

## Expert consensus on immune checkpoint inhibitors for non-small cell lung cancer

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批注 [o1]: Please confirm the added titles to corresponding authors.

## Supplementary Table 1. Immunotherapy clinical trials in non-small cell lung cancer

### Supplementary Table 1.1. Clinical trials for early-stage NSCLC

Trial	Study Type	Enrolment Stage	Enroll ment	Stage Distrib	Treat ment Mode	Treatment Drugs	Media n Follow	Surge ry	R0 Resec tion	MPR Rate (%)	pCR Rate (%)	Media n EFS/D	Med ian	Grad e 3-4/5	Sur gery Dela
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			<b>Number</b>	<b>Population</b>			<b>Survival</b>	<b>Rate</b>	<b>Rate</b>			<b>FS/RF</b>	<b>OS</b>	<b>TRAEs</b>	<b>Quality of Life</b>
			<b>(n)</b>	<b>(%)</b>			<b>(m)</b>	<b>(%)</b>	<b>(%)</b>			<b>S (m)</b>	<b>(m)</b>	<b>(%)</b>	<b>(%)</b>
CheckMate-159 <sup>[18]</sup>	II	I-III A (7th)	21	I 19 II 48 III 10	IO→Surgery	Neoadjuvant nivolumab 3mg/kg,q2w,2 cycles	12 (post-operative)	100	95	45	15	RFS: 67 (HR=0.61)	NA	45.4	0
Neostar <sup>[24]</sup>	II	I-III A (single-station N2) (7th)	23 vs 21	NA	IO/IO+IO→Surge	Neoadjuvant nivolumab 3mg/kg, q2w,3 cycles vs Neoadjuvant nivolumab 3mg/kg,q2w,3 cycles + ipilimumab 1mg/kg,q.6w,1 cycle	22.2	96 vs 81	100 vs 100	22s 38	9 vs 29	NR	NR	13 vs 10	NA

NeoCO AST <sup>[25]</sup>	II	IA3 ~ IIIA	26 vs 21 vs 20 vs 16	NA	IO/IO +IO→ Surge ry	Neoadjuvant Durvalumab(D) vs Neoadjuvant Durvalumab + Oleclumab (D+O) or Monalizumab (D+M) or Danvatirsen (D+Da)	NA	NA	NA	11.1 vs 19 vs 30 vs	3.7 vs 9.5 vs 10 vs 12.5	NA	NA	0 vs 4.8 vs 0 vs 6.3	NA
Check Mate81 6 <sup>[27]</sup>	III	IB(≥4 cm) ~ IIIA(7 th)	179 vs 179	IB/II 36 vs 34 IIIA 63 vs 64	IO+C →Sur gery	Neoadjuvant nivolumab 360mg,q3w,3 cycles + chemo vs Neoadjuvant chemo	21	83.2 vs 75.4	83.2 vs 77.8	36.9 vs 8.9 ( OR=	24 vs 2.2 ( OR=	EFS:31 .6 vs 20.8	NR vs NR(	33.5 vs 36.9	3.4 vs 5.1
										5.70)	13.94, P <	(HR=0. 63,P=0.	HR= 0.57, P=0.		

TD-FOREK NOW <sup>[28]</sup> 1	II	IIIA/II IB(T3 N2)	43 vs 45	IIIA 70 vs 80 IIIB 30 vs 20	IO+C →Sur gery	Neoadjuvant camrelizumab 200mg, q3w,3cycles + chemo vs Neoadjuvant chemo	14.1	93 vs 93.3	92.5 vs 85.7	65.1 vs 15.6( OR=1 0.13,P < 0.001)	32.6 vs 8.9(O R=4.9 5,P=0. 008)	EFS: NR vs NR (HR=0. 52) DFS: NR vs NR (HR=0. 54)	NA vs 11.1	25.6 vs 2.4	12.5
EAST ENERG GY <sup>[29]</sup>	II	IB ~ IIIA, PD- L1≥1 %	24	IB 4 IIA 17 IIB 38 IIIA 42	IO +VEG FRi→ Surge ry	Neoadjuvant pembrolizumab 200mg + Ramucirumab 10mg/kg,q3w,2cyc les	NA	91.7	87.5	50	25	NR	NA	37.5	NA

