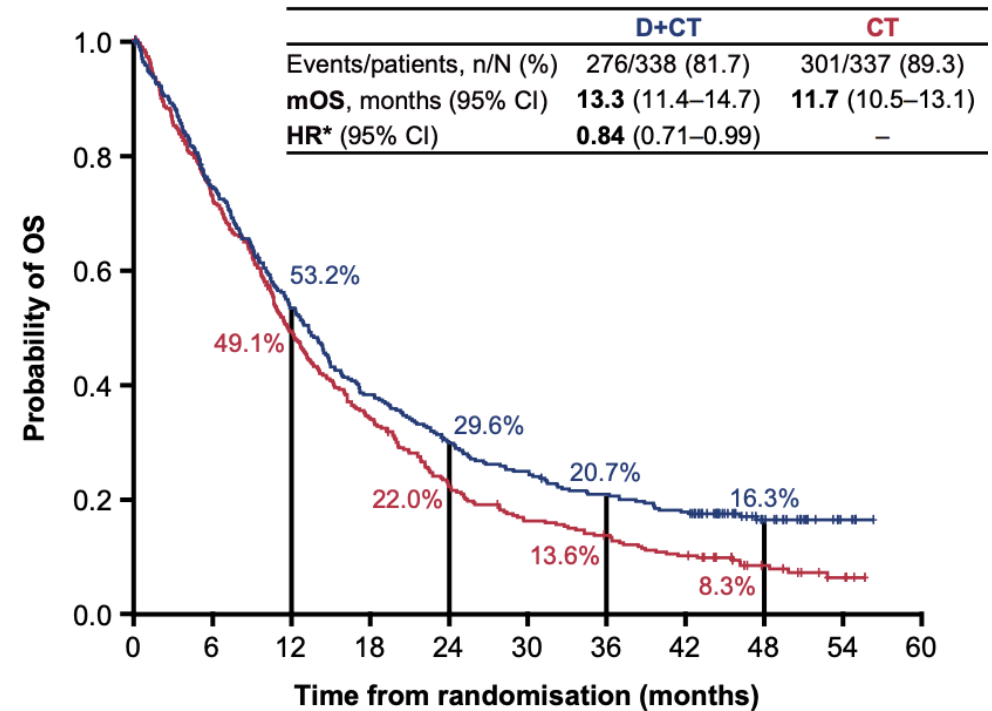
Durable long-term OS benefit for T+D+CT vs CT with HR 0.75 and estimated 25.0% alive at 3 yrs vs 13.6%

T+D+CT vs CT



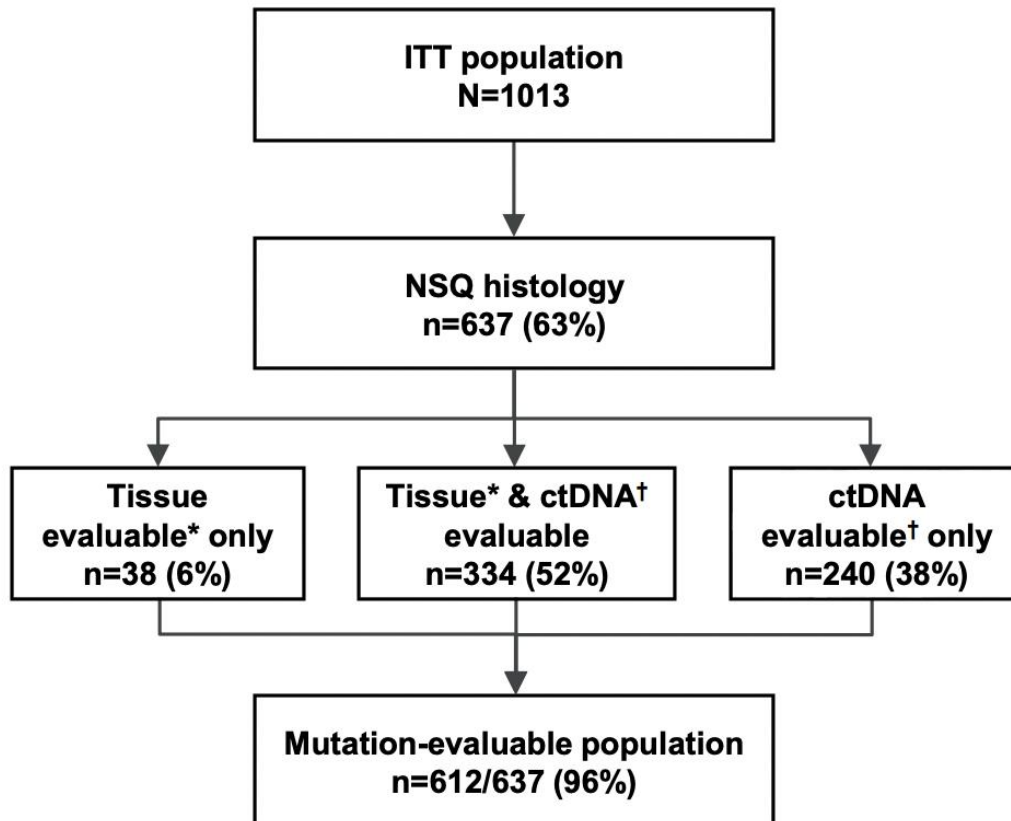
No. at risk		0	6	12	18	24	30	36	42	48	54	60
T+D+CT	338	256	183	137	109	89	83	70	32	6	0	
CT	337	236	160	111	71	51	42	31	14	5	0	

