Rapidly Evolving Landscape of Therapies

Neoadjuvant treatment	Surgery	Adjuvant treatment
FDA Approved: Nivolumab + chemo x 3 cycles[1]		FDA Approved: Chemo → atezolizumab ~ 1 yr (PD-L1 ≥ 1%)[2] FDA Approved: Chemo (optional) pembrolizumab ~ 1 yr[3]
FDA Approved: Pembrolizumab + chemo x 4 cycles[4]		Pembrolizumab ~ 1 yr
FDA Approved 10/3/24: Nivolumab + chemo x 4 cycles[5]		Nivolumab ~ 1 yr
FDA Approved 8/15/24: Durvalumab + chemo x 4 cycles[6]		Durvalumab ~ 1 yr
Toripalimab + chemo x 3 cycles[7]		Toripalimab + chemo x 1 cycle Toripalimab ~ 1 yr

1. Forde PM, et al. *N Engl J Med.* 2022;386(21):1973-1985. 2. Felip E, et al. *Lancet.* 2021;398(10308):1344-1357.
3. O'Brien M, et al. *Lancet Oncol.* 2022;23(10):1274-1286. 4. Wakelee H, et al. *N Engl J Med.* 2023;389(6):491-503.
5. Cascone T, et al. N *Engl J Med.* 2024;390(19):1756-1769. 6. Heymach JV, et al. *N Engl J Med.* 2023;389(18):1672-1684.
7. Lu S, et al. *JAMA.* 2024;331(3);201-211.

Phase III Neoadjuvant/Perioperative Chemo-Immunotherapy Studies

	CheckMate 816[1,2]	KEYNOTE-671[3,4,5]	AEGEAN[6,7]	CheckMate 77T[8]	Neotorch[9]
Design	Neoadj Nivo-chemo vs chemo	Peri-op Pembro-chemo vs placebo-chemo	Peri-op Durva-chemo vs placebo-chemo	Peri-op Nivo-chemo vs placebo-chemo	Peri-op Tori-chemo vs placebo-chemo
Trial Size	N = 358	N = 797	N = 740	N = 461	N = 501
Stage	IB-IIIA (AJCC 7th)	II-IIIB (AJCC 8th)	II-IIIB (AJCC 8th)	IIA-IIIB (AJCC 8th)	II-III (AJCC 8th)
Placebo	No	Yes	Yes	Yes	Yes
Adj IO	No	Yes	Yes	Yes	Yes
% Stage III[#]	64%	70%	71%	64%	81%
IIIA	- 64%	- 55%	- 46%	- N/A	-67.3%
IIIB	- 0%	- 15%	- 25%	- N/A	-32.2%
pCR rate (95% CI)	24% (18.0 – 31.0)	18% (14.5 – 22.3)	17% (13.5 – 21.5)	25% (19.8 – 31.5)	28% (22.1 – 35.0)
Median f/u	41.4mo	36.6mo	11.7mo	25.4mo	18.3mo
EFS HR (95% CI)	0.68 (0.49-0.93) – **ITT**	0.59 (0.48 – 0.72) – **ITT**	0.68 (0.53-0.88) – **ITT**	0.58 (0.42-0.81) – **ITT**	0.40 (0.27-0.57)
PD-L1[*] <1%	0.87 (?)	0.75 (0.56-1.01)	0.76 (0.49-1.17)	0.73 (0.47-1.15)	0.65 (0.33-1.23)
PD-L1[*] ≥1%	0.46 (?)	0.47 (0.36-0.63)[%]	Unknown	0.52 (0.35-0.78)	
PD-L1[*] 1%-49%	0.63 (?)	0.52 (0.36-0.73)	0.70 (0.46-1.05)	0.76 (0.46-1.25)	0.31 (0.17-0.54)
PD-L1[*] ≥50%	0.29 (?)	0.48 (0.33-0.71)	0.60 (0.35-1.01)	0.26 (0.12-0.55)	0.31 (0.15-0.60)
% ≥G3 AEs (G5)	41% (0%)	45% (1.0%)	32% (1.8%)	47% (0.9%)	63% (3.0%)
FDA approved	Resectable NSCLC tumor ≥4cm or node positive	Resectable NSCLC tumor ≥4cm or node positive	FDA Approved 8.15.24	FDA Approved 10.3.24	N/A