NCT02904954 <sup>[32]</sup>	II	I~IIIA (7th)	30 vs 30	I 37 vs 26 II 16 vs 33 IIIA 47 vs 40	IO+R T→S surgery	Neoadjuvant SBRT + durvalumab 1200mg, q3w,2cycles vs Neoadjuvant durvalumab 1200mg,q3w,2cycles	NA	87 vs 87	96 vs 88	53.3 vs 6.7	30.7 vs 0	NA	NA	32 vs 25	3 vs 3
IMpower010 <sup>[36]</sup>	III	IB(≥4cm)~IIA(7th)	507 vs 498	IB 13 vs 12 II 47 vs 47 IIIA 40 vs 42	Surge ry→C +IO	Adjuvant atezolizumab 1200mg q3w,16cycles vs Adjuvant BSC	32.8	NA	NA	NA	NA	DFS:II ~ IIIA PD-L1 PD-TC≥1% :NR vs TC≥35.3 (HR=0.66,P=0.0039)	II ~ IIIA PD-TC≥1% TC≥1% NR vs NR	22 vs 12	NA

														( HR		
														=0.7		
														1)		
KEYN OTE- 091 <sup>[37]</sup>	III	IB(≥4 cm)~I IIA(7 th)	590 vs 587	IB 14 vs14 II 56 vs 58 IIIA 30 vs 28	Surge ry→I O es vs Adjuvant placebo	Adjuvant pembrolizumab 200mg,q3w,18cycl es vs Adjuvant placebo	35.6	NA	NA	NA	NA	DFS:53 .6 vs 42(HR =0.76,P =0.001 4)	NR vs NR( HR= 0.87, P=0. 17)	34.1 vs 25.8	NA	
KEYN OTE- 671 <sup>[38]</sup>	III	II~III B(N2)	397 vs 400	II 30 vs 30 IIIA 55 vs 56 IIIB	IO+C →Sur gery →IO	Neoadjuvant pembrolizumab 200mg, q3w,4cycles + chemo → adjuvant	25.2	82.1 vs 79.4	92 vs 84.2	30.2 vs 11 (HR= 19.2,p <0.00 001)	18.1 vs 4 (HR= 14.2,p <0.00 001)	EFS:18 .3 vs 7.2 (HR=0. 58,P<0. 00001)	NR vs 54.2 (HR =0.7 2,P= 2,P= 2,P=	45.2 vs 37.8	NA	







→ adjuvant  
 placebo

IO: Immunotherapy; C: Chemotherapy; Chemo: Chemotherapy; RT: Radiotherapy; VEGFRi: VEGF Receptor Inhibitor; MPR: Major Pathological Response; pCR: Pathological Complete Response; EFS: Event-Free Survival; DFS: Disease-Free Survival; RFS: Recurrence-Free Survival; OS: Overall Survival; TRAEs: Treatment-Related Adverse Events; q3W: every 3 weeks; q4W: every 4 weeks; NR: Not Reached; NE: Not Evaluable; HR:Hazard Ratio; SBRT: Stereotactic Body Radiotherapy; OR: Odds Ratio.

**Supplementary Table 1.2 Clinical trials for locally advanced NSCLC**

<b>Trial name</b>	<b>Study type</b>	<b>Enrollment criteria</b>	<b>Enrollment number</b>	<b>Stage distribution (%)</b>	<b>Treatment regimen</b>	<b>Treatment drugs</b>	<b>Median follow-up (m)</b>	<b>Median PFS (m)</b>	<b>Median OS (m)</b>	<b>ORR (%)</b>	<b>DoR (m)</b>	<b>Grade 3-4 TRAEs (%)</b>	<b>Treatment discontinuation due to AEs (%)</b>
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PACIFIC <sup>[50]</sup>	III	Unresectable Stage III, no progression after CCRT, PS 0-1	473 vs 236	IIIA 53 IIIB 45	CCRT →IO	Consolidation durvalumab 10mg/kg, q2w, 12 months vs Consolidation placebo	34.2	16.9 vs 5.6 (HR = 0.55, P<0.0001)	47.5 vs 29.1 (HR = 18.3 vs 0.72, P<0.001)	29.8 vs 18.4	NR vs 18.4	29.9 vs 26.1	15.4 vs 9.8
GEMSTONE-301 <sup>[51]</sup>	III	Unresectable Stage III, no progression after CCRT/SCRT, PS 0-1	255 vs 126	IIIA 28 IIIB 55 IIIC 16	CCRT/SCRT →IO	Consolidation sugemalimab 1200 mg, q3w, 24 months vs Consolidation placebo	14.3	9.0 vs 5.8 (HR = 0.64, p=0.0026)	NR	24.5 vs 25.2	24.1 vs 6.9	9.0 vs 6.0	11 vs 5
PACIFIC-R <sup>[52]</sup>	Real-world	Unresectable Stage III	1399	IA ~ IIB 5 IIIA 43 IIIB/IIIC 51	CRT→IO	Consolidation durvalumab, 10mg/kg, q2w	23.5	21.7 (19.1-24.5)	NR	NA	NA	NA	16.5 (permanent discontinuation)