D+CT vs CT

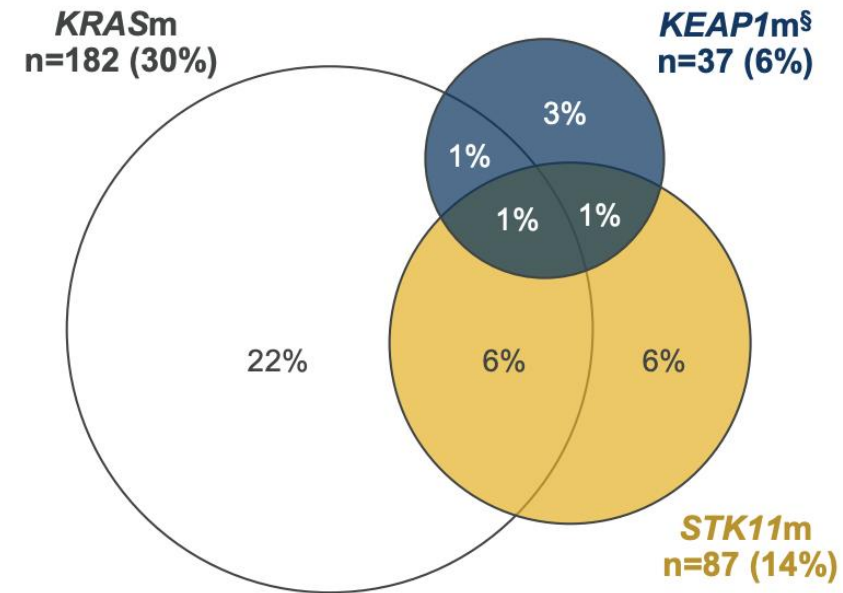


No. at risk		0	6	12	18	24	30	36	42	48	54	60
D+CT	338	247	176	126	97	81	67	57	26	5	0	
CT	337	236	160	111	71	51	42	31	14	5	0	

Prevalence of *STK11*, *KEAP1* and *KRAS* Mutations in Patients from POSEIDON with NSQ Histology

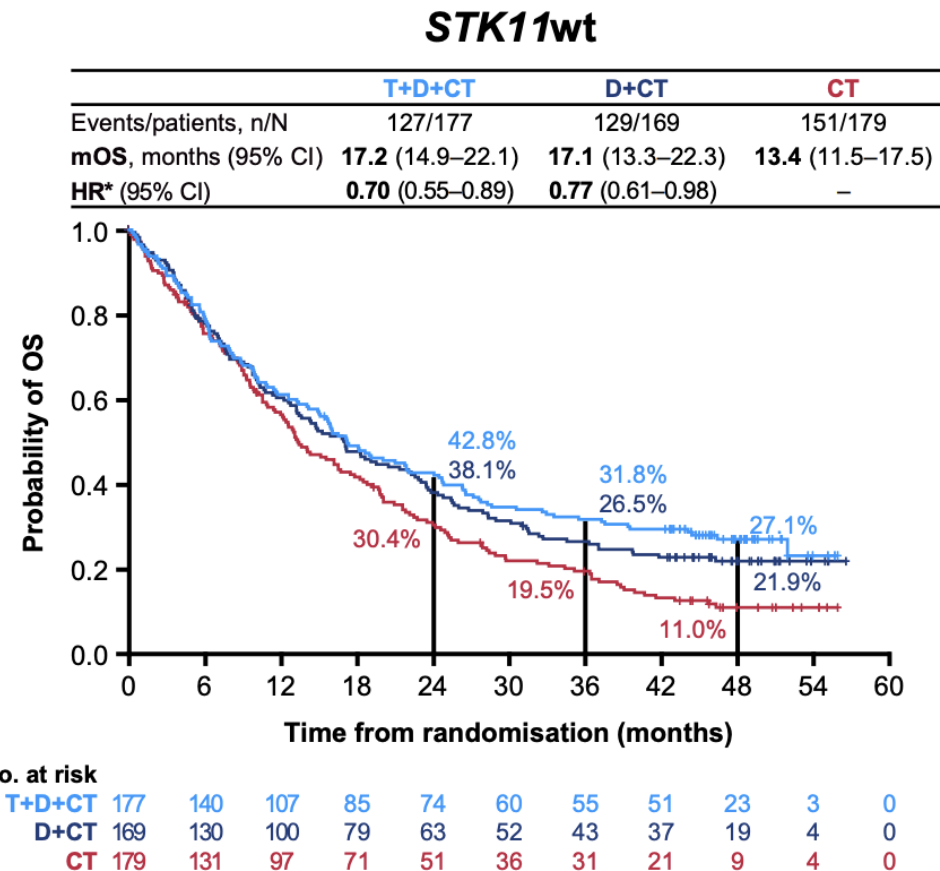
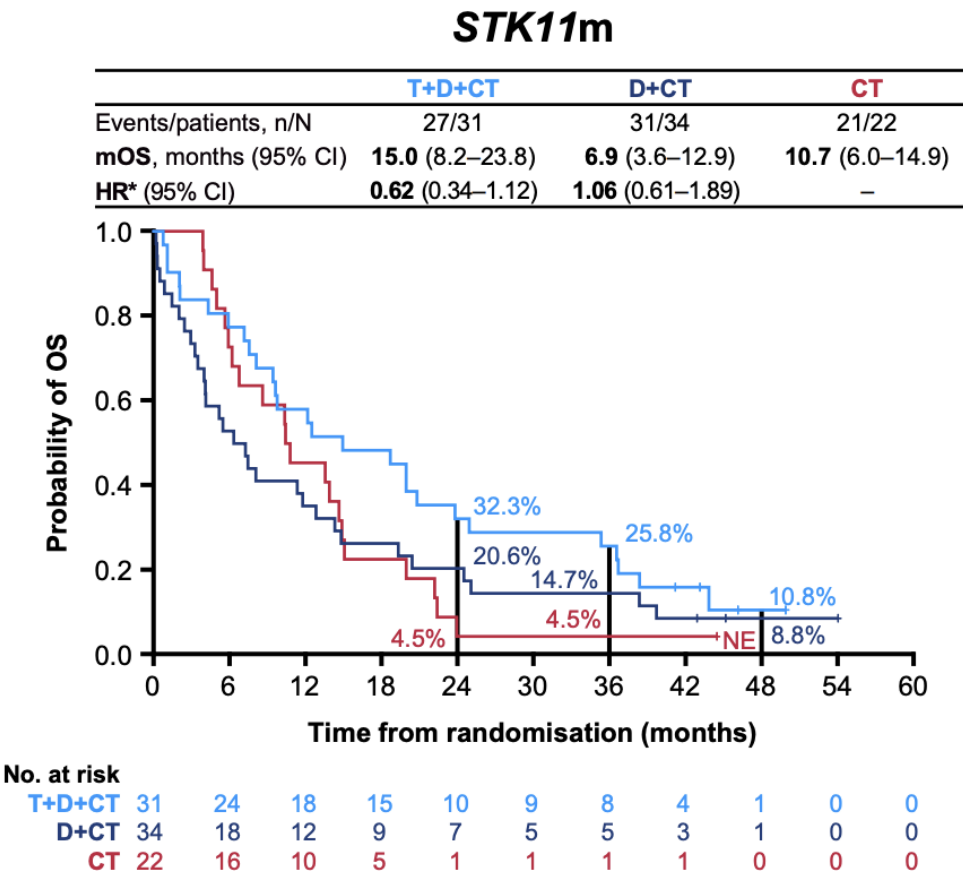


