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Is Perioperative Immunotherapy the New Standard of Care?

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What is the Gold Standard for Clinical Trial Outcomes?

--Overall Survival--

What is the Main Goal Desired by Patients With NSCLC?

--The treatment that helps them live longest--

Randomized Phase III Trials, Resectable NSCLC

	Perioperative Treatment?	EFS HR	OS HR
CM 816	No	0.63	?
KN-671	Y	0.59	0.72
CM 77T	Y	0.58	?
AEGEAN	Y	0.68	?
RATIONALE-315	Y	0.56	0.62 (Interim Analysis)

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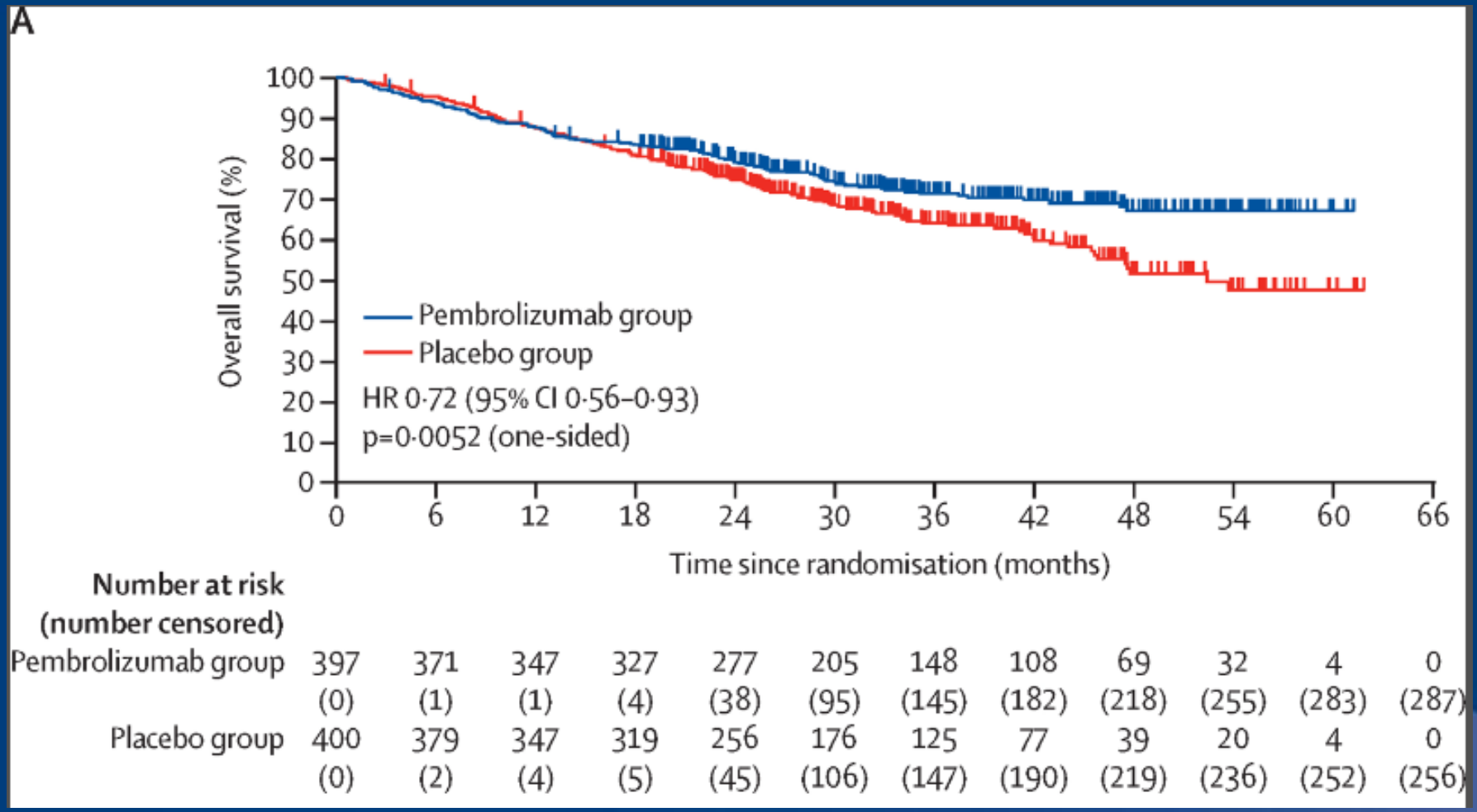
KEYNOTE-671 Overall Survival



Number at risk (number censored)												
Pembrolizumab group	397 (0)	371 (1)	347 (1)	327 (4)	277 (38)	205 (95)	148 (145)	108 (182)	69 (218)	32 (255)	4 (283)	0 (287)
Placebo group	400 (0)	379 (2)	347 (4)	319 (5)	256 (45)	176 (106)	125 (147)	77 (190)	39 (219)	20 (236)	4 (252)	0 (256)

