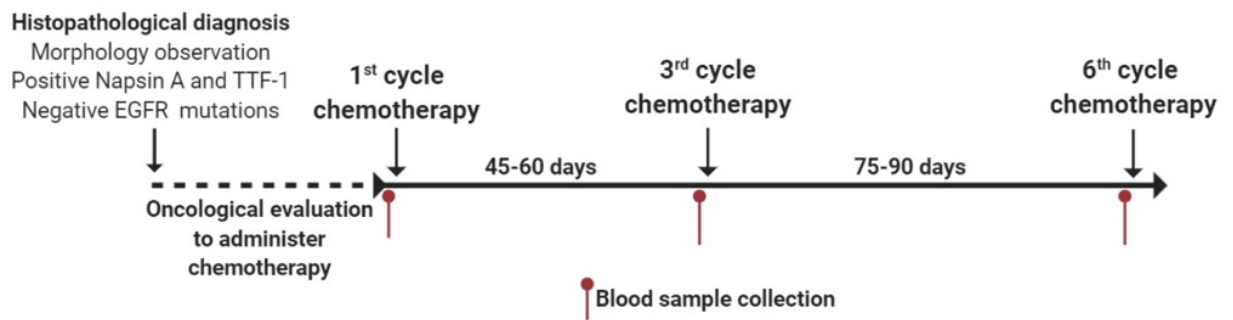