Mutation-evaluable population[‡]
(n=612; **96%** of randomised patients with NSQ histology)

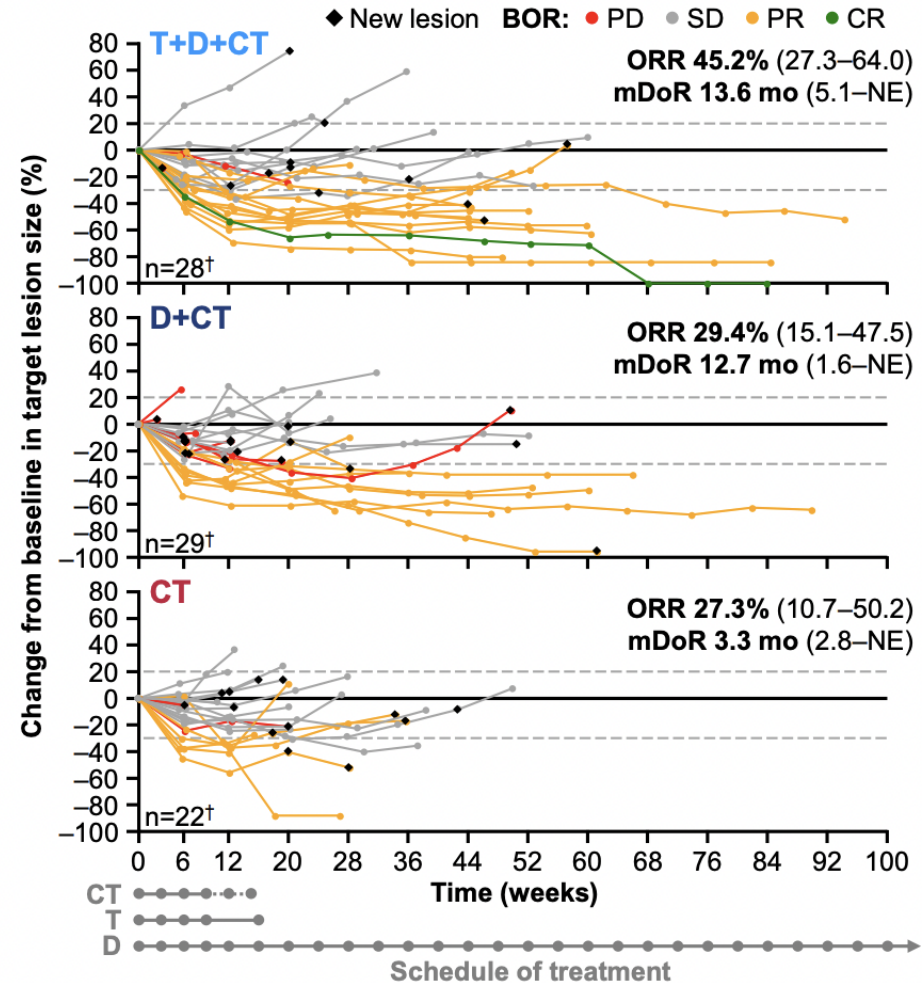
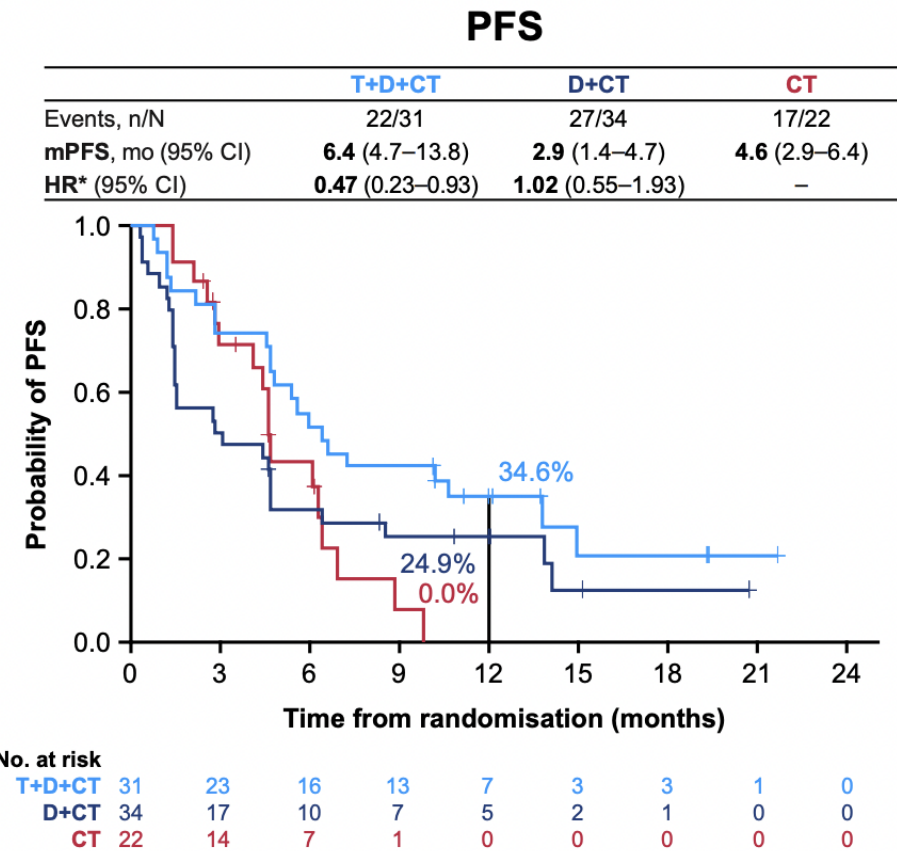


