

Table 1. Studies featuring NSCLC patient cohorts in which a certain peripheral blood immune cell type predicts or monitors the response to ICIs

Cell type/measure	Cell count method	ICI	Number of patients	Association with response to ICIs	Statistical test and p-value	References
ALC	Absolute cell count	Nivolumab	22	High ALC at baseline and after 6 weeks of treatment correlates with longer OS	Log-rank test ($p_{T0} = 0.0059$; $p_{Tn} = 0.0016$)	[31]
	Absolute cell count	Nivolumab	79 (55%)	High ALC at baseline correlates with longer OS and PFS	Multivariate Cox regression ($p_{OS} = 0.003$, $p_{PFS} = 0.023$) Log-rank test ($p_{OS} = 4.7 \times 10^{-5}$)	[32]
		Pembrolizumab	52 (37%)			
		Atezolizumab	11 (8%)			
	Absolute cell count	Nivolumab	134	High ALC at baseline is associated with longer OS and	Multivariate Cox regression ($p_{OS} = 0.03$, $p_{PFS} = 0.04$)	[33]
	Absolute cell count	Nivolumab	174 (75%)	High ALC at baseline and after 1 month of treatment is associated with better objective response, OS and PFS	T-test ($p_{T0} = 0.02$, $p_{Tn} = 0.02$) Multivariate Cox regression ($p_{T0-OS} = 0.035$, $p_{Tn-OS} = 0.005$, $p_{T0-PFS} = 0.006$, $p_{Tn-PFS} = 0.001$)	[34]
Pembrolizumab		54 (24%)				
Atezolizumab		3 (1%)				
ANC	Absolute cell count	Nivolumab	134	Low ANC at baseline is associated with longer OS and PFS	Multivariate Cox regression ($p_{OS} = 0.03$, $p_{PFS} = 0.001$)	[33]
	Absolute cell count	Anti-PD-1	88	Low ANC after 8 weeks of treatment is associated with better clinical response	T-test ($p = 0.017$)	[69]
		Anti-PD-L1				
Absolute cell count	Nivolumab	146 (93%)	Low ANC at baseline is associated with longer OS	Multivariate Cox regression ($p = 0.02$)	[70]	
NLR	Absolute cell count	Anti-PD-1	88	Low NLR at baseline is associated with longer time to treatment discontinuation, time to disease progression and OS	Log-rank test ($p_{TD} = 0.037$, $p_{DP} = 0.047$, $p_{OS} = 0.019$)	[69]
		Anti-PD-L1				
	Absolute cell count	Nivolumab	146 (93%)	Low NLR at baseline is associated with longer OS and PFS	Multivariate Cox regression ($p_{OS} = 0.01$; $p_{PFS} = 0.008$)	[70]
		Pembrolizumab	11 (7%)			
	Absolute cell count	Nivolumab	175	Low NLR at baseline is associated with longer OS and PFS	Multivariate Cox regression ($p_{OS} = 0.002$, $p_{PFS} = 0.04$) Log-rank test ($p_{OS} = 0.01$, $p_{PFS} = 0.04$)	[71]
Absolute cell count	Nivolumab	52	Low NLR at baseline is associated with longer OS and PFS	Multivariate Cox regression ($p_{OS} < 0.001$, $p_{PFS} = 0.007$)	[72]	

