

**Differential prognostic effect of systemic inflammation in patients with
NSCLC treated with immunotherapy or chemotherapy: a post hoc analysis of
the phase III OAK trial**

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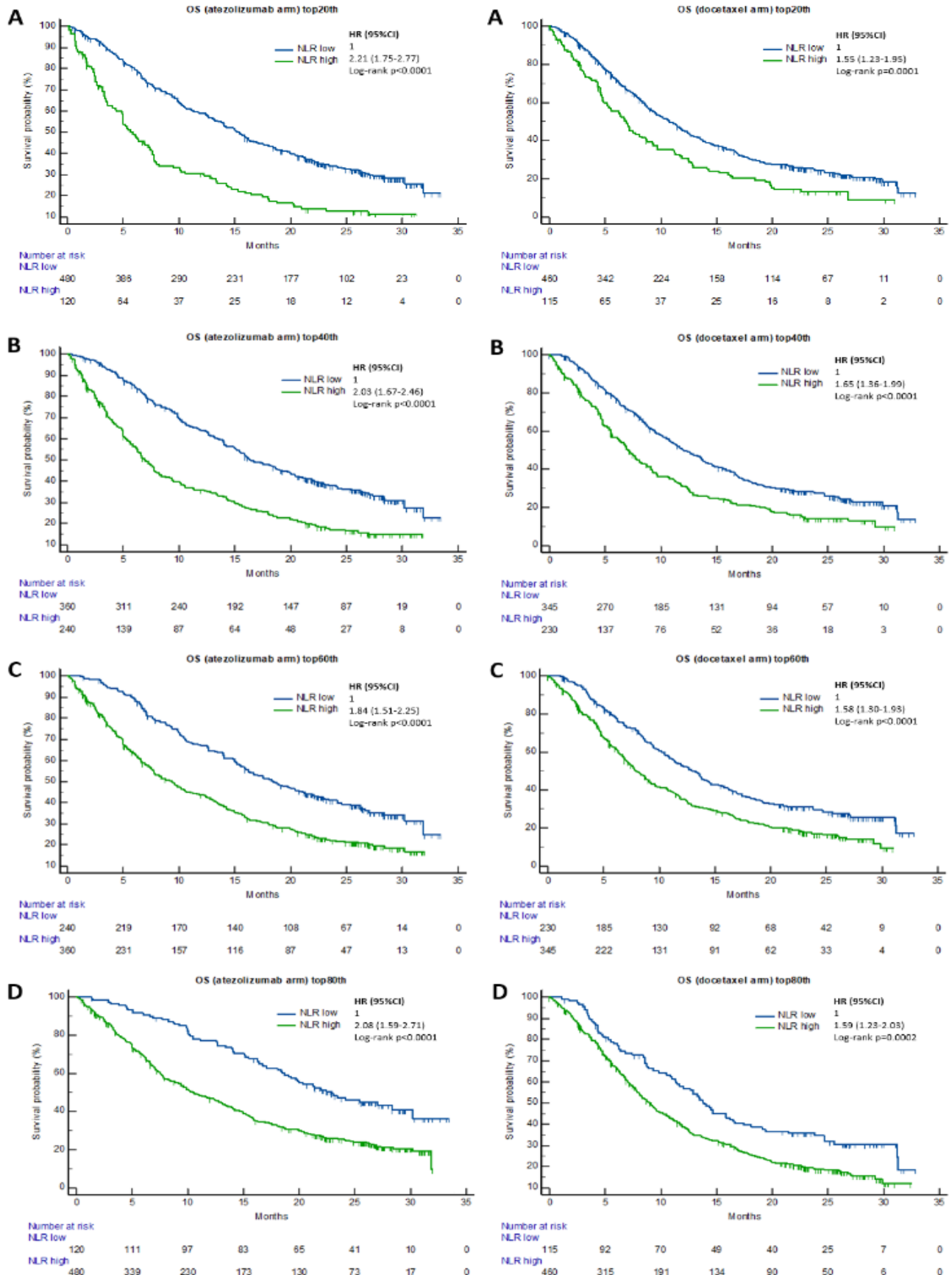
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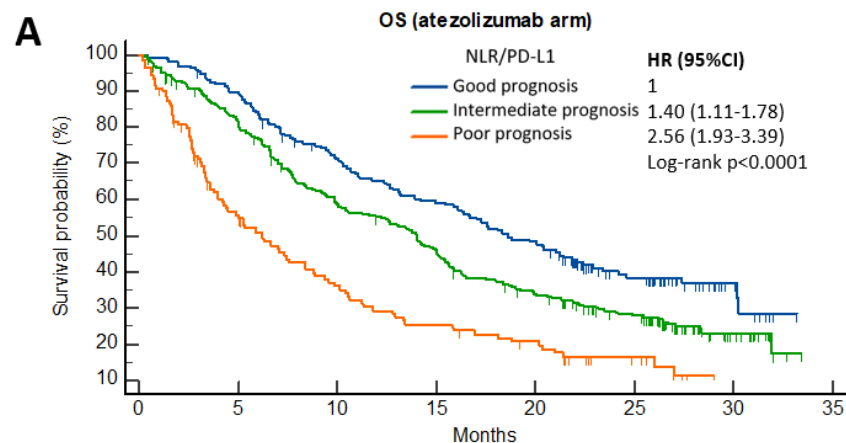
Supplementary Table 1. Pooled population multivariable models for the risk of disease progression/death (Progression Free Survival) and the risk of death (Overall Survival). Backward stepwise selection with enter $p < 0.05$, remove $p > 0.1$ applied.

