

Supplementary Table S12. Subgroup analysis of the 1,229 line chemotherapy, anti-PD-(L)1, and chemotherapy + anti-PD-(L)1 validation cohort

Variable	Subgroup	Comparison	IRS-UL					IRS-IL					IRS-H								
			Treatments (n)	aHR	95%CI Lower	95%CI Upper	Events (n)	P	Treatments (n)	aHR	95%CI Lower	95%CI Upper	Events (n)	P	Treatments (n)	aHR	95%CI Lower	95%CI Upper	Events (n)	P	
All		PD-(L)1 + Chemo vs. Chemo	345	1.012	0.675	1.517	228	0.9551	494	0.658	0.460	0.943	304	0.0225	390	0.610	0.409	0.911	218	0.0157	
		PD-(L)1 + Chemo vs. PD-(L)1		0.815	0.481	1.379		0.4455		0.876	0.585	1.310		0.5182		1.503	0.943	2.395		0.087	
		PD-(L)1 vs. Chemo		1.242	0.814	1.895		0.3151		0.752	0.543	1.041		0.0858		0.406	0.280	0.589		<0.0001	
Line of Therapy	1st Line	PD-(L)1 + Chemo vs. Chemo	237	0.819	0.478	1.404	151	0.4681	363	0.654	0.437	0.979	221	0.0392	316	0.591	0.376	0.929	173	0.0226	
		PD-(L)1 + Chemo vs. PD-(L)1		0.743	0.374	1.475		0.3953		0.948	0.581	1.548		0.8317		1.487	0.877	2.522		0.141	
		PD-(L)1 vs. Chemo		1.103	0.634	1.919		0.7289		0.690	0.458	1.040		0.0762		0.397	0.262	0.602		<0.0001	
>1st line	PD-(L)1 + Chemo vs. Chemo	108	1.663	0.877	3.153	77	0.1195	131	0.690	0.305	1.557	83	0.3711	74	1.270	0.456	3.534	45	0.6472		
	PD-(L)1 + Chemo vs. PD-(L)1		1.237	0.527	2.905		0.6254		0.664	0.299	1.472		0.3131		2.496	0.717	8.681		0.1505		
	PD-(L)1 vs. Chemo		1.344	0.689	2.623		0.3859		1.039	0.558	1.934		0.9038		0.509	0.149	1.738		0.2809		
Tumor Type	NSCLC	PD-(L)1 + Chemo vs. Chemo	50	0.620	0.194	1.986	30	0.4211	156	0.607	0.337	1.094	105	0.0967	216	0.551	0.321	0.946	117	0.0307	
		PD-(L)1 + Chemo vs. PD-(L)1		0.394	0.117	1.326		0.1324		0.559	0.303	1.031		0.0627		1.206	0.687	2.119		0.5143	
		PD-(L)1 vs. Chemo		1.576	0.601	4.128		0.355		1.086	0.667	1.768		0.7396		0.457	0.289	0.721		0.0008	
	Remaining 4	PD-(L)1 + Chemo vs. Chemo	295	0.990	0.656	1.495	198	0.9617	338	0.699	0.459	1.065	0	0.0954	174	0.628	0.349	1.127	101	0.119	
		PD-(L)1 + Chemo vs. PD-(L)1		0.837	0.472	1.484		0.5416		1.199	0.674	2.132		0.537		2.385	0.996	5.711		0.051	
		PD-(L)1 vs. Chemo		1.183	0.737	1.900		0.4857		0.583	0.369	0.922		0.0211		0.263	0.126	0.551		0.0004	
	Esophagago.	PD-(L)1 + Chemo vs. Chemo	93	0.938	0.219	4.023	67	0.9309	122	1.867	0.763	4.566	78	0.1716							
		PD-(L)1 + Chemo vs. PD-(L)1		0.368	0.075	1.809		0.2184		4.219	1.148	15.504		0.0302							
		PD-(L)1 vs. Chemo		2.551	1.228	5.299		0.0121		0.442	0.173	1.129		0.088							
	Remaining 3	PD-(L)1 + Chemo vs. Chemo	202	0.990	0.625	1.568	131	0.9659	216	0.549	0.322	0.936	121	0.0275							
		PD-(L)1 + Chemo vs. PD-(L)1		1.318	0.641	2.710		0.4526		1.131	0.576	2.222		0.7206							
		PD-(L)1 vs. Chemo		0.751	0.381	1.480		0.4083		0.485	0.273	0.862		0.0136							
Age	<65 yrs	PD-(L)1 + Chemo vs. Chemo	211	1.004	0.592	1.702	141	0.9891	252	0.928	0.562	1.532	148	0.7689	184	0.990	0.567	1.728	98	0.9705	