Study	Phase	Population	n	Stratification	Randomization	Intervention	n	OS (%)	OS (95% CI)	HR	95% CI	OS (%)	OS (95% CI)
PACIFIC-6 <sup>[53]</sup>	II	Unresectable Stage III, no progression after SCRT, PS 0-2	117	IIIA 378 IIIB 50 IIIC 11	SCRT→IO	Consolidation durvalumab 1500mg,q4w,24 cycles	11(PFS) 13(OS)	10.9 (7.3-15.6)	25.0 (25.0-NE)	17.1 (11.1-25.8)	NR	18.8	21.4
DUARET <sup>[54]</sup>	II	Unresectable Stage III, unfit for chemo, ECOG 0-2	150	NA	RT→IO	Consolidation durvalumab 1500mg,q4w,12 months	7.65	8	15.9	26.5	NA	34	NA
COAST <sup>[56]</sup>	II	Unresectable Stage III, no progression	Durvalumab (D): 66, Oleclumab 55	IIIA 46 IIIB/C 55	CCRT →IO	Durvalumab (D) q4w ± Oleclumab (O) q2w/	11.5	D+O: HR=0.44 (0.26-0.75)	NA	D:17.9 D+O: 30.0	NA	D:39.4 D+O: 40.7	D:16.7 D+O: 15.3

		after CCRT, ECOG 0-1	(O): 59, Monalizumab (M): 61			Monalizumab(M)) q2w,12months		D+M: HR=0.42 (0.24-0.72)		D+M: 35.5		D+M: 27.9	D+M: 14.8
AFT-16 <sup>[57]</sup>	II	Unresectable Stage III, PS 0-1	64	NA	IO→CC RT→IO	Atezolizumab 25.1 1200 mg q3W (4 cycles induction →17cycles consolidation)		23.7 (13.2-NE)	NE	NA	NA	one G4 Guilla in- Barré, oneC G3 pneu moniti s and colitis	NA
EP05.01-004 <sup>[58]</sup>	Retrospective	Unresectable Stage III,	31	IIIA 13 IIIB 64	IO+C→ CRT	A:Induction chemoimmunotherapy vs	19.9	30.6 (29.2-NA)	NR	A vs B 54.8vs 93.5	NA	22.6% G2, 3.2% G3	NA

		bulky tumor (≥5 cm or LN ≥2 cm)		IIIC 23		B:Induction chemoimmunotherapy + CRT						pneumonitis	
NICOL AS <sup>[59]</sup>	II	Locally advanced, Stage III, PS 0-1	79	IIIA 35 IIIB 63	CRT+I O→IO	Concurrent nivolumab 360 mg q3w → consolidation nivolumab 480 mg, q4W, 1 year	21	12.7 (10.1- 22.8)	38.8 (26.8-NE)	73.4(6 2.3- 82.7)	11.0 (8.6- 20.7)	27	4.4
DETR RED Part1 <sup>[62]</sup>	II	Unresectable Stage III	10	NA	CRT→IO	Atezolizumab 1200 mg q3w (for 1 year)	39.2	18.9	26.5	NA	NA	NA	NA
DETR REDPart 2 <sup>[62]</sup>	II	Unresectable Stage III	30	NA	CRT+I O→IO	Concurrent atezolizumab → consolidation atezolizumab(12	39.2	15.1 (HR=1.30, p = 0.54)	NR (HR= 0.71 , p = 0.51)	NA	NA	NA	NA