Absolute cell count		Nivolumab	17 (49%)	Low NLR after treatment is associated with longer OS at baseline and with better clinical response	Univariate Cox regression ($p_{OS} = 0.03$)	[73]	
		Pembrolizumab	18 (51%)		Log-rank test ($p_{OS} = 0.017$) ANOVA ($p_{CR} = 0.019$)		
Absolute cell count		Nivolumab	31 (57%)	Low NLR after 6 weeks of treatment is associated with longer OS and PFS	Multivariate Cox regression ($p_{OS} = 0.003$, $p_{PFS} < 0.001$)	[75]	
		Pembrolizumab	23 (43%)		Log-rank test ($p_{OS} < 0.001$, $p_{PFS} < 0.001$)		
Absolute cell count		Nivolumab	101	Low NLR after 2 and 4 weeks of treatment is associated with longer PFS	Log-rank test ($p_{T2} = 0.0053$, $p_{T4} = 0.0052$)	[76]	
dNLR	Absolute cell count	Pembrolizumab	221	Low dNLR at baseline in responders, and it is associated with longer OS and PFS	T-test ($p < 0.001$)	[74]	
					Log-rank test ($p_{OS} < 0.001$, $p_{PFS} < 0.001$)		
AMC	Absolute cell count	Nivolumab	146 (93%)	Low AMC at baseline is associated with longer PFS	Multivariate Cox regression ($p = 0.02$)	[70]	
		Pembrolizumab	11 (7%)				
PD-1 ⁺ CD8 ⁺ T cells	Flow cytometry	Nivolumab	31	Higher percentage of PD-1 ⁺ CD8 ⁺ T cells in responders, and it correlates with longer OS and PFS	Mann-Whitney U test ($p < 0.01$)	[38]	
		Nivolumab	25 (32%)		Higher fold-change in the percentage of proliferating PD-1 ⁺ CD8 ⁺ T cells between baseline and 1 week after treatment is associated with a better durable clinical benefit (DCB), OS and PFS		Log-rank test ($p_{OS} = 0.005$, $p_{PFS} = 0.009$)
		Pembrolizumab	54 (68%)				T-test ($p = 0.001$) Multivariate Cox regression ($p_{OS} = 0.007$, $p_{PFS} < 0.001$) Log-rank test ($p_{OS} = 0.037$, $p_{PFS} = 0.002$)
CD137 ⁺ CD8 ⁺ T cells	Flow cytometry	Nivolumab	109	Higher percentage of CD137 ⁺ CD8 ⁺ T cells at baseline in responders, and it is associated with longer OS and PFS	T-test ($p = 0.02$)	[41]	
		Pembrolizumab			Log-rank test ($p_{OS} = 0.00052$, $p_{PFS} = 0.0031$)		
CD45RA ⁺ CCR7 ⁻ CD8 ⁺ T cells	Flow cytometry	Nivolumab	71	Higher frequency of CD45RA ⁺ CCR7 ⁻ CD8 ⁺ T cells before and after treatment in responders	Mann-Whitney U test ($p_{T0} < 0.05$, $p_{Tn} < 0.05$)	[42]	
CX3CR1 ⁺ CD8 ⁺ T cells	Flow cytometry	Nivolumab	2 (6%)	Higher increase in CX3CR1 ⁺ CD8 ⁺ T cells frequency between baseline and 12 weeks after treatment in responders, and it correlates with longer OS and PFS	Mann-Whitney U test ($p < 0.0001$)	[44]	
		Pembrolizumab	34 (94%)		Log-rank test ($p_{OS} = 0.0136$, $p_{PFS} = 0.0033$)		
Central memory to effector CD8 ⁺ T cell ratio	Flow cytometry	Nivolumab	22	High central memory to effector CD8 ⁺ T cell ratio at baseline correlates with longer PFS	Mann-Whitney U test ($p < 0.05$)	[43]	

Central memory to effector CD4 ⁺ T cell ratio	Flow cytometry	Nivolumab	22	High central memory to effector CD4 ⁺ T cell ratio at baseline correlates with longer PFS	Mann-Whitney U test ($p < 0.05$)	[43]
CD27 ⁻ CD28 ⁻ CD4 ⁺ T cells	Flow cytometry	Nivolumab	8 (16%)	Higher percentage of CD27 ⁻ CD28 ⁻ CD4 ⁺ T cells before and after treatment in responders, and it is associated with a longer PFS	Mann-Whitney U test ($p_T < 0.001$) Log-rank test ($p_{PFS} = 0.001$)	[51]
		Pembrolizumab	22 (43%)			
PD-1 ⁺ CD4 ⁺ T cells	Flow cytometry	Nivolumab	5 (23%)	High percentage of PD-1 ⁺ CD4 ⁺ T cells (not clear at what timepoint) is associated with longer PFS	Log-rank test ($p = 0.034$)	[50]
		Pembrolizumab	11 (50%)			
		Atezolizumab	6 (27%)			
CD62L ^{low} CD4 ⁺ Th1 cells	Flow cytometry	Nivolumab	126	Higher percentage of CD62L ^{low} CD4 ⁺ Th1 cells at baseline in responders	T-test ($p < 0.0001$)	[52]
	Flow cytometry	Nivolumab	126	Lower percentage of Tregs at baseline in responders	T-test ($p = 0.034$)	[52]
Tregs	Flow cytometry	Nivolumab	16 (22%)	Decreasing percentage of Tregs after treatment in responders	Paired t-test ($p = 0.034$)	[54]
		Pembrolizumab	31 (42%)			
		Atezolizumab	27 (36%)			
	Flow cytometry	Nivolumab	132	Higher percentage of Tregs after treatment in responders, and it is associated with longer OS and PFS	T-test ($p = 0.008$) Log-rank test ($p_{OS} = 0.01$, $p_{PFS} = 0.008$)	[55]
		Pembrolizumab				
PD-1 ⁺ Tregs	Flow cytometry	Nivolumab	16 (22%)	Decreasing percentage of PD-1 ⁺ Tregs after treatment in responders	Paired t-test ($p < 0.001$)	[54]
		Pembrolizumab	31 (42%)			
		Atezolizumab	27 (36%)			
Treg to Lox-1 ⁺ gMDSC ratio	Flow cytometry	Nivolumab	63	Higher Treg to Lox-1 ⁺ gMDSC ratio after treatment in responders, and it is associated with a longer PFS	$p_T = 0.0011$ (statistical test not clear) Log-rank test ($p_{PFS} = 0.0079$)	[85]
NK cell to Lox-1 ⁺ gMDSC ratio	Flow cytometry	Nivolumab	62	Higher NK cell to Lox-1 ⁺ gMDSC ratio after treatment in responders, and it is associated with a longer OS and PFS	T-test ($p_{NK} < 0.0001$) Log-rank test ($p_{OS} = 0.012$, $p_{PFS} < 0.0001$) ROC curve analysis (AUC = 0.866; $p < 0.0001$)	[61]
NK cells	Flow cytometry	Nivolumab	31	Higher number of NK cells at baseline in responders, and it is associated with	Mann-Whitney test ($p_{NK} < 0.01$) Log-rank test ($p_{OS} = 0.014$,	[38]