		PD-(L)1 + Chemo vs. PD-(L)1		0.992	0.490	2.009		0.9824		1.176	0.661	2.093		0.5804		2.189	1.123	4.266		0.0214	
		PD-(L)1 vs. Chemo		1.012	0.575	1.780		0.9679		0.788	0.492	1.262		0.3223		0.452	0.263	0.778		0.0042	
>=65 yrs	PD-(L)1 + Chemo vs. Chemo	134	1.093	0.556	2.145	87	0.7971	242	0.468	0.277	0.790	146	0.0045	206	0.362	0.199	0.658	120	0.0009		
	PD-(L)1 + Chemo vs. PD-(L)1		0.604	0.254	1.438		0.2545		0.637	0.353	1.150		0.1344		1.072	0.551	2.086		0.8377		
	PD-(L)1 vs. Chemo		1.809	0.886	3.693		0.1037		0.735	0.462	1.169		0.1928		0.338	0.198	0.576		0.0001		
Gender	Male	PD-(L)1 + Chemo vs. Chemo	143	0.691	0.334	1.430	93	0.3189	240	1.245	0.737	2.102	155	0.4126	216	0.548	0.312	0.964	121	0.0368	
		PD-(L)1 + Chemo vs. PD-(L)1		1.005	0.430	2.353		0.9901		1.823	0.975	3.408		0.0601		1.083	0.566	2.069		0.8103	
		PD-(L)1 vs. Chemo		0.687	0.353	1.337		0.2692		0.683	0.407	1.146		0.149		0.506	0.310	0.827		0.0066	
Female	PD-(L)1 + Chemo vs. Chemo	202	1.113	0.672	1.846	135	0.677	254	0.434	0.253	0.745	149	0.0025	174	0.722	0.400	1.302	97	0.2786		
	PD-(L)1 + Chemo vs. PD-(L)1		0.582	0.287	1.178		0.1326		0.505	0.278	0.914		0.0242		2.408	1.198	4.843		0.0137		
	PD-(L)1 vs. Chemo		1.913	1.063	3.442		0.0304		0.860	0.548	1.352		0.5142		0.300	0.167	0.537		0.0001		
PD-L1 qTP expression (tertile)	1	PD-(L)1 + Chemo vs. Chemo	248	1.152	0.720	1.844	165	0.5556	239	0.783	0.491	1.247	161	0.3026	97	0.928	0.448	1.922	58	0.8407	
		PD-(L)1 + Chemo vs. PD-(L)1		0.997	0.502	1.981		0.9934		0.980	0.569	1.687		0.9421		2.639	0.914	7.622		0.0729	
		PD-(L)1 vs. Chemo		1.155	0.643	2.076		0.6293		0.799	0.489	1.305		0.3694		0.352	0.143	0.866		0.023	
	2	PD-(L)1 + Chemo vs. Chemo	137		0.445	0.190	1.040	70	0.0616		0.461	0.177	1.197	70	0.1117	123	0.872	0.426	1.785	69	0.7081
		PD-(L)1 + Chemo vs. PD-(L)1		0.965	0.480	1.944	0.9213		0.403		0.189	0.857	0.0183								
		PD-(L)1 vs. Chemo			0.380	0.133	1.088		0.0715		0.279	0.126	0.618		0.0016						
	3	PD-(L)1 + Chemo vs. Chemo	118		0.628	0.222	1.777	73	0.3811		0.604	0.309	1.181	73	0.1406	170	0.734	0.331	1.628	91	0.4473
		PD-(L)1 + Chemo vs. PD-(L)1			0.714	0.306	1.669		0.4373												
		PD-(L)1 vs. Chemo			0.557	0.215	1.445		0.229												
	PD-L1 tert 2 or 3	PD-(L)1 + Chemo vs. Chemo	97		1.282	0.660	2.492	63	0.4638												
		PD-(L)1 + Chemo vs. PD-(L)1																			
			PD-(L)1 vs. Chemo																		

Subgroup analysis of the 1,229 line chemotherapy, anti-PD-(L)1, and chemotherapy + anti-PD-(L)1 validation cohort (from Figure) 4 is shown. For all subgroups (those with ≥ 50 treatment lines per IRS group are shown), the number of treatment lines in the subgroup, the adjusted hazard ratio (aHR), 95% lower and upper confidence intervals (CI), the number of events in the subgroup, and the p-value (those significant in green) are shown. When < 50 treatment lines per group were present, remaining groups were combined and shown (as indicated).