	Progression Free Survival	Overall Survival
VARIABLE	HR (95% CI); <i>p</i> - value	HR (95% CI); <i>p</i> - value
Age ≥ 65 years vs < 65 years	-	-
Sex Male vs Female	-	-
ECOG PS ≥2 vs 0-1	1.29 (1.14-1.46); $p = 0.0001$	1.72 (1.48-1.98); $p < 0.0001$
Smoking status Current/former vs never smokers	0.81 (0.69-0.95); $p = 0.0118$	-
Histology type Squamous vs Non-squamous.	1.16 (1.01-1.34); $p = 0.0288$	1.51 (1.31-1.75); $p < 0.0001$
Number of metastatic sites > 2 vs ≤ 2	1.38 (1.22-1.56); $p < 0.0001$	1.63 (1.42-1.88); $p < 0.0001$
Number of prior therapies 1 vs 2	0.82 (0.72-0.95); $p < 0.0001$	-

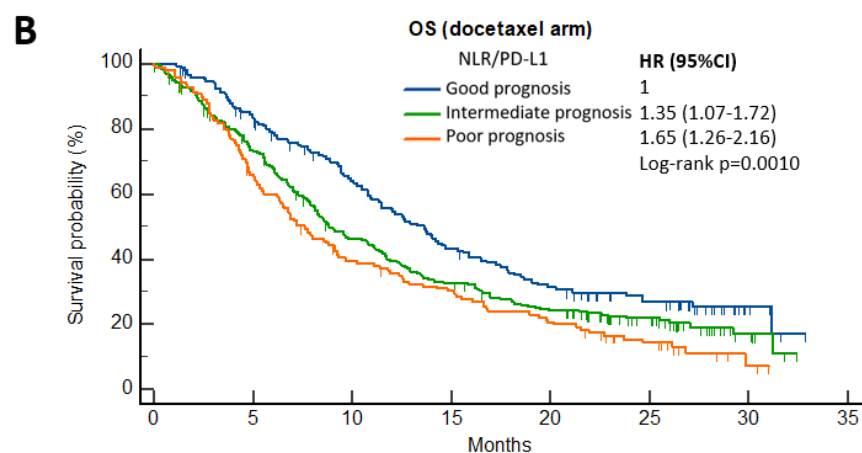
Supplementary Figure 1: Kaplan-Meier survival estimates for Overall Survival according to increasing percentiles of the NLR as cut-offs. **A) Top 20th percentile** Atezolizumab cohort: NLR-low: 15.4 months (95%CI: 13.8-16.6; 315 events) vs NLR-high: 7.8 months (95%CI: 4.8-7.6; 100 events). Docetaxel cohort: NLR-low: 10.9 months (95%CI: 9.4-12.0; 336 events) vs NLR-high: 6.8 months (95%CI: 5.1-8.6; 95 events). **B) Top 40th percentile** Atezolizumab cohort: NLR-low: 16.4 months (95%CI: 15.0-19.2; 228 events) vs NLR-high: 6.9 months (95%CI: 5.8-8.2; 187 events). Docetaxel cohort: NLR-low: 12.0 months (95%CI: 10.7-13.8; 244 events) vs NLR-high: 7.1 months (95%CI: 5.9-8.2; 187 events). **C) Top 60th percentile** Atezolizumab cohort: NLR-low: 18.5 months (95%CI: 15.8-21.9; 148 events) vs NLR-high: 9.3 months (95%CI: 7.6-11.2; 267 