Spicer J et al, Lancet 2024

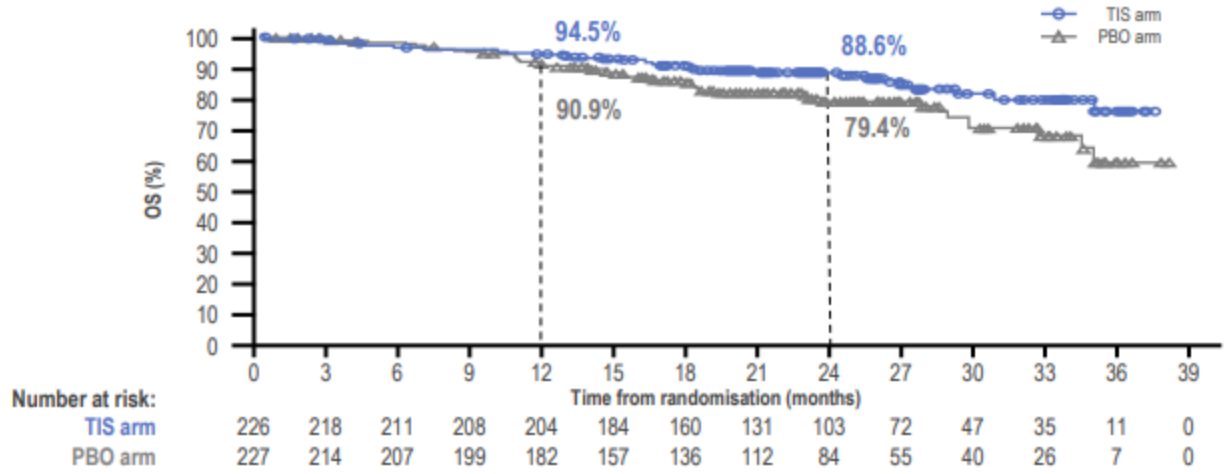
RATIONALE-315 Overall Survival

Overall Survival

BARCELONA 2024 ESMO congress

ITT Analysis Set

	Events (%)	Median (95% CI), months	HR (95% CI)	*P*-value
TIS arm	31 (13.7)	NR (NE, NE)	**0.62 (0.39, 0.98)**	0.0193
PBO arm	45 (19.8)	NR (35.0, NE)		



Number at risk:														
TIS arm	226	218	211	208	204	184	160	131	103	72	47	35	11	0
PBO arm	227	214	207	199	182	157	136	112	84	55	40	26	7	0

An OS benefit trend (HR=0.62 [95% CI: 0.39, 0.98]; one-sided *P*=0.0193) was observed favouring perioperative TIS

OS was defined as the time from the date of randomisation to the date of death due to any cause.
Abbreviations: CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; NE, not evaluable; NR, not reached; OS, overall survival; PBO, placebo; TIS, tislelizumab.

Dongsheng Yue

Yue D et al, ESMO 2024

Questions From the Data

- Are the results definitely due to perioperative treatment?
  - Unknown
- Are the results specific to the immunotherapy (or chemotherapy) agent?
  - (Probably not)
- Are there specific subgroups that benefit more/less?
  - Most likely

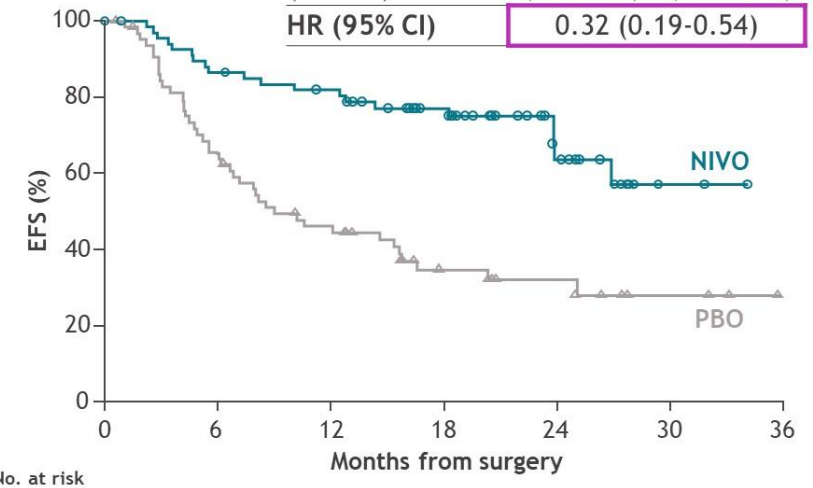
CM 77T, Evaluation of N2 Disease

CheckMate 77T: clinical outcomes with perioperative NIVO by nodal status

Landmark EFS from definitive surgery

Stage III N2

	NIVO (n = 70)	PBO (n = 66)
Median EFS, mo (95% CI)	NR (23.8-NR)	8.9 (6.1-15.6)
HR (95% CI)	0.32 (0.19-0.54)	

