Supplementary Online Content

Kazandjian D, Gong Y, Keegan P, Pazdur R, Blumenthal GM. Prognostic value of the lung immune prognostic index for patients treated for metastatic non–small cell lung cancer. *JAMA Oncol.* Published online July 25, 2019. doi:10.1001/jamaoncol.2019.1747

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Summary of Selected Clinical Studies

Study	EXPERIMENTAL DRUG	CONTROL	# OF PATIENTS	PATIENT POPULATION
LUX-Lung 3	afatinib	platinum doublet	345	1L EGFRm
Oak	atezolizumab	docetaxel	850	2L
Poplar	atezolizumab	docetaxel	287	2L
ALTa	brigatinib	brigatinib	222	2L ALK+
Profile 1007	crizotinib	pemetrexed/docetaxel	347	2L ALK+
Profile 1014	crizotinib	platinum doublet	343	1L ALK+
checkmate 017	nivolumab	docetaxel	272	2L squamous histology
checkmate 057	nivolumab	docetaxel	582	2L non-squamous histology
aura3	osimertinib	platinum doublet	419	2L T790M EGFRm
flaura	osimertinib*	gefitinib/erlotinib	556	1L EGFRm
Keynote 010	pembrolizumab	docetaxel	691	2L PD-L1+

*For the FLAURA study, both experimental and control arms were pooled in the targeted therapy arm for the purpose of the pooled analysis.
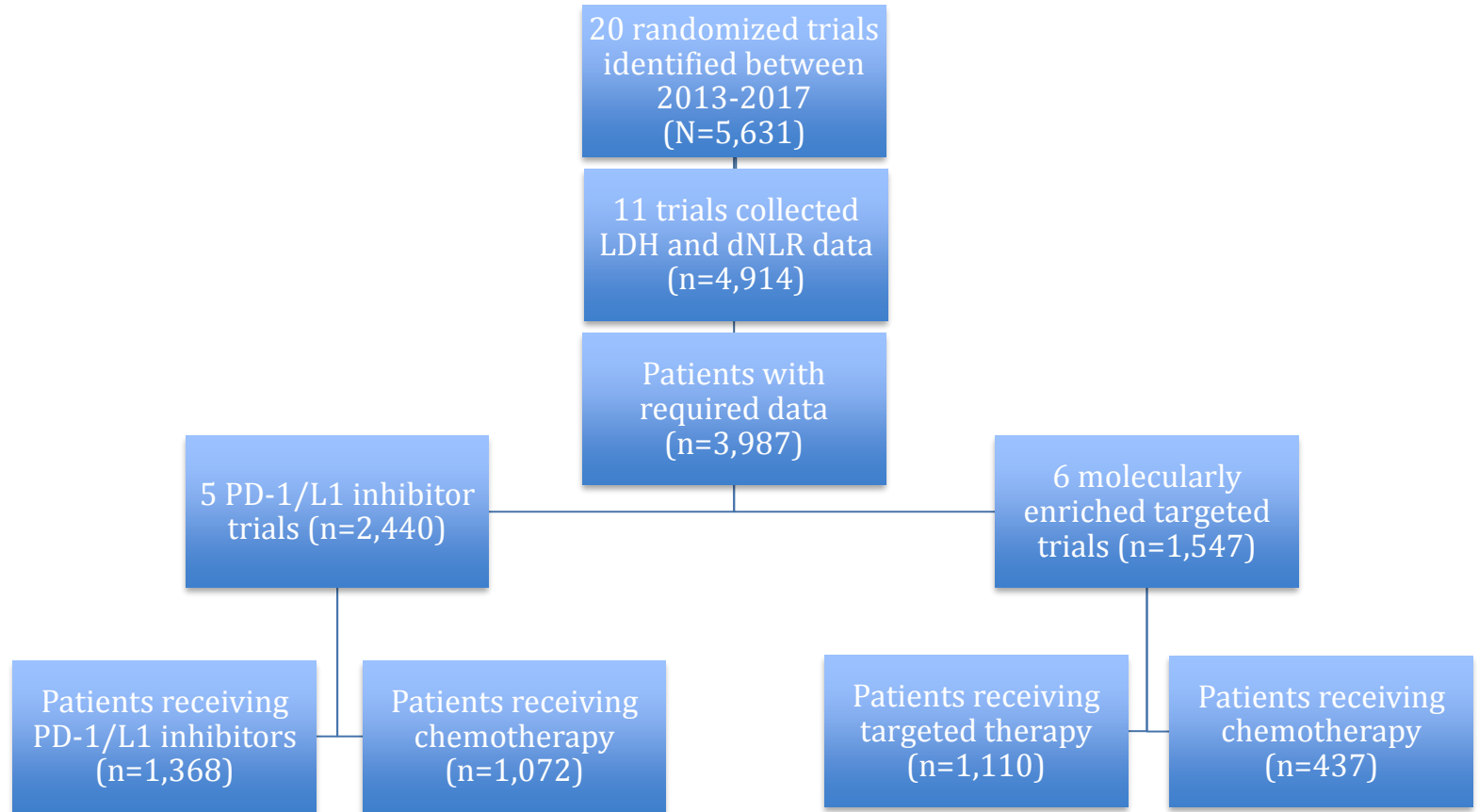
Abbreviations: 1L: first-line treatment; EGFRm: patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have activating epidermal growth factor receptor (EGFR) mutations; 2L: second-line treatment; ALK+: patients with NSCLC whose tumors are anaplastic lymphoma kinase (ALK) positive; T790M EGFRm: patients with metastatic EGFR T790M mutation-positive NSCLC; PD-L1+: patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%).