Updated OS by *STK11* Mutation Status

OS benefit observed for T+D+CT vs CT in *STK11*m with HR 0.62 and estimated 25.8% alive at 3 yrs vs 4.5%



PFS and Response in *STK11m* Subgroup



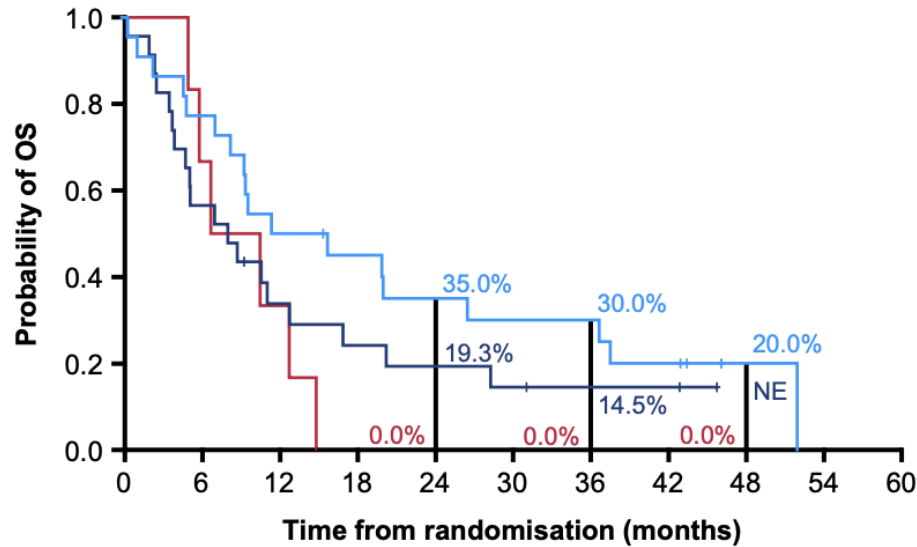
BOR, best objective response; CR, complete response; mDoR; median duration of response; mPFS, median PFS; NE, not estimable; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease

Updated OS by *KEAP1* Mutation Status

OS benefit observed for T+D+CT vs CT in *KEAP1*m with HR 0.43 (small sample size)

*KEAP1*m

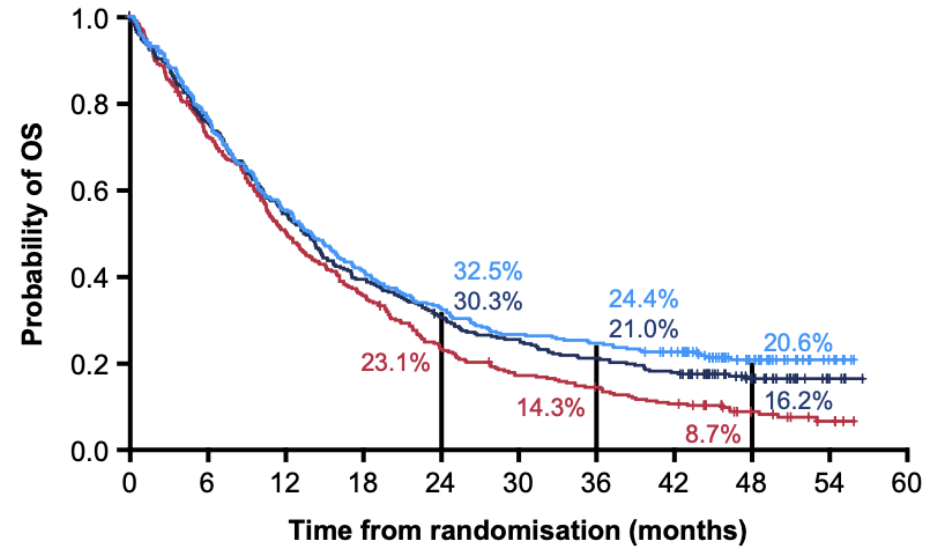
	T+D+CT	D+CT	CT
Events/patients, n/N	18/22	19/23	6/6
mOS, months (95% CI)	13.7 (7.2–26.5)	8.1 (4.0–12.9)	8.7 (5.1–NE)
HR* (95% CI)	0.43 (0.16–1.25)	0.77 (0.31–2.15)	–



No. at risk	0	6	12	18	24	30	36	42	48	54	60
T+D+CT	22	17	11	9	7	6	6	4	1	0	0
D+CT	23	13	7	5	4	3	2	2	0	0	0
CT	6	4	2	0	0	0	0	0	0	0	0