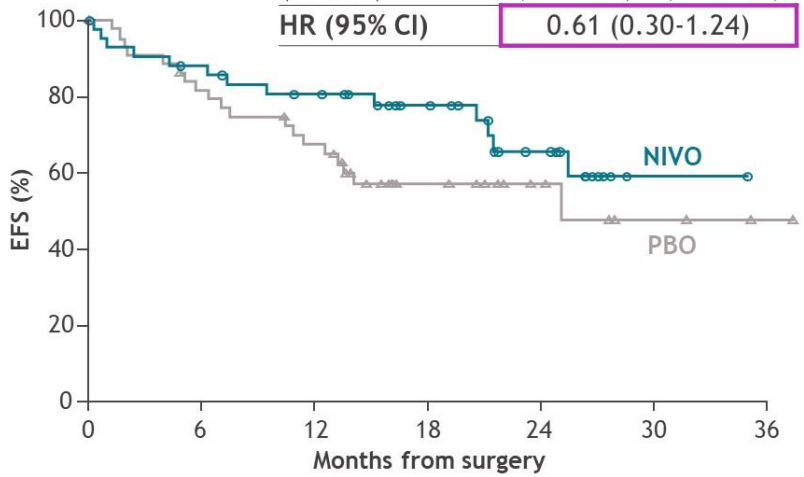


No. at risk

NIVO	70	58	52	37	16	3	0
PBO	66	41	27	14	8	3	0

Stage III non-N2

	NIVO (n = 45)	PBO (n = 45)
Median EFS, mo (95% CI)	NR (21.4-NR)	25.0 (12.5-NR)
HR (95% CI)	0.61 (0.30-1.24)	



	45	36	31	23	13	1	0
	45	35	28	13	7	3	1

Median follow-up (range): 25.4 months (15.7-44.2).

Cascone T et al, ASCO 2024

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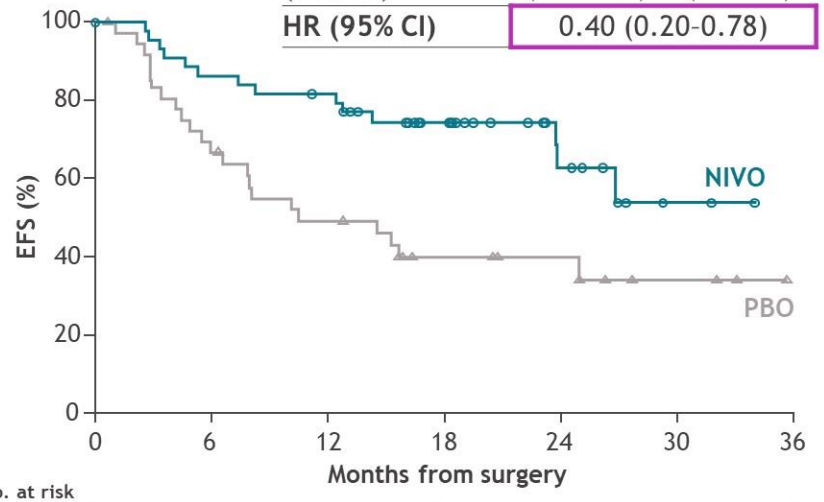
CM 77T, Evaluation **BY** N2 Disease

CheckMate 77T: clinical outcomes with perioperative NIVO by nodal status

Landmark EFS from definitive surgery

Stage III N2 single-station[a]

	NIVO (n = 45)	PBO (n = 37)
Median EFS, mo (95% CI)	NR (23.7-NR)	10.5 (6.0-NR)
HR (95% CI)	0.40 (0.20-0.78)	

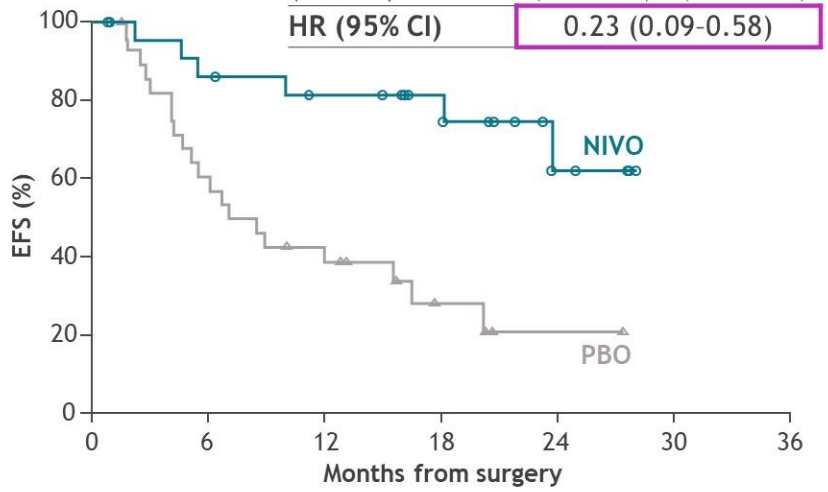


No. at risk

NIVO	45	38	35	24	11	3	0
PBO	37	24	17	10	7	3	0

Stage III N2 multi-station[a]

	NIVO (n = 24)	PBO (n = 29)
Median EFS, mo (95% CI)	NR (18.2-NR)	7.8 (4.7-16.5)
HR (95% CI)	0.23 (0.09-0.58)	



	24	19	16	12	4	0	0
	29	17	10	4	1	0	0

Median follow-up (range): 25.4 months (15.7-44.2). [a]N2 subcategory was not reported in 1 patient in the NIVO arm.