events). Docetaxel cohort: NLR-low: 13.3 months (95%CI: 10.9-14.6; 158 events) vs NLR-high: 7.9 months (95%CI: 7.1-9.1; 273 events). **D) Top 80th percentile** Atezolizumab cohort: NLR-low: 22.9 months (95%CI: 18.7-30.2; 66 events) vs NLR-high: 10.5 months (95%CI: 9.3-12.8; 349 events). Docetaxel cohort: NLR-low: 13.8 months (95%CI: 11.4-16.6; 77 events) vs NLR-high: 9.1 months (95%CI: 7.9-10.1; 354 events).



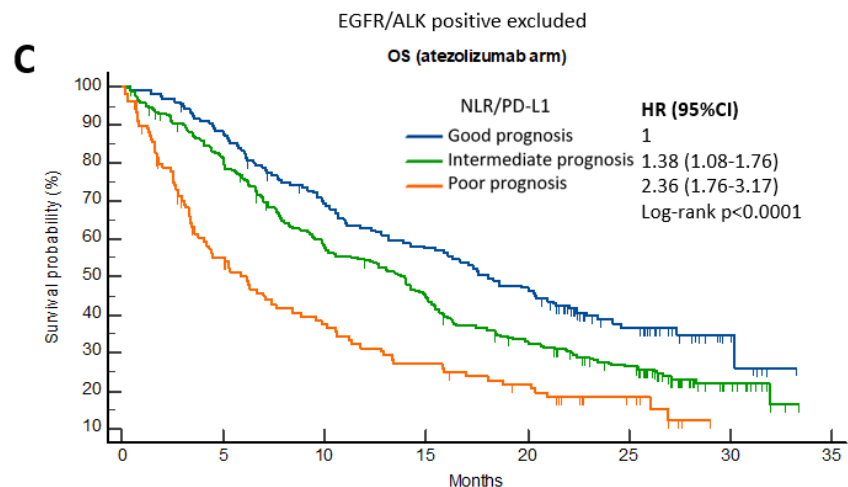
Supplementary Figure 2: Kaplan-Meier survival estimates for Overall Survival according to the NLR/PD-L1 complementation. A) Atezolizumab cohort including oncogene addicted patients. 0 factors: 18.6 months (95%CI: 16.1-22.1; 104 events) vs 1 factor: 14.0 months (95%CI: 11.6-15.1; 217 events) vs 2 factors: 6.2 months (95%CI: 4.2-8.4; 94 events). **B) Docetaxel cohort including oncogene addicted patients:** 0 factors: 13.6 months (95%CI: 10.9-15.9; 102 events) vs 1 factor: 8.8 months (95%CI: 8.0-11.1; 214 events) vs 2 factors: 7.6 months (95%CI: 6.3-9.2; 115 events). **C) Atezolizumab cohort excluding EGFR/ALK positive patients:** 0 factors: 18.1 months (95%CI: 14.9-22.1; 97 events) vs 1 factor: 13.9 months (95%CI: 10.4-15.1; 196 events) vs 2 factors: 6.2 months (95%CI: 4.0-8.8; 84 events). **D) Docetaxel cohort excluding EGFR/ALK positive patients:** 0 factors: 13.3 months (95%CI: 10.8-15.6; 97 events) vs 1 factor: 8.3 months (95%CI: 7.5-9.6; 203 events) vs 2 factors: 7.6 months (95%CI: 6.2-9.2; 105 events).