*KEAP1*wt

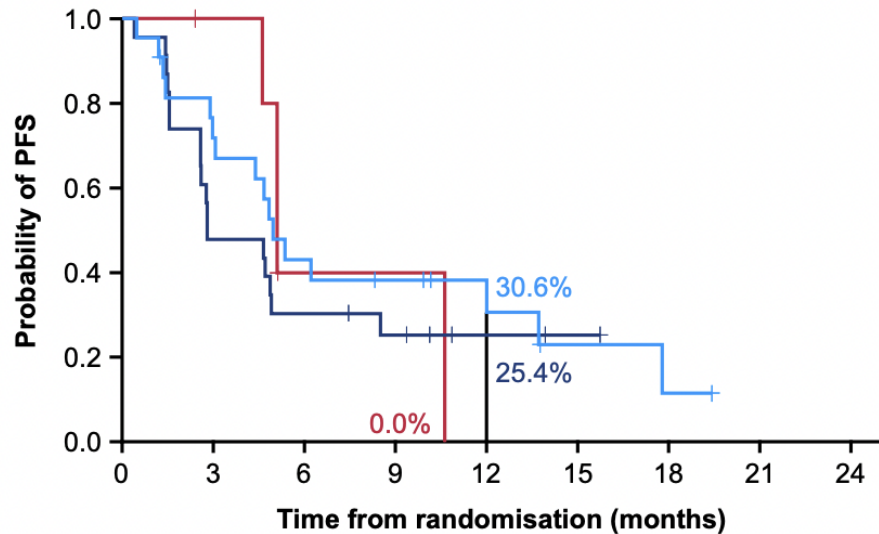
	T+D+CT	D+CT	CT
Events/patients, n/N	236/303	253/307	278/312
mOS, months (95% CI)	14.0 (11.8–16.1)	13.5 (11.7–14.9)	12.2 (10.6–13.9)
HR* (95% CI)	0.75 (0.63–0.89)	0.81 (0.69–0.97)	–



No. at risk	0	6	12	18	24	30	36	42	48	54	60
T+D+CT	303	230	165	123	97	79	73	63	30	6	0
D+CT	307	230	165	119	91	76	63	53	26	5	0
CT	312	221	153	108	69	50	41	30	14	5	0

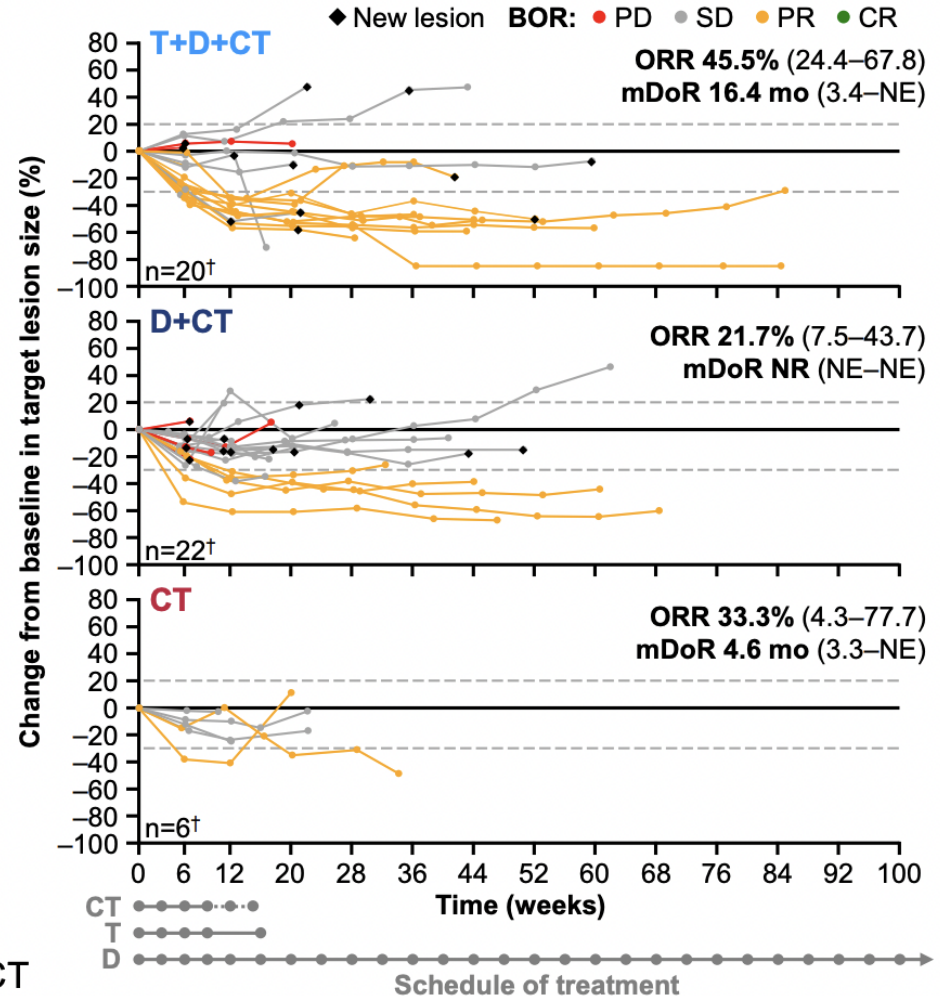
PFS and Response in *KEAP1m* Subgroup

	T+D+CT	D+CT	CT
Events, n/N	16/22	17/23	4/6
mPFS, mo (95% CI)	5.0 (3.0–13.7)	2.8 (2.6–4.9)	5.1 (4.6–NE)
HR* (95% CI)	0.94 (0.33–3.35)	1.51 (0.55–5.25)	–