Cascone T et al, ASCO 2024

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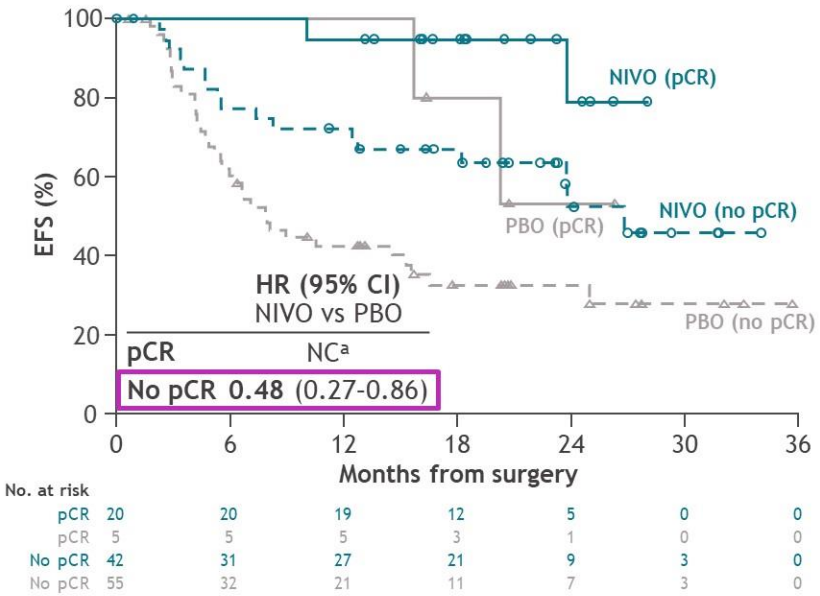
CM 77T, Evaluation by pCR

Landmark EFS from definitive surgery by pCR status

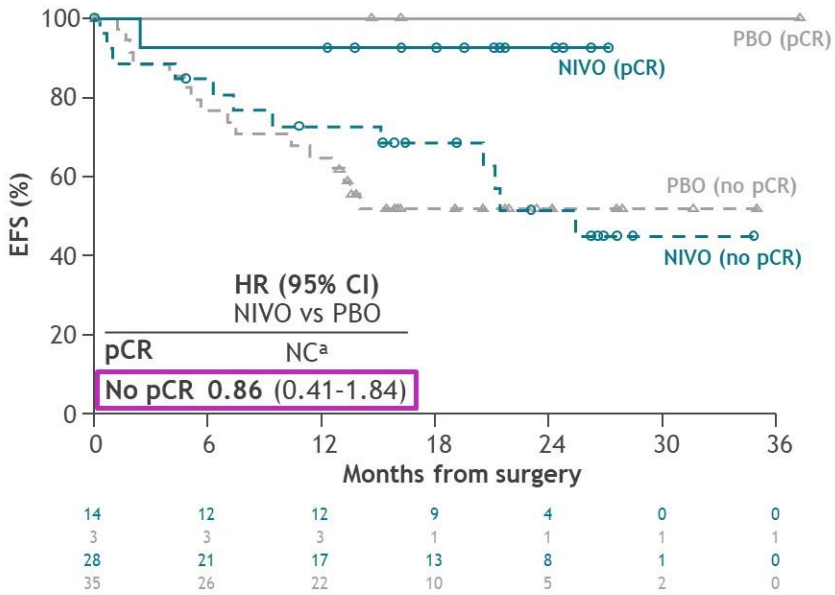
Stage III N2



No. at risk

pCR	20	20	19	12	5	0	0
pCR	5	5	5	3	1	0	0
No pCR	42	31	27	21	9	3	0
No pCR	55	32	21	11	7	3	0

Stage III non-N2



	14	12	12	9	4	0	0
	3	3	3	1	1	1	1
	28	21	17	13	8	1	0
	35	26	22	10	5	2	0

Landmark EFS HRs for no pCR[a]: 0.59[b] (single-station N2) and 0.36[c] (multi-station N2)[d]

Median follow-up (range): 25.4 months (15.7-44.2). [a]HRs were NC for patients with pCR as there were < 10 patients in either treatment arm. [b,c]95% CI: [b]0.29-1.20; [c]0.12-1.09. [d]N2 subcategory was not reported in 1 patient in the NIVO arm.