[#]CheckMate 816 – AJCC 7th, AEGEAN/KEYNOTE-671 – AJCC 8th; *IHC per 28-8 in CheckMate 816, per SP263 in AEGEAN, per 22C3 in KEYNOTE-671; [%]subgroup from ASCO/NEJM 2023 publication.
Adj, adjuvant; AE, adverse event; durva, durvalumab; G, grade; ITT, intention-to treat; N/A, not applicable; neoadj, neoadjuvant; pembro, pembrolizumab; peri-op, perioperative; TBA, to be announced; tori, toripalimab. 1. Forde PM, et al. *N Engl J Med*. 2022;386(21):1973-1985. 2. Forde PM, et al. ELCC 2023. Abstract 840. 3. Wakelee H, et al. ASCO 2023. Abstract LBA100. 4. Wakelee H, et al. *N Engl J Med*. 2023;389(6):491-503. 5. Spicer JD, et al. ESMO 2023. Abstract LBA56. 6. Heymach JV, et al. AACR 2023. Abstract CT005. 7. Heymach JV, et al. *N Engl J Med*. 2023;389(18):1672-1684. 8. Cascone T, et al. *N Engl J Med*. 2024;390(19):1756-1769. 9. Lu S, et al. *JAMA*. 2024;331(3);201-211.

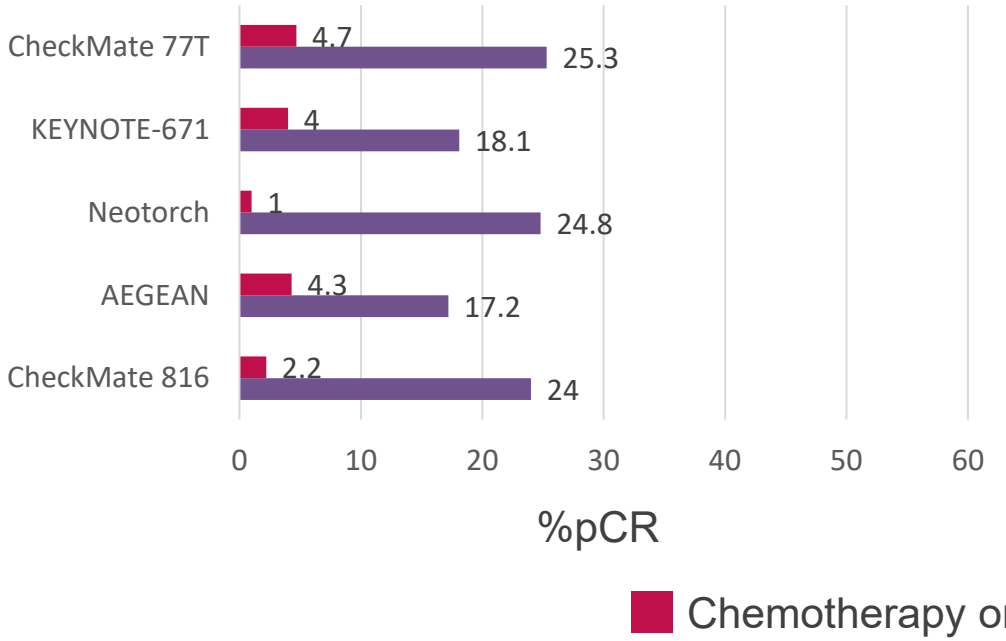
Overall Survival Results Summary

Immunotherapy Setting	Trial	Median f/u	HR (95% CI)	P value
Neoadjuvant + Adjuvant	**KEYNOTE-671**[1]	36.6 mo	0.72 (0.56, 0.93)	0.00517
	Neotorch[2]	18.3 mo	0.62 (0.38, 1.00)	0.05
Neoadjuvant	**CheckMate 816**[3]	57.6 mo	0.71 (0.47, 1.07)	0.045
Adjuvant	**IMpower010**[4]	45.3 mo	ITT Stage IB-IIIA: 0.995 (0.78, 1.28) Stage II-IIIA: 0.95 (0.74, 1.24) Stage II-IIIA, PD-L1 TC ≥ 1%: 0.71 (0.49, 1.03)	0.966 0.721 0.067
	IMpower010[5]	65.0 mo	Stage II-IIIA, PD-L1 TC ≥ 15: 0.77 (0.56, 1.06)	
	KEYNOTE-091[6]	35.6 mo	0.87 (0.67, 1.15)	0.17