				longer OS and PFS	$p_{\text{PFS}} = 0.025$	
	Mass cytometry	Nivolumab	3 (33%)	Higher frequency of NK cells at baseline and 6 weeks after treatment in responders	T-test ($p_{\text{T0}} < 0.05$, $p_{\text{Tn}} < 0.05$)	[60]
		Pembrolizumab	6 (67%)			
PD-L1 ⁺ monocytes	Flow cytometry	Nivolumab	17 (49%)	Low frequency of PD-L1 ⁺ monocytes is associated with longer OS and PFS	Univariate Cox regression ($p_{\text{OS}} = 0.01$, $p_{\text{PFS}} = 0.015$)	[78]
		Pembrolizumab	18 (51%)			
	Flow cytometry	Nivolumab	17 (49%)	High percentage of mMDSCs is associated with longer OS at baseline and better clinical response after treatment	Univariate Cox regression ($p_{\text{OS}} = 0.039$)	[73]
		Pembrolizumab	18 (51%)			
	Flow cytometry	Nivolumab	61	Lower frequency of mMDSCs after treatment in responders, and it is associated with longer OS and PFS	Mann-Whitney U test ($p_{\text{mMDSC}} < 0.05$)	[81]
mMDSCs	Flow cytometry	Nivolumab	132	Low frequency of mMDSCs at baseline is associated with longer OS and PFS	Log-rank test ($p_{\text{OS}} = 0.03$, $p_{\text{PFS}} = 0.01$)	[82]
		Pembrolizumab				
	Flow cytometry	Nivolumab	3 (14%)	Low frequency of mMDSCs at baseline in responders, and it is associated with longer OS and PFS	Mann-Whitney U test ($p = 0.045$)	[83]
		Pembrolizumab	5 (23%)			
		Atezolizumab	10 (45%)			
		Combination	4 (18%)			
	Flow cytometry	Nivolumab	132	Low frequency of gMDSCs at baseline is associated with longer OS and PFS	Log-rank test ($p_{\text{OS}} = 0.04$, $p_{\text{PFS}} = 0.03$)	[82]
		Pembrolizumab				
gMDSCs	Flow cytometry	Nivolumab	53	High frequency of gMDSCs at baseline is associated with better clinical response, longer PFS and OS	Mann-Whitney U test ($p_{\text{gMDSC}} = 0.02$)	[84]
					Multivariate Cox regression ($p_{\text{OS}} = 0.01$, $p_{\text{PFS}} = 0.003$)	
PD-L1 ⁺ cDC1 mDCs	Flow cytometry	Nivolumab	17 (49%)	Low frequency of PD-L1 ⁺ cDC1 mDCs is associated with longer OS and PFS	Log-rank test ($p_{\text{OS}} = 0.035$, $p_{\text{PFS}} = 0.031$)	[78]
		Pembrolizumab	18 (51%)			
PD-L1 ⁺ pDCs	Flow cytometry	Nivolumab	17 (49%)	Low frequency of PD-L1 ⁺ pDCs is associated with longer OS and PFS	Univariate Cox regression ($p_{\text{OS}} = 0.005$, $p_{\text{PFS}} = 0.004$)	[78]
		Pembrolizumab	18 (51%)			
					Log-rank test ($p_{\text{OS}} = 0.001$, $p_{\text{PFS}} = 0.001$)	

DCs	Flow cytometry	Nivolumab	17 (49%)	High percentage of DCs at baseline and after treatment is associated with longer OS at baseline and better clinical response	Univariate Cox regression ($p_{OS} = 0.015$)	[73]
		Pembrolizumab	18 (51%)		Log-rank test ($p_{OS} = 0.005$) ANOVA ($p_{TO-CR} = 0.009$, $p_{TN-CR} = 0.001$)	