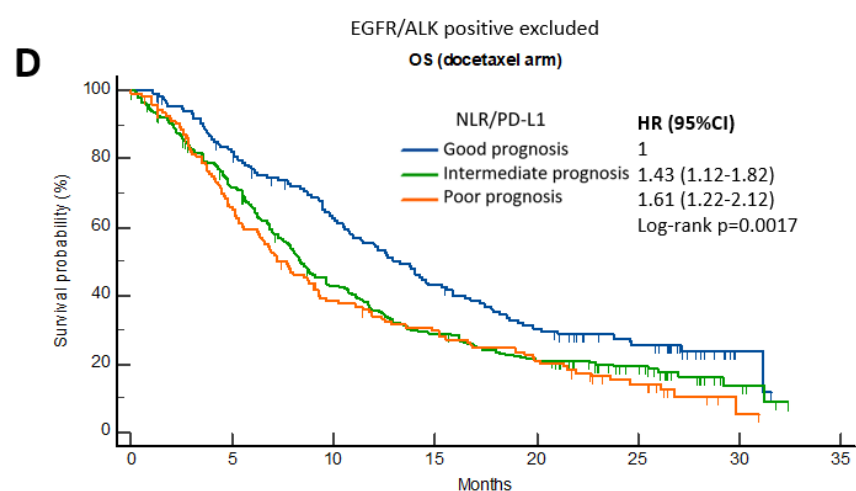
Number at risk	0	5	10	15	20	25	30	35
0 factors	172	152	118	98	80	42	11	0
1 factor	307	237	171	131	95	64	16	0
2 factors	121	61	38	27	20	8	0	0



Number at risk	0	5	10	15	20	25	30	35
0 factors	150	120	87	59	42	26	5	0
1 factor	286	200	123	86	62	35	6	0
2 factors	139	87	51	38	26	14	2	0