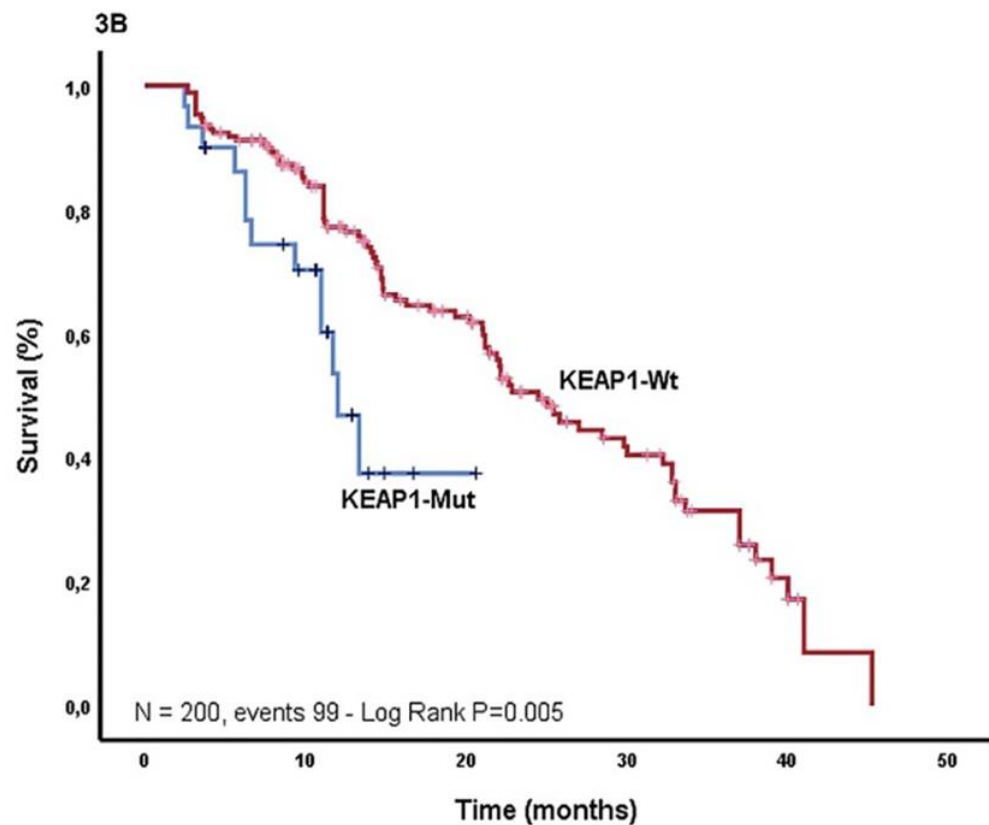
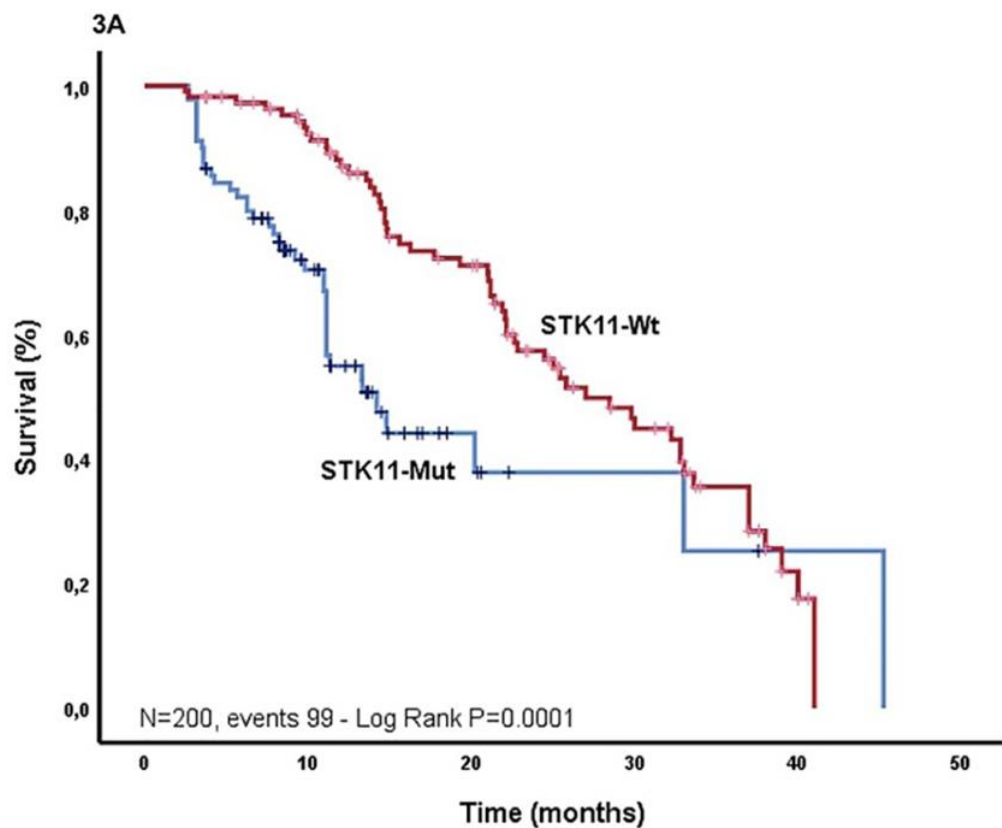


No. at risk	0	3	6	9	12	15	18	21	24
T+D+CT	22	15	9	7	4	2	1	0	0
D+CT	23	11	7	5	2	1	0	0	0
CT	6	5	1	1	0	0	0	0	0