eTable 2. Summary of Key Demographics and Disease Characteristics of Pooled Cohorts

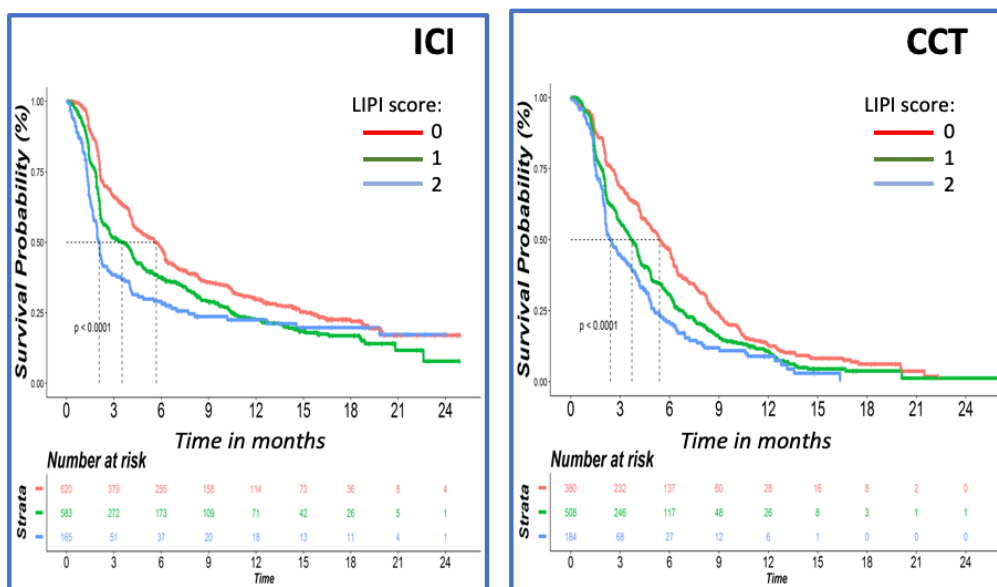| Variable	ICI Studies		TT Studies	
	ICI (n=1,368)	CCT (n=1,072)	TT (n=1,110)	CCT (n=437)
Age ≥ 65	561 (41%)	475 (44%)	341 (31%)	102 (23%)
Male	834 (61%)	657 (61%)	430 (39%)	164 (38%)
Smoker	1,036 (76%)	773 (72%)	407 (37%)	136 (31%)
Squamous	363 (27%)	294 (27%)	Not applicable	
ECOG 0	425 (31%)	351 (33%)	518 (47%)	248 (57%)
ECOG 1	940 (69%)	719 (67%)	562 (51%)	178 (41%)
ECOG ≥2	3 (0%)	1 (0%)	29 (3%)	11 (3%)
ECOG unknown	0 (0%)	1 (0%)	1 (0%)	0 (0%)
EGFRm	Not applicable		587 (53%)	140 (32%)
ALK+			523 (47%)	297 (68%)