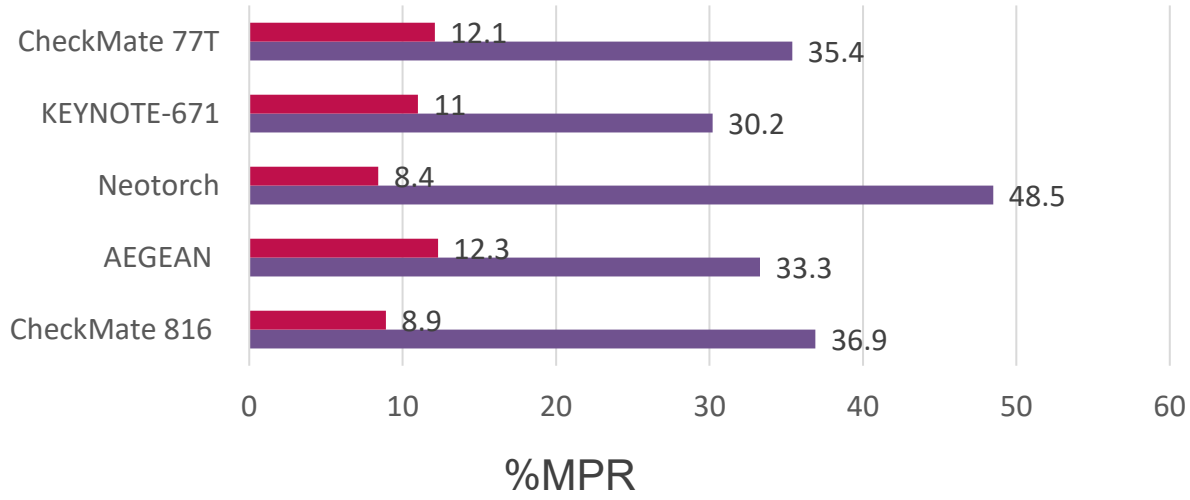
1. Spicer JD, et al. ESMO 2023. Abstract LBA56. 2. Lu S, et al. *JAMA* 2024;331(3):201-211.
3. Spicer JD, et al. ASCO 2024. Abstract LBA8010. 4. Felip E, et al. *Ann Oncol*. 2023;34(10):907-919.
5. Wakelee HA, et al. ASCO 2024. Abstract LBA8035. 6. O'Brien M, et al. *Lancet Oncol*. 2022;23(10):1274-1286.

Comparison of Pathologic Responses

pCR
Pathologic Complete Response
No viable tumor at resection



MPR
Major Pathologic Response
≤10% viable tumor at resection



Chemotherapy only Comparator*

* Comparators for the studies: AEGEAN, durvalumab + chemotherapy; CheckMate 77T/816, nivolumab + chemotherapy; KEYNOTE-671, pembrolizumab + chemotherapy; Neotorch, toripalimab + chemotherapy.

Forde PM, et al. *N Engl J Med*. 2022;386(21):1973-1985. Heymach JV, et al. *N Engl J Med*. 2023:389(18):1672-1684. Lu S, et al. *JAMA*. 2024;331(3):201-211. Wakelee H, et al. *N Engl J Med*. 2023;389(6):491-503. Cascone T, et al. *N Engl J Med*. 2024;390(19):1756-1769.

Surgical Outcomes in Trials With Neoadjuvant Chemoimmunotherapy in Stage III NSCLC

	Underwent Definitive Surgery (Exp vs Control, %)	Delay in Surgery (Exp vs Control, %)	R0 (% who Underwent Surgery)	Surgery-Related AE (%)
CheckMate 816[1]	83.2 vs 75.4	20.8 vs 17.8	83.2 vs 77.8	Grade 3 or 4: 11.4 vs 14.8
KEYNOTE-671[2]	82.1 vs 79.4	NA	92.0 vs 84.2	Grade 3-5: 25.8 vs 21.5 Grade 5: 2.8 vs 1.6
CheckMate 77T[3]	77.7 vs 76.7	15.7 vs 14.2	89.3 vs 90.4	Grade 3 or 4: 11.8 vs 11.8
AEGEAN[4]	80.6 vs 80.7	14.5 vs 16.8#	94.7 vs 91.3	NA

#, a surgical delay is defined as surgery occurring more than 40 days after the last dose of study treatment in the neoadjuvant period; AE, adverse events; Exp, experimental treatment; NA, not available.

1. Forde PM, et al. *N Engl J Med*. 2022;386(21):1973-1985. 2. Wakelee H, et al. *N Engl Med*. 2023;389(6):491-503.
3. Cascone T, et al. *N Engl J Med*. 2024;390(19):1756-1769. 4. Heymach JV, et al. *N Engl J Med*. 2023;389(18):1672-1684.