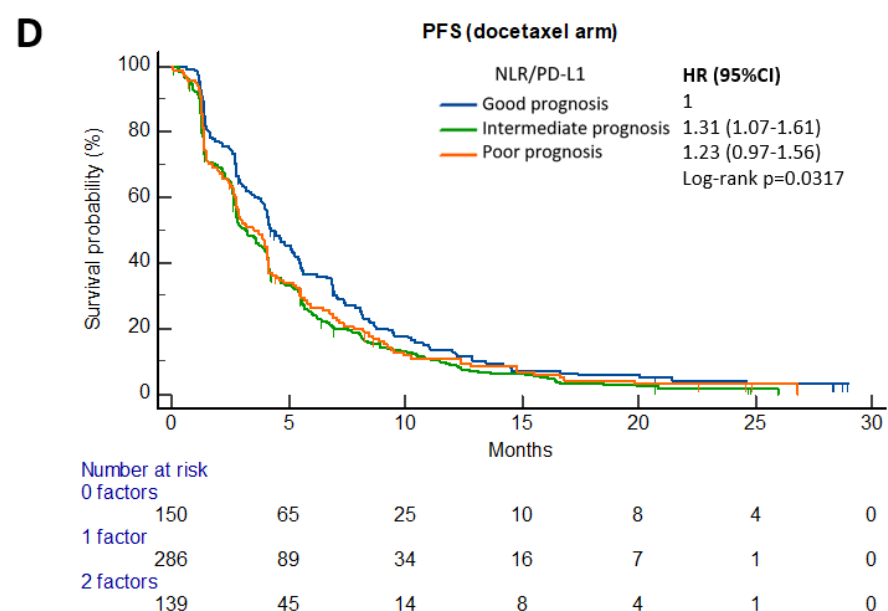
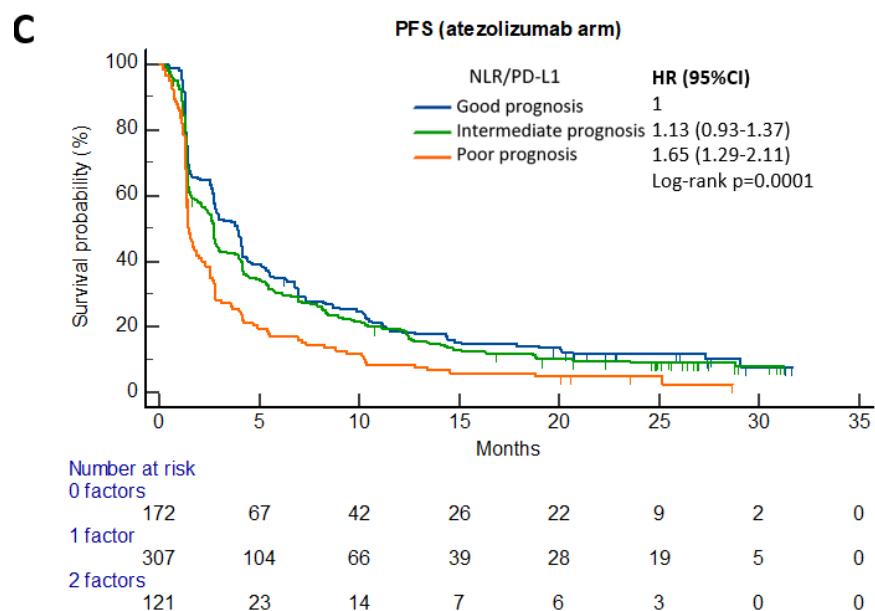