NSQ: HR vs CT 0.61 (0.20–2.29) T+D+CT; 1.18 (0.40–4.29) D+CT



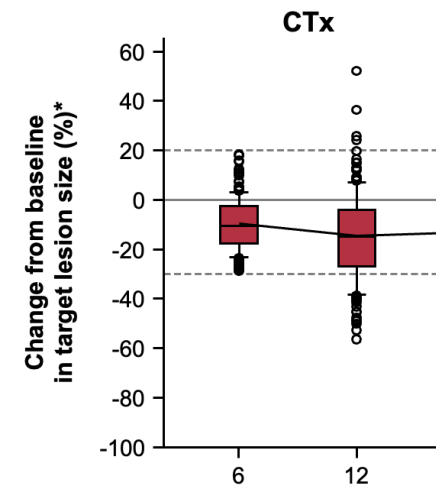
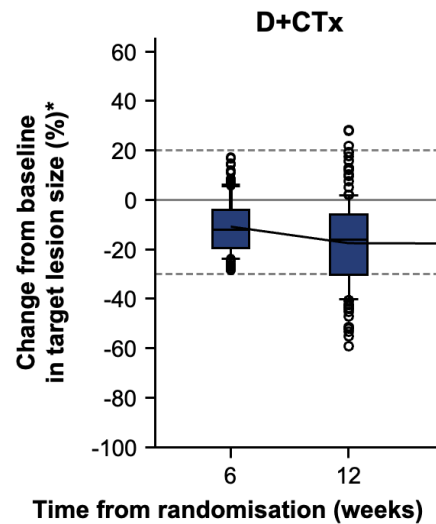
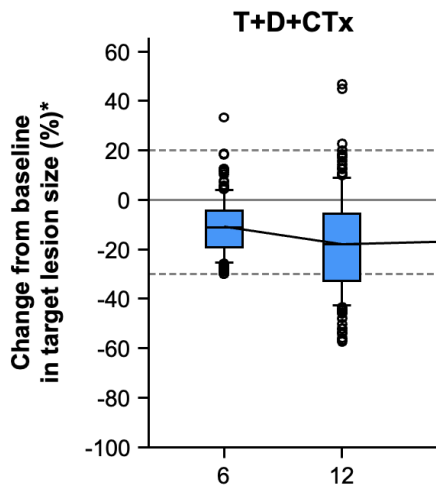
STRIKE Registry – Avaliação do impacto de mutações em STK11 e KEAP1 na população latino-americana.



Response by CTx cycle: patients with SD after C2

22.9% improved to PR after C4 and a reduction in median target lesion size occurred vs C2 in all arms

	T+D+CTx	D+CTx	CTx	Total
SD after C2 and PR after C4, n/N	47/180	42/179	39/201	128/560
% (95% CI)	26.1 (19.9–33.2)	23.5 (17.5–30.4)	19.4 (14.2–25.6)	22.9 (19.4–26.6)
Median change from baseline in target lesion size,* %				
C2	-11.15	-12.20	-10.60	–
C4	-18.00	-16.10	-14.95	–

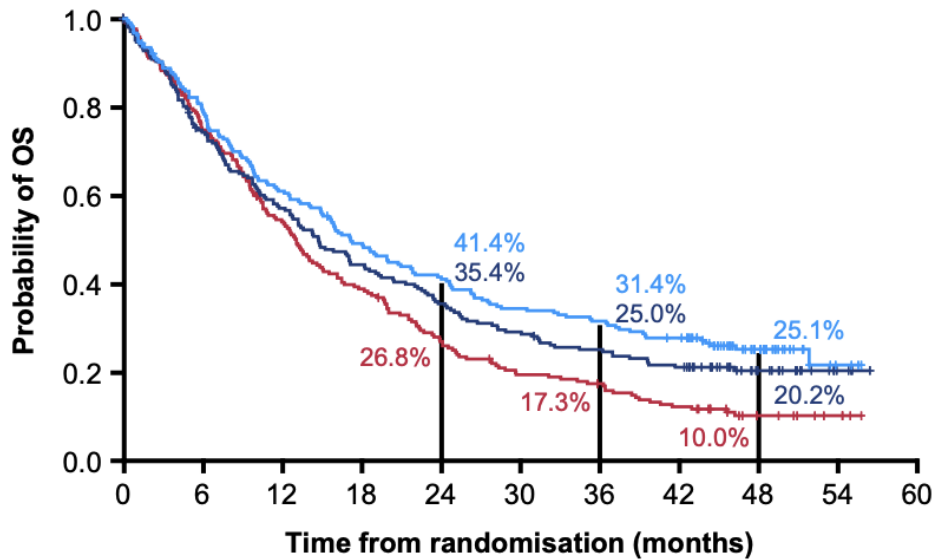


Updated OS by Histology

OS benefit with T+D+CT vs CT more pronounced in NSQ with HR 0.68 and estimated 31.4% alive at 3 yrs vs 17.3%

NSQ

	T+D+CT	D+CT	CT
Events/patients, n/N	158/214	162/209	183/214
mOS, months (95% CI)	17.2 (14.9–21.8)	14.8 (11.8–18.3)	13.1 (10.6–15.1)
HR* (95% CI)	0.68 (0.55–0.85)	0.80 (0.64–0.98)	–