Cascone T et al, ASCO 2024

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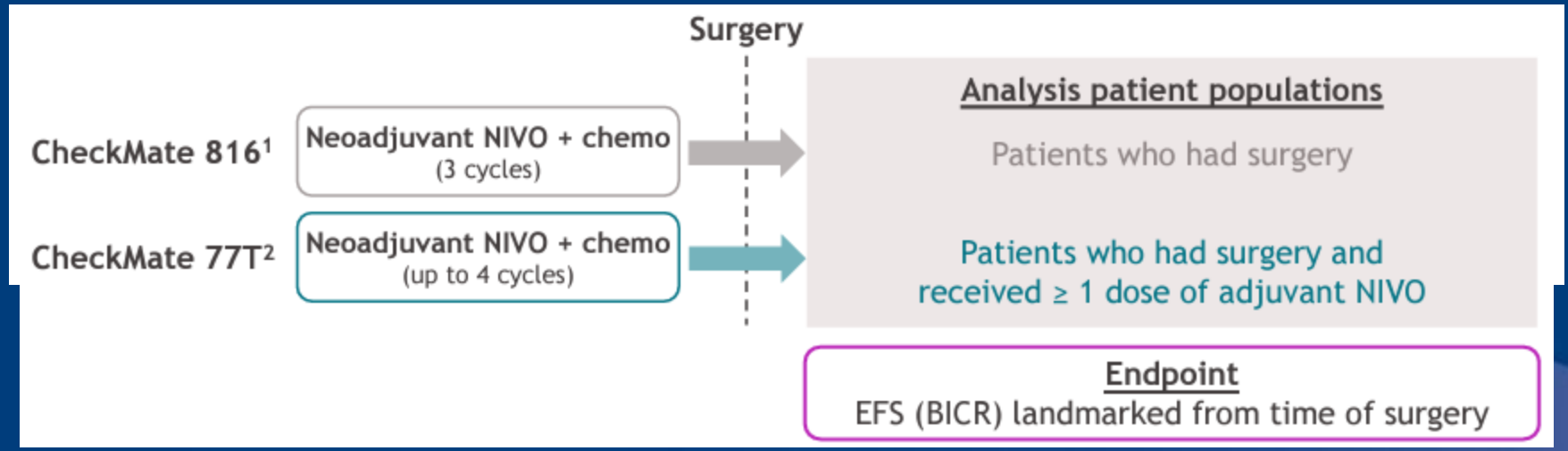
Questions From the Data

- Do the results prove benefit of perioperative treatment?
  - No, but intriguing evidence
- Does this give information to select who gets adjuvant immunotherapy?
  - Not yet

2024 World Conference on Lung Cancer
SEPTEMBER 7-10, 2024 | SAN DIEGO, CA USA

Perioperative vs neoadjuvant nivolumab for resectable NSCLC: patient-level data analysis of CheckMate 77T vs CheckMate 816

Patrick M. Forde,[1] Solange Peters,[2] Jessica Donington,[3] Stephanie Meadows-Shropshire,[4] Phuong Tran,[4] Stefano Lucherini,[5] Cinthya Coronado Erdmann,[6] Hong Sun,[6] Tina Cascone[7]



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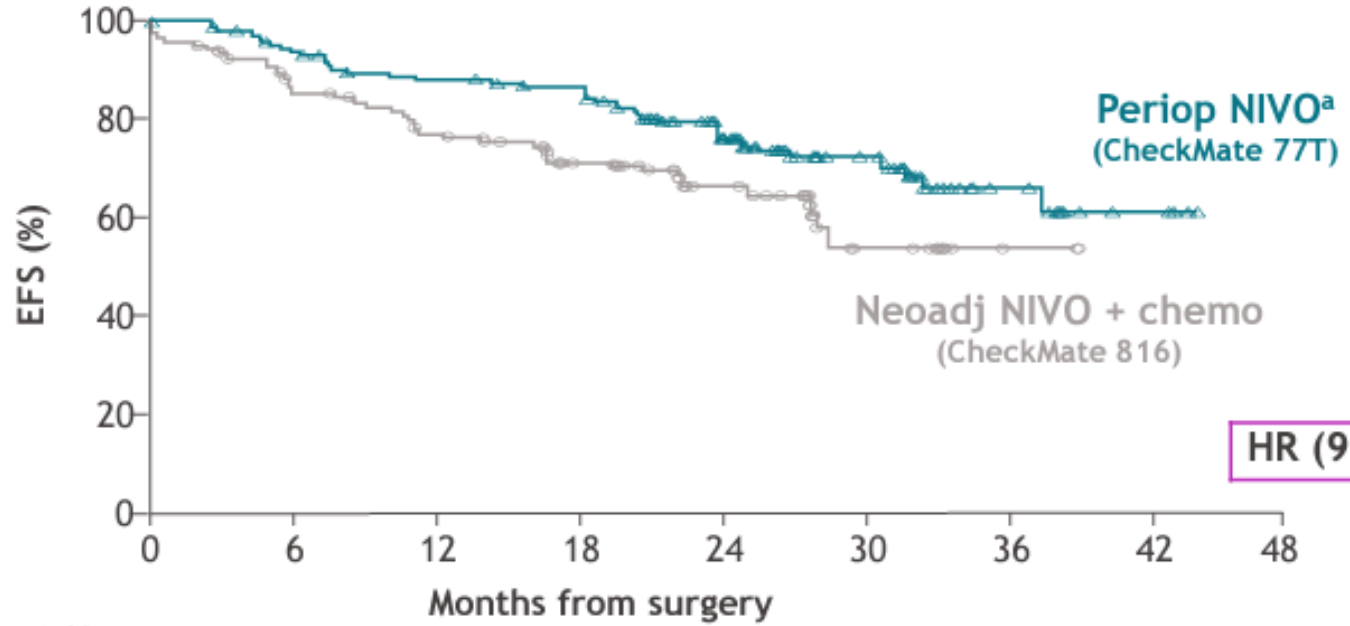
CM 816 v CM 77T: Meta-Analysis