Abbreviations: ICI: Immune checkpoint inhibitor; TT: targeted therapy; CCT: cytoxic chemotherapy; ECOG PS: Eastern Cooperative Oncology Group performance status; EGFRm: patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have activating epidermal growth factor receptor (EGFR) mutations; ALK+: patients with NSCLC whose tumors are anaplastic lymphoma kinase (ALK) positive.

eFigure 1. Flow Chart of Clinical Studies and Patients Selected for Analysis

eFigure 2. Progression-Free Survival Based on LIPI Score and Treatment: ICI Studies
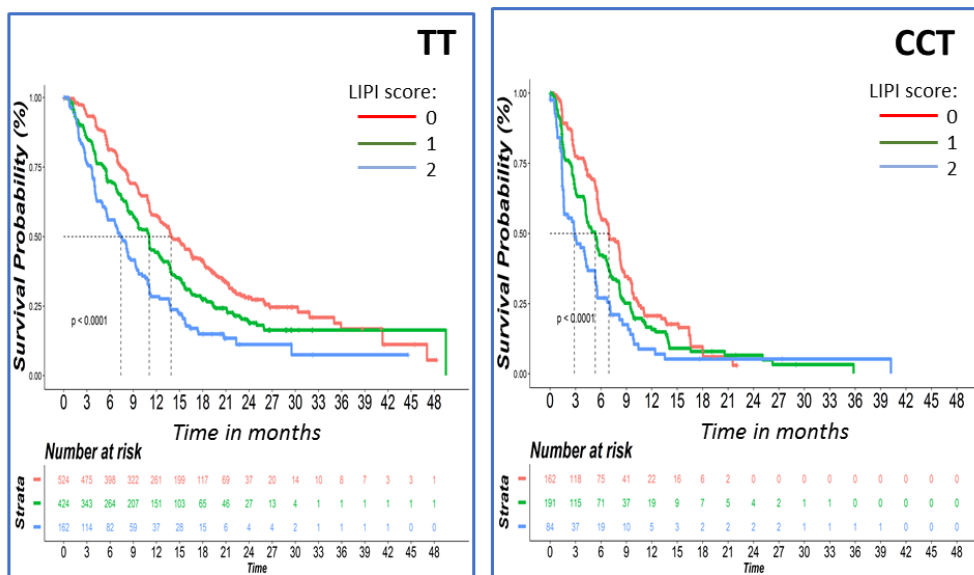
Abbreviations: LIPI, lung immune prognostic index; ICI, immune checkpoint inhibitor; CCT, cytotoxic chemotherapy; HR, hazard ratio; PFS, progression-free survival.