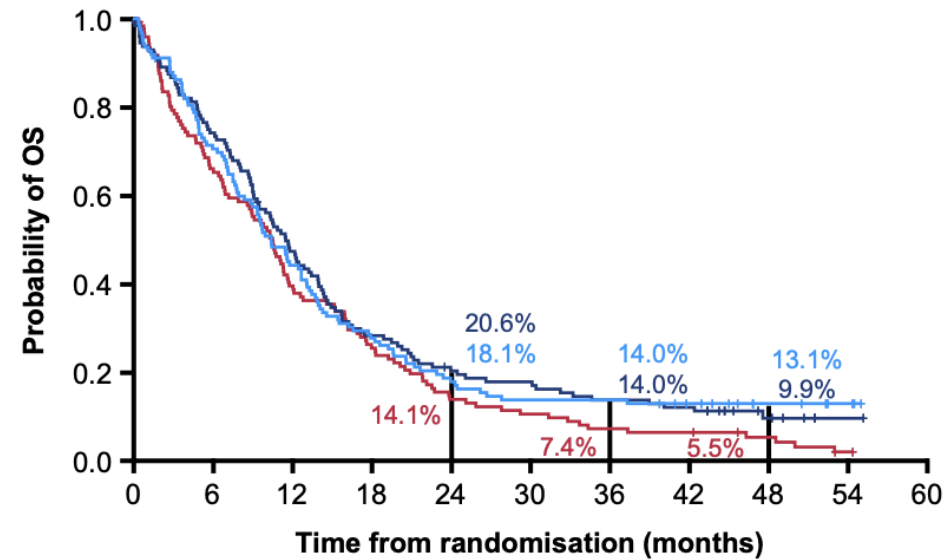


No. at risk

T+D+CT	214	169	129	103	87	72	66	57	25	3	0
D+CT	209	152	116	90	72	59	50	42	20	4	0
CT	214	155	111	79	54	38	33	23	9	4	0

SQ

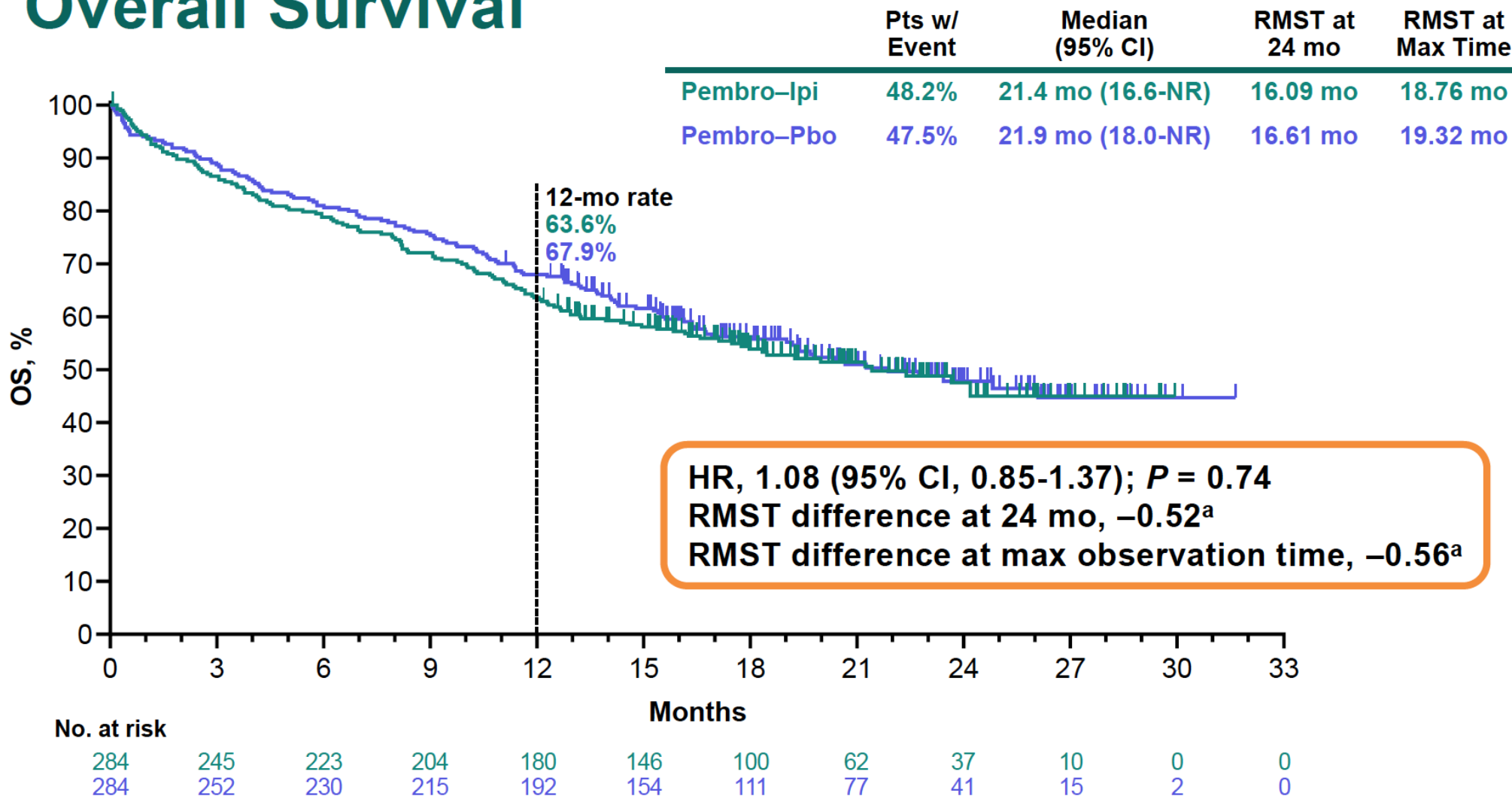
	T+D+CT	D+CT	CT
Events/patients, n/N	106/124	113/128	117/122
mOS, months (95% CI)	10.4 (8.4–12.7)	11.5 (9.4–14.0)	10.5 (8.0–11.7)
HR* (95% CI)	0.83 (0.64–1.08)	0.81 (0.63–1.06)	–

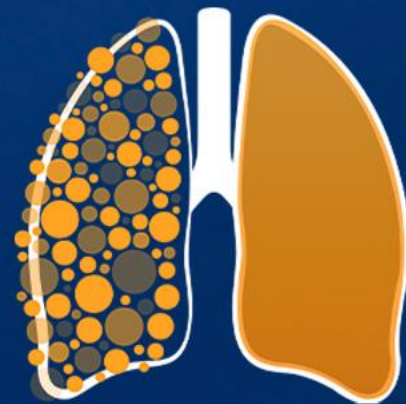


No. at risk

T+D+CT	124	87	54	34	22	17	17	13	7	3	0
D+CT	128	95	60	36	25	22	17	15	6	1	0
CT	122	80	48	32	17	13	9	8	5	1	0

Overall Survival





12º SIMPÓSIO
INTERNACIONAL DE

CÂNCER DE
PULMÃO

2ª JORNADA ONCONNECTION MULTICARE

2024

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GERENCIAMENTO E PRODUÇÃO