Landmark EFS (BICR) from definitive surgery



	Weighted (ATE)[b]	
	Periop NIVO[a] (n = 139.4[c])	Neoadj NIVO + chemo (n = 147.5[c])
HR (95% CI)	0.61 (0.39-0.97)	

No. at risk

Periop NIVO	139.4	128.0	118.1	112.9	79.7	42.5	13.0	3.1	0
Neoadj N+C	147.5	121.0	106.2	84.2	39.1	12.1	2.2	0	0

- HR (95% CI): ATT[d] weighted analysis, 0.56 (0.35-0.90); unweighted analysis, 0.59 (0.38-0.92)

Forde P et al, IASLC WCLC 2024

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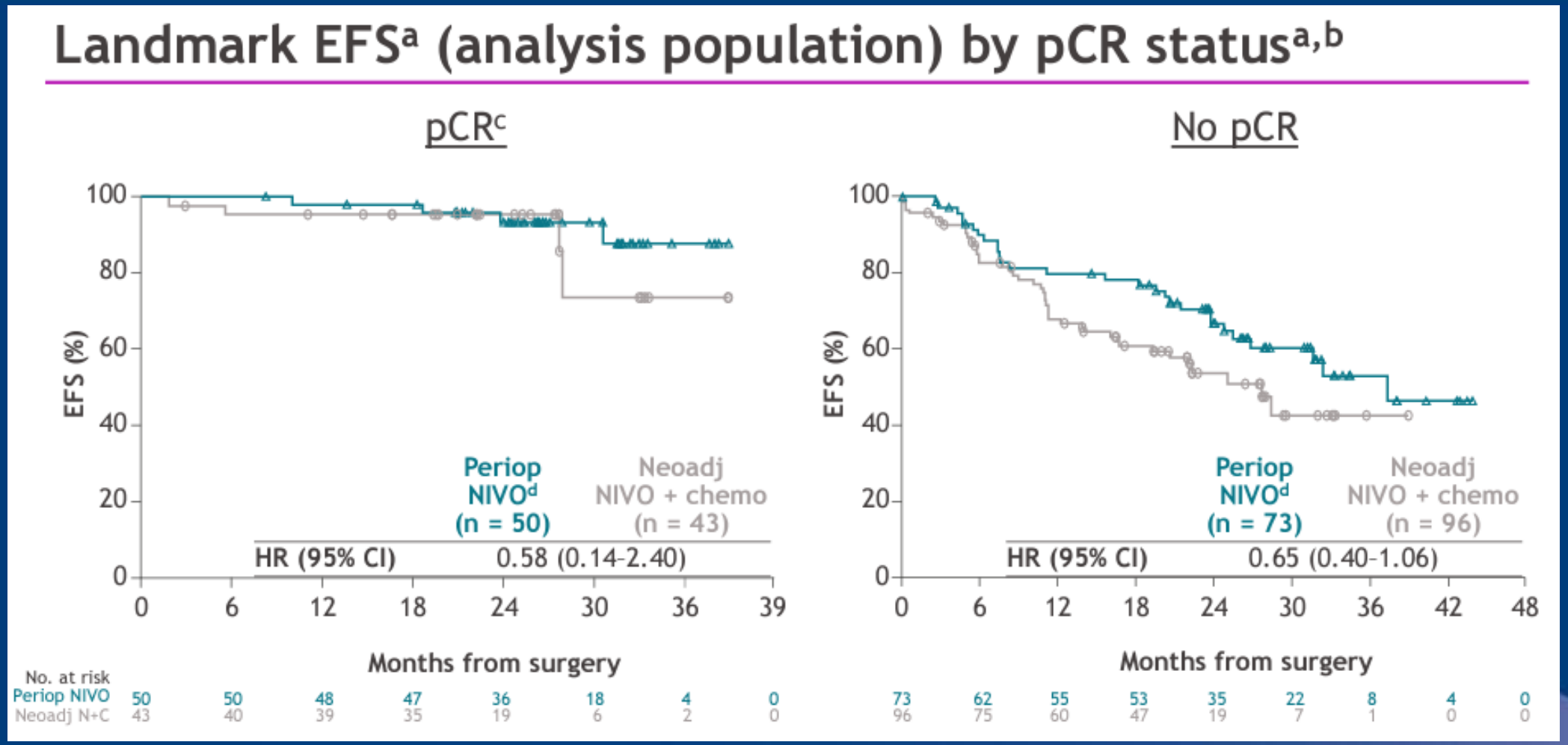
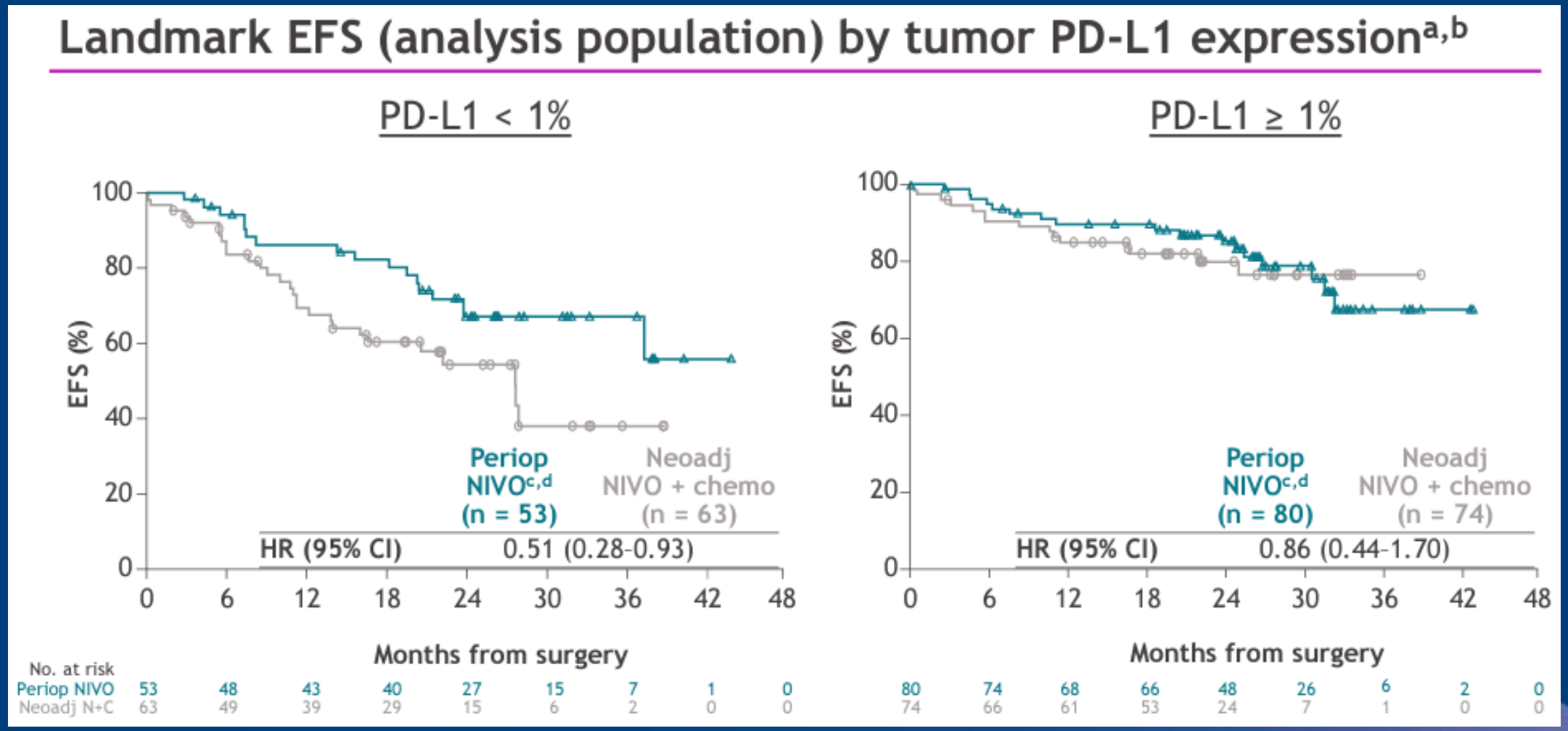
CM 816 v CM 77T: Meta-Analysis