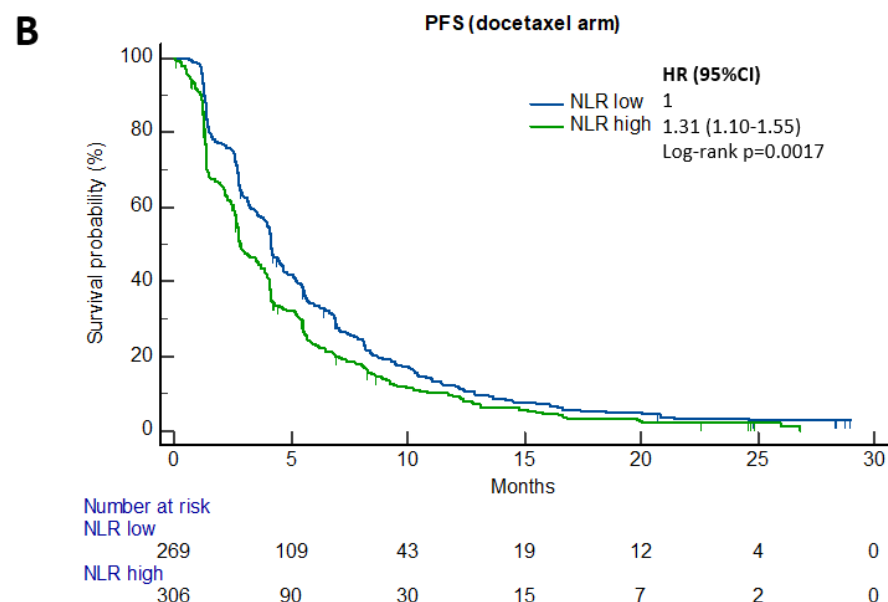
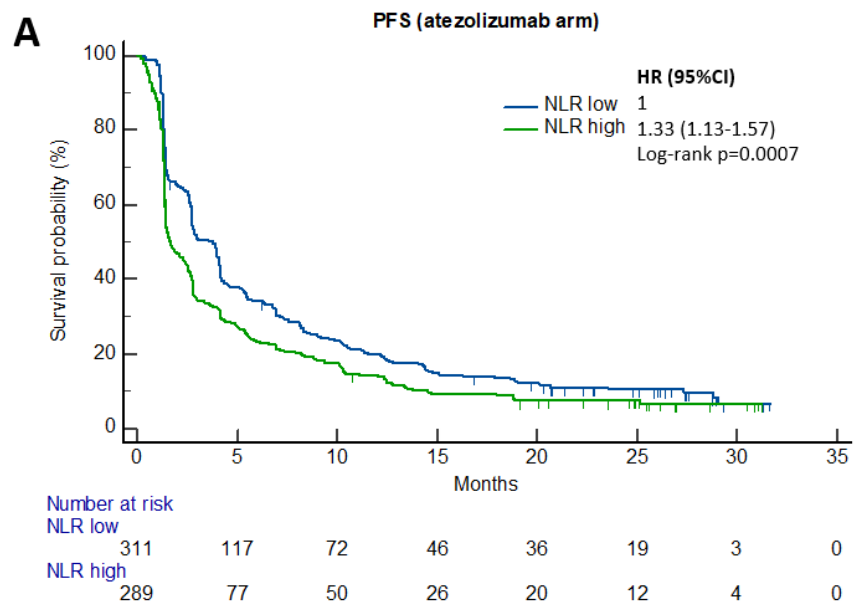