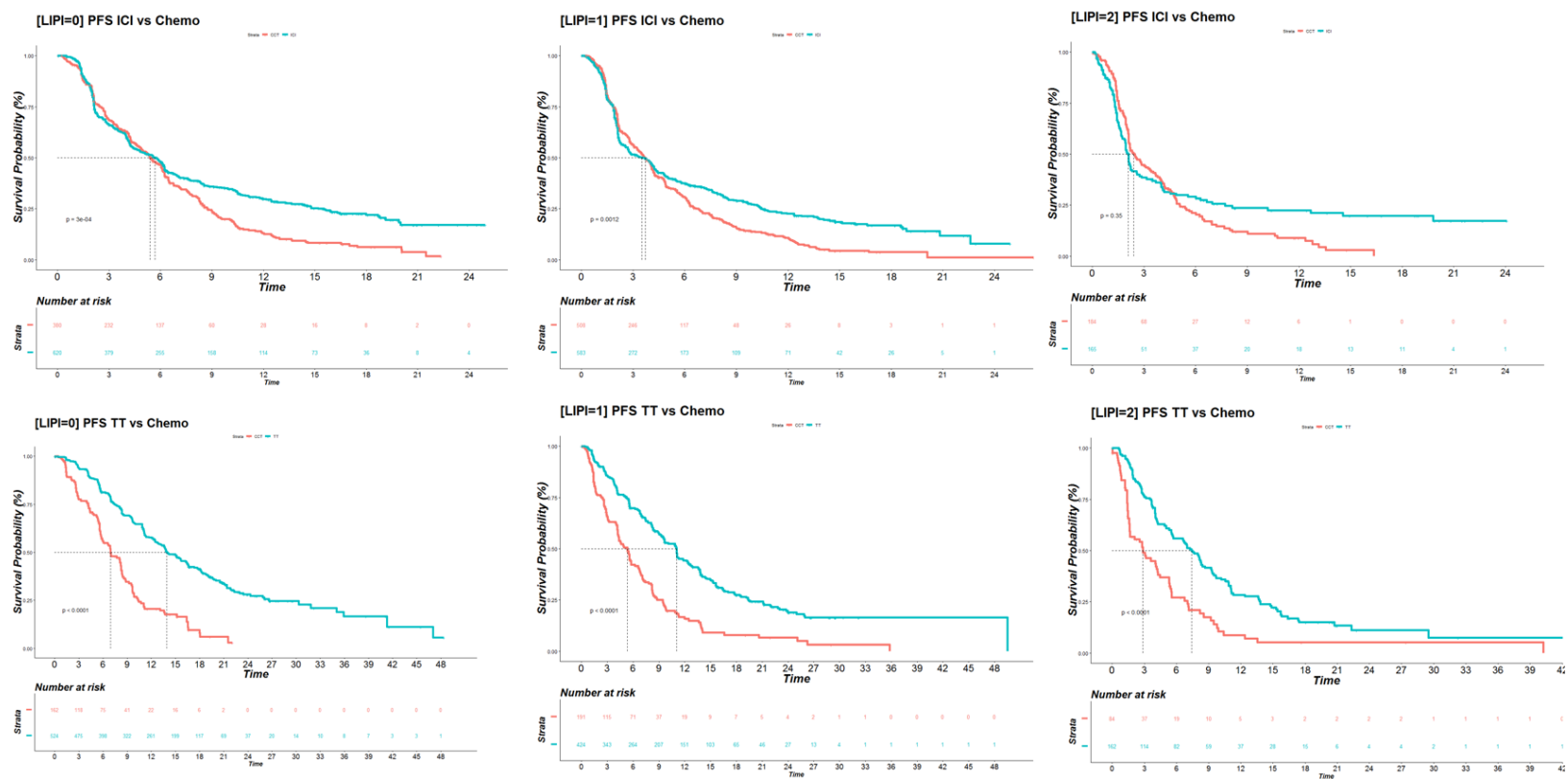|		ICI			CCT		
	LIPI	0	1	2	0	1	2
	(n)	620	583	165	380	508	184
PFS	HR (95%CI)	0.59 (0.48, 0.72)	0.79 (0.64, 0.98)	1	0.56 (0.45, 0.68)	0.78 (0.64, 0.95)	1
	Median months (95%CI)	5.7 (4.6, 6.2)	3.5 (2.7, 4.2)	2.1 (1.7, 2.3)	5.4 (4.7, 6.1)	3.7 (3.2, 4.1)	2.4 (2.1, 3.4)
	Global Log Rank	P <0.0001			P <0.0001		

eFigure 3. Progression-Free Survival Based on LIPI Score and Treatment: TT Studies