00 mg,q3w, 1 year)													
KETN	II	Unresectabl	sq+nsq vs	IIIA/III	IO+C	Pembrolizumab	18.5	30.6 vs	NR vs NR	70.5	NR vs	64.3	33.9 vs
OTE-		e Stage III,	nsq	B/IIIC :	→CRT+	200	vs	NR		vs	NR	vs	18.6
799 <sup>[60]</sup>		ECOG 0–1	112	37/56/7	IO→IO	mg,q3w,17cycle	13.7			70.6		50.0	
			vs 102	vs		s							
				38/41/2		(induction+conc							
				1		urrent+consolida							
						tion)							

CCRT: Concurrent chemoradiotherapy; SCRT: Sequential chemoradiotherapy; IO: Immunotherapy; RT: Radiotherapy; PFS: Progression-free survival; OS: Overall survival; ORR: Objective response rate; DoR: Duration of response; TRAEs: Treatment-related adverse events; AE: Adverse event; q3w: every 3 weeks; q4w: every 4 weeks; vs: versus; NR: Not reached; NE: Not estimable; NA: Not available; CRT: Concurrent radiotherapy; HR: Hazard Ratio.

**Supplementary Table 1.3 Clinical trials for stage IV NSCLC**

<b>Trial name</b>	<b>Study type</b>	<b>Enrollment stage</b>	<b>Sample size (n)</b>	<b>Treatment regimen</b>	<b>Median follow-up (m)</b>	<b>Median PFS (m)</b>	<b>Median OS (m)</b>	<b>ORR (%)</b>	<b>≥ Grade 3 TRAEs (%)</b>
IMPOWER110 <sup>[67]</sup>	III	IV	554	Atezolizumab vs chemotherapy	31.3	8.2 vs 5.0	20.2 vs 14.7	40.2 vs 28.6	40. vs 16.7
KEYNOTE-024 <sup>[68]</sup>	III	IV	305	Pembrolizumab vs chemotherapy	59.9	7.7 vs 5.5	26.3 vs 13.4	46.1 vs 31.1	31.2 vs 53.3
KEYNOTE-407 <sup>[73]</sup>	III	IV	559	Pembrolizumab + chemo vs placebo + chemo	7.8	6.4 vs 4.8	15.9 vs 11.3	57.9 vs 38.4	69.8 vs 68
RATIONALE307 <sup>[74]</sup>	III	IIIB/IV	360	A: Tislelizumab + paclitaxel + carboplatin B: Tislelizumab + nab-paclitaxel + carboplatin C: Paclitaxel + carboplatin	8.6	A: 7.7 B: 7.7 C: 5.5	A: 26.1 B: 23.3 C: 14.0	A: 72.5 B: 74.8 C: 49.6	A:88.3% B:86.4% C:83.8%
CameLsq <sup>[75]</sup>	III	IIIB/IV	389	Camrelizumab + carboplatin + paclitaxel vs	53.5	11.0 vs 6.5	27.4 vs 15.5	64.8 vs 36.7	73.6 vs 71.9

				placebo + carboplatin + paclitaxel						
ORIENT-12 <sup>[80]</sup>	III	IIIB/IV	357	Sintilimab + gemcitabine + platinum	8	6.7 vs 4.9	NR vs NR	44 vs 35.4	86.6 vs	83.1
				vs placebo + gemcitabine + platinum						
ASTRUM-004 <sup>[81]</sup>	III	IIIB/IV	537	Serplulimab + nab-paclitaxel + carboplatin	32.9	9.9 vs 5.8	27.4 vs 18.4	67.5 vs 44.5	44.6 vs	38.7
				vs placebo + nab-paclitaxel + carboplatin						
CheckMate9LA <sup>[85]</sup>	III	IV	719	Nivolumab + ipilimumab + chemo	36.1	6.7 vs 5.3	15.8 vs 11.0	37.7 vs 25.1	48 vs	38
				vs chemo						
CheckMate-078 <sup>[106]</sup>	III	IIIB/IV	504	Nivolumab vs docetaxel	10.4	2.8 vs 2.8	12 vs 9.6	16.6 vs 4.2	10 vs	47