Number at risk	0	5	10	15	20	25	30	35
0 factors	156	136	105	87	71	36	10	0
1 factor	271	208	149	114	81	57	14	0
2 factors	110	55	36	26	19	8	0	0

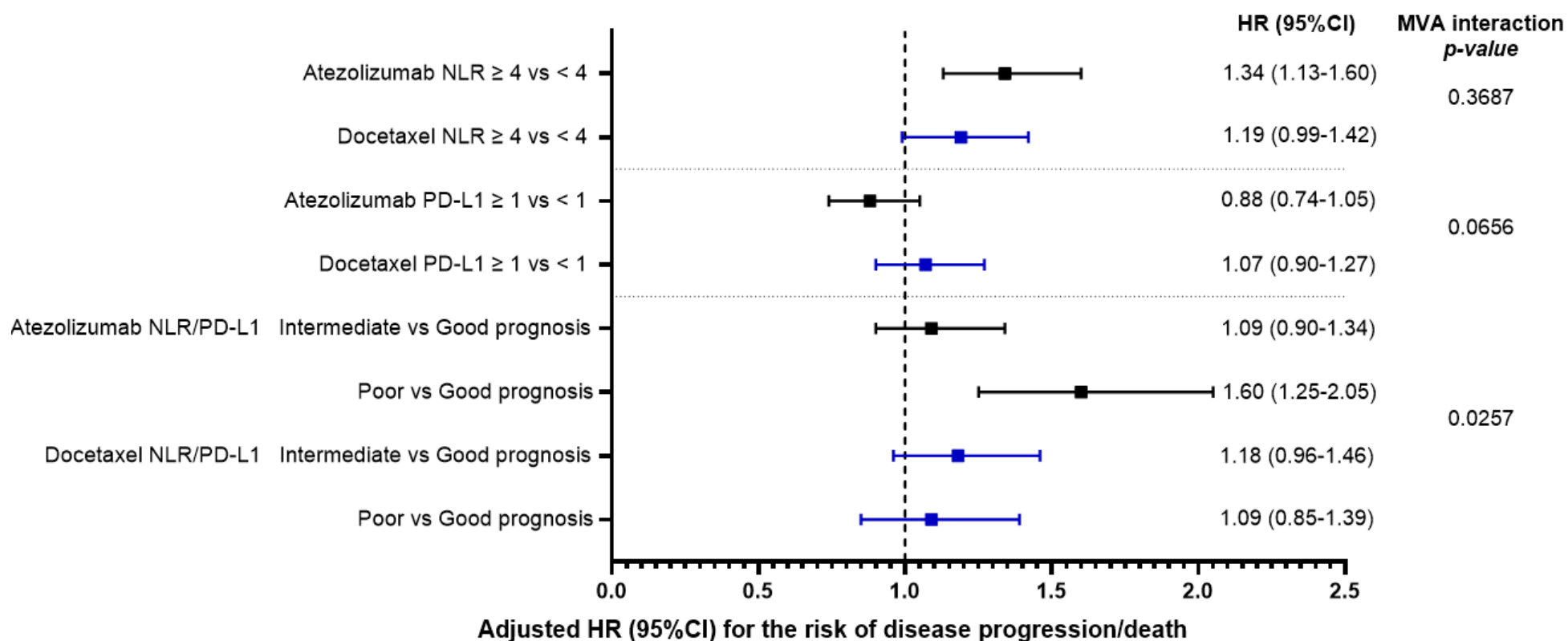


Number at risk	0	5	10	15	20	25	30	35
0 factors	137	109	80	55	38	23	3	0
1 factor	262	179	104	69	50	28	5	0
2 factors	127	79	45	34	24	13	1	0

Supplementary Figure 3: Kaplan-Meier survival estimates for Progression Free Survival according to the NLR. A) Atezolizumab cohort: NLR-low: 3.7 months (95%CI: 2.7-4.1; 279 events) vs NLR-high: 1.6 months (95%CI: 1.4-2.4; 263 events). **B) Docetaxel cohort:** NLR-low: 4.1 months (95%CI: 3.9-4.7; 252 events) vs NLR-high: 2.8 months (95%CI: 2.7-3.7; 284 events). Kaplan-Meier survival estimates for Progression Free Survival according to the NLR/PD-L1 complementation. **C) Atezolizumab cohort:** 0 factors: 3.9 months (95%CI: 2.7-4.1; 153 events) vs 1 factor: 2.7 months (95%CI: 2.3-2.9; 276 events) vs 2 factors: 1.5 months (95%CI: 1.4-1.9; 113 events). **D) Docetaxel cohort:** 0 factors: 4.2 months (95%CI: 3.9-5.4; 139 events) vs 1 factor: 3.2 months (95%CI: 2.7-3.9; 268 events) vs 2 factors: 3.5 months (95%CI: 2.7-4.1; 129 events).



Supplementary Figure 4: Forest plot graph reporting the adjusted HR for the risk of disease progression/death across the two cohorts (including EGFR/ALK positive patients), according to the NLR, PD-L1 expression and NLR/PD-L1 complementation. Adjusting factors were ECOG-PS (1 vs 0), histology (squamous vs non-squamous), number of metastatic sites (≤ 2 vs > 2), smoking status (former/current vs never smoker), and number of prior therapies (1 vs 2). The interaction terms through the same multivariable model including the pooled population. MVA: multivariable.



Supplementary Figure 5: Violin plot reporting the median baseline NLR (Log10) according to the mutational status of the selected genes of interest. A) TP53, B) KRAS, C) KEAP1, D) STK11, E) EGFR, F) SMARCA4, G) ARID1A, H) DDR genes (BRCA1/2, RAD51, RAD51C, CHEK2, ATM, ATR).