Abbreviations: LIPI, lung immune prognostic index; TT, targeted therapy; CCT, cytotoxic chemotherapy; HR, hazard ratio; PFS, progression-free survival.
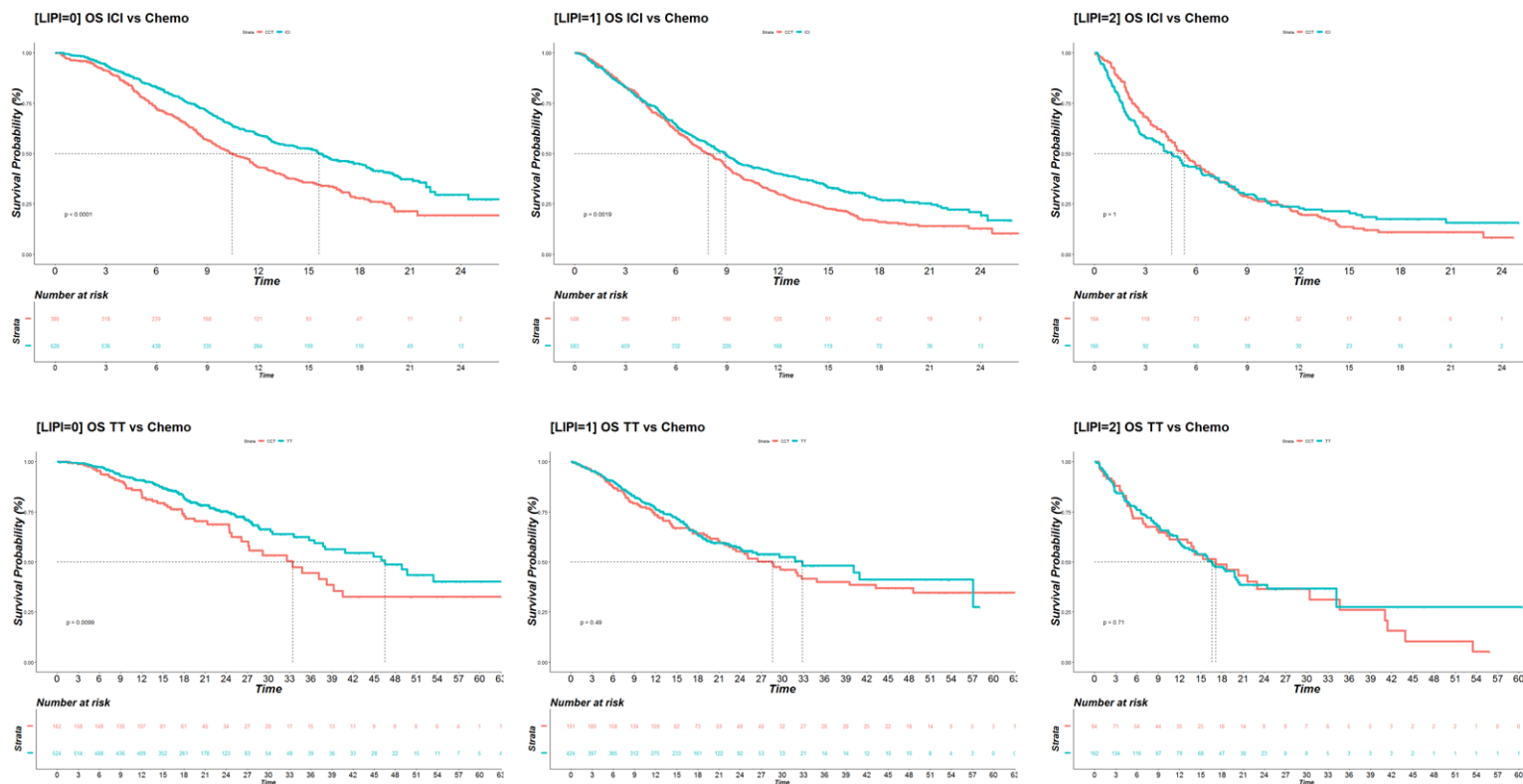

		TT			CCT		
	LIPI	0	1	2	0	1	2
	(n)	524	424	162	162	191	84
P F S	HR (95%CI)	0.46 (0.37, 0.57)	0.67 (0.54, 0.83)	1	0.51 (0.38, 0.69)	0.70 (0.53, 0.93)	1
	Median months (95%CI)	13.9 (12.9, 15.7)	11.1 (9.6, 11.8)	7.4 (5.5, 8.6)	6.9 (5.8, 8.2)	5.3 (4.2, 5.8)	2.9 (1.6, 4.3)
	Global Log Rank	P <0.0001			P <0.0001		

eFigure 4. Kaplan Meier Progression-Free Survival Estimates by Treatment Arm for Each of the LIPI Categories

Abbreviations: LIPI, lung immune prognostic index; PFS, progression-free survival; ICI, immune checkpoint inhibitor; chemo, chemotherapy; TT, targeted therapy; Time, time in months.

eFigure 5. Kaplan Meier Overall Survival Estimates by Treatment Arm for Each of the LIPI Categories

Abbreviations: LIPI, lung immune prognostic index; PFS, overall survival; ICI, immune checkpoint inhibitor; chemo, chemotherapy; TT, targeted therapy; Time, time in months.