RATIONALE303 <sup>[107]</sup>	III	IIIB/IV	805	Tislelizumab vs docetaxel	16	4.2 vs 2.6	16.9 vs 11.9	22.6 vs 7.0	42.1 vs 74.8
KEYNOTE-189 <sup>[112]</sup>	III	IV	616	Pembrolizumab + chemo vs chemo	64.6	9.0 vs 4.9	22.0 vs 10.6	48.3 vs 19.9	72.8 vs 67.3
CAMEL <sup>[113]</sup>	III	IV	412	Camrelizumab + chemo vs chemo	65.2	11.0 vs 6.5	27.1 vs 19.8	60.5 vs 38.6	73.6 vs 71.9
ORIENT-11 <sup>[115]</sup>	III	IIIB/IV	397	Sintilimab + chemo vs placebo + chemo	30.8	9.2 vs 5.0	24.2 vs 16.8	51.9 vs 29.8	61.7 vs 58.8
RATIONALE304 <sup>[116]</sup>	III	III	334	Tislelizumab + pemetrexed + platinum vs pemetrexed + platinum	16.1	9.7 vs 7.6	21.6 vs 14.9	57.4 vs 36.9	67.6 vs 53.6
IMpower132 <sup>[118]</sup>	III	IV	578	Atezolizumab + pemetrexed + platinum vs pemetrexed + platinum	14.8	7.6 vs 5.2	18.1 vs 13.6	47 vs 32	47 vs 32
GEMSTONE-302 <sup>[117]</sup>	III	IV	479	Sugemalimab + chemo vs placebo + chemo	25.4	9.0 vs 4.9	25.4 vs 16.9	63.4 vs 40.3	64 vs 66

IMpower130 <sup>[120]</sup>	III	IV	724	Atezolizumab + nab-paclitaxel + carboplatin vs nab-paclitaxel + carboplatin	18.5	7.0 vs 5.5	18.6 vs 13.9	49.2 vs 31.9	81 vs 71
CHOICE-01 <sup>[119]</sup>	III	IIIB/IV	450	Toripalimab + chemo vs chemo	19.4	8.4 vs 5.6	23.8 vs 17.1	58.60 vs 26.50	78.6 vs 82.1
IPSOS <sup>[87]</sup>	III	IIIB/IV	453	Atezolizumab vs chemo	41	4.2 vs 4.0	10.3 vs 9.2	27.4 vs 7.9	33.3 vs 52.2
OAK <sup>[110]</sup>	III	IIIB/IV	1225	Atezolizumab vs docetaxel	21	2.8 vs 4.0	15.7 vs 10.3	14 vs 13	37 vs 54
IMpower150 subgroup analysis <sup>[66]</sup>	III	IV	1202	Atezolizumab + bevacizumab + platinum + paclitaxel vs bevacizumab + platinum + paclitaxel	20	9.7 vs 6.1	19.2 vs 14.9	63.5 vs 48.0	66.7 vs 58.9
ORIENT-31 <sup>[133]</sup>	III	IIIB/IV	444	Sintilimab + bevacizumab + platinum + pemetrexed vs	9.8	6.9 vs 4.3	14.6 vs 9.9	48.1 vs 34.8	51.4 vs 35.1

				platinum + pemetrexed						
NCT03647956 <sup>[273]</sup>	II	IV	40	Atezolizumab + bevacizumab + platinum + pemetrexed	17	9.4	18.9 vs 13.4	62.5	40	
CheckMate 722 <sup>[274]</sup>	III	IV	294	Nivolumab + pemetrexed + platinum	18.2	5.6 vs 5.4	13.4 vs 12.1	31 vs 27	45 vs 34.7	
KEYNOTE-789 <sup>[275]</sup>	III	IV	492	pemetrexed + platinum Pembrolizumab + pemetrexed + platinum	42	6.5 vs 4.4	17.1 vs 12.4	29.0 vs 27.1	51.4 vs 37.2	
CT18 <sup>[276]</sup>	II	IV	40	pemetrexed + platinum Toripalimab + pemetrexed + platinum	Data cutoff: Jan 2020	7.5	14.4	50	40	

PFS: progression-free survival; OS: overall survival; ORR: objective response rate; TRAEs: treatment-related adverse events; chemo: chemotherapy; NR: not reached; NA: not available; Sq: squamous; Non-Sq: non-squamous; PD-L1: programmed death-ligand 1; ECOG:Eastern Cooperative Oncology Group; PS: performance status.