Forde P et al, IASLC WCLC 2024

CM 816 v CM 77T: Meta-Analysis



Forde P et al, IASLC WCLC 2024

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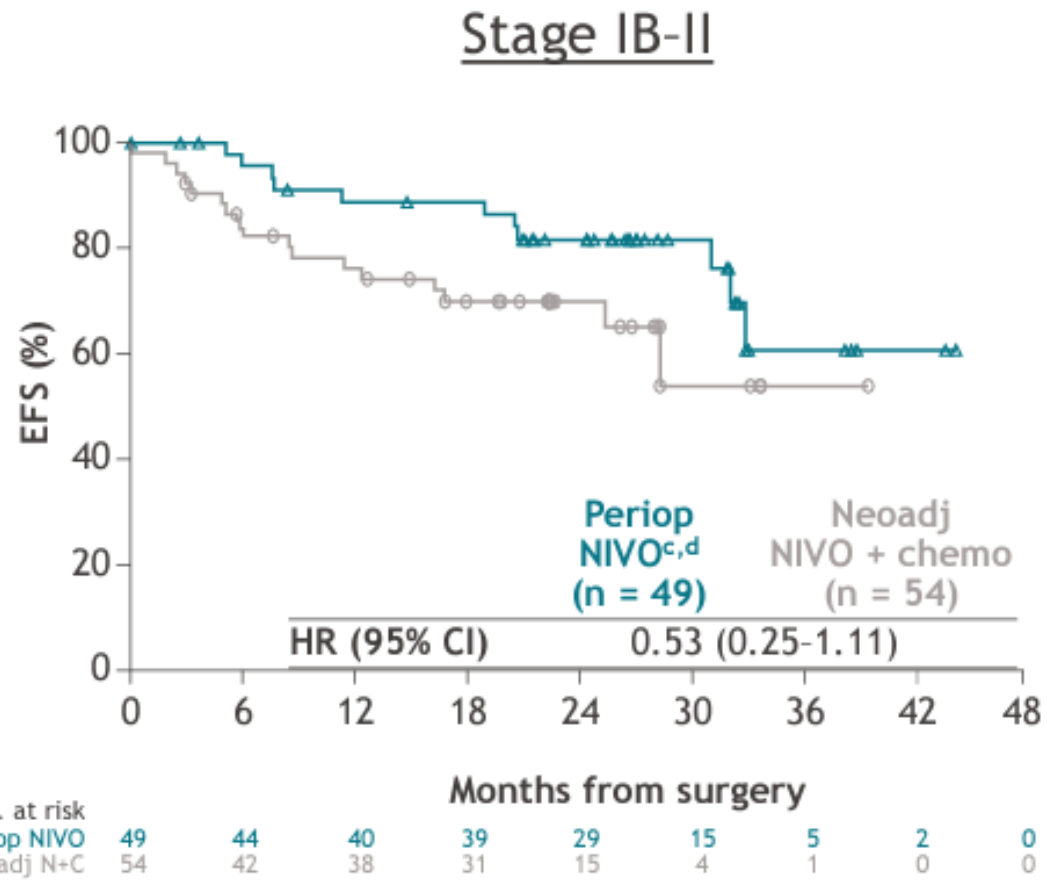
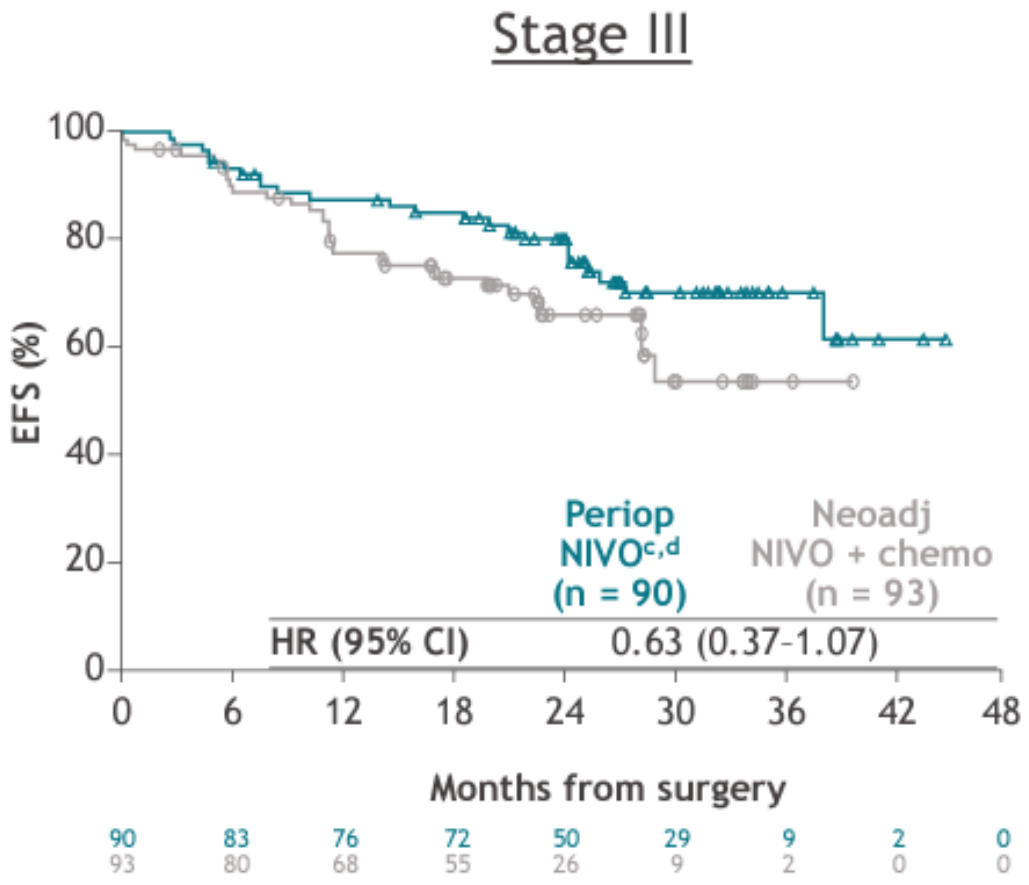
CM 816 v CM 77T: Meta-Analysis

Landmark EFS (analysis population) by clinical stage[a,b]





Forde P et al, IASLC WCLC 2024

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Questions From the Data

- Do the results prove benefit of perioperative treatment?
  - No, but strong evidence
- Does this give information to select who gets adjuvant immunotherapy?
  - Not yet
- Are there patient populations more tempting for adjuvant immunotherapy?
  - Yes
- Can we definitely select who should NOT receive adjuvant immunotherapy?
  - Not yet

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How Do We Decide?

- Patients with pCR?
  - Less benefit with adjuvant?
- Patients with PD-L1 negative?
  - Benefit with adjuvant
- Patient with Stage II (Benefit), without pCR (Benefit), PD-L1 positive (No Benefit)?

- All hypothesis-generating but not ready for clinic tomorrow

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What Will Help Us Move Forward?

- Head to head comparative studies
- Including different populations (pCR vs no, etc)
- Novel perioperative combination trials

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What Treatment Schedule Has Been Shown to Help Patients Live the Longest?

Is Perioperative Immunotherapy Is the New Standard of Care?