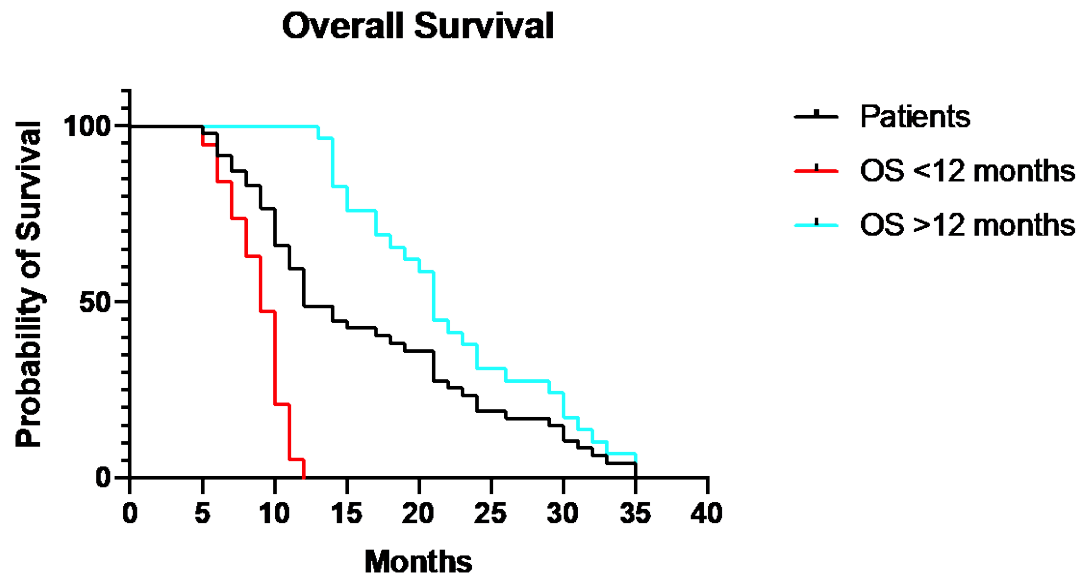
**Supplementary Table S1.** Patients characteristics at 3<sup>rd</sup> and 6<sup>th</sup> cycle of treatment.

| Characteristic                                               | 3 <sup>rd</sup> cycle of treatment |                               |                              |             | <i>p</i>           | 6 <sup>th</sup> cycle of treatment |                              |        |  | <i>p</i> |
|--------------------------------------------------------------|------------------------------------|-------------------------------|------------------------------|-------------|--------------------|------------------------------------|------------------------------|--------|--|----------|
|                                                              | Total Group                        | Patients with:                |                              | Total Group |                    | Patients with:                     |                              |        |  |          |
|                                                              |                                    | shorter survival <sup>1</sup> | longer survival <sup>1</sup> |             |                    | shorter survival <sup>1</sup>      | longer survival <sup>1</sup> |        |  |          |
| n                                                            | 53                                 | 22                            | 31                           | -           | 53                 | 22                                 | 31                           | -      |  |          |
| Clinical parameters                                          |                                    |                               |                              |             |                    |                                    |                              |        |  |          |
| Leukocytes (10 <sup>3</sup> /mm <sup>3</sup> ) <sup>2</sup>  | 6.4 (5.3-8.2)                      | 7.1 (5.4-10)                  | 5.8 (4.9-8)                  | 0.1346      | 6.2 (5.2-8)        | 7.8 (5.6-11.8)                     | 5.8 (4.4-8.6)                | 0.0761 |  |          |
| Lymphocytes (10 <sup>3</sup> /mm <sup>3</sup> ) <sup>2</sup> | 1.8 (1.5-2.2)                      | 1.7 (1.5-2.1)                 | 1.8 (1.5-2.3)                | 0.9388      | 1.5 (1.1-2.3)      | 1.3 (0.9-2.3)                      | 1.7 (1.4-2.2)                | 0.2094 |  |          |
| TGF-β (ng/mL) <sup>2</sup>                                   | 19.5 (12.5-29.8)                   | 16 (8.4)                      | 19.6 (13.3-25.7)             | 0.2178      | 18.7 (12.2-27.8)   | 17.4 (13.3-27.2)                   | 18.1 (10.8-27.6)             | 0.8074 |  |          |
| HMGB-1 (ng/mL) <sup>2</sup>                                  | 1.9 (1.3-2.7)                      | 1.9 (1.4-2.7)                 | 1.9 (1.2-2.8)                | 0.8902      | 2 (1.4-2.9)        | 1.9 (0.9-2.7)                      | 2 (1.4-3.0)                  | 0.3895 |  |          |
| IL-6 (pg/mL) <sup>2</sup>                                    | 3 (1.6-5.4)                        | 3.7 (2.6-5.3)                 | 2.7 (1.5-5.4)                | 0.3873      | 3.8 (1.9-8.1)      | 5.7 (2.2-12.9)                     | 2.8 (1.8-6.4)                | 0.1701 |  |          |
| NLR <sup>2</sup>                                             | 1.8 (1.5-2.5)                      | 2.2 (1.6-3.5)                 | 1.7 (1.5-2.2)                | 0.1274      | 2.1 (1.5-3)        | 2.9 (2-6.1)                        | 1.8 (1.2-2.2)                | 0.0008 |  |          |
| SII <sup>2</sup>                                             | 605.8 (432.8-813.2)                | 625.2 (433.7-818)             | 605.8 (414.5-834.2)          | 0.8346      | 593.4 (345.9-1093) | 1062 (517.7-2278)                  | 411.5 (293.6-729.5)          | 0.001  |  |          |
| T-lymphocytes (%) <sup>3</sup>                               |                                    |                               |                              |             |                    |                                    |                              |        |  |          |
| CD4+                                                         | 39.45 ± 3.31                       | 44.7 ± 6.49                   | 36.82 ± 3.74                 | 0.2746      | 41.81 ± 3.28       | 49.46 ± 4.75                       | 37.56 ± 4.11                 | 0.1599 |  |          |
| Th1 (%) <sup>3</sup>                                         | 12.40 ± 2.57                       | 15.38 ± 3.71                  | 7.43 ± 2.31                  | 0.0838      | 11.33 ± 2.34       | 13.61 ± 3.30                       | 7.23 ± 2.41                  | 0.1178 |  |          |
| Th2 (%) <sup>3</sup>                                         | 2.81 ± 0.38                        | 2.91 ± 0.49                   | 2.63 ± 0.62                  | 0.9070      | 2.77 ± 0.34        | 2.86 ± 0.41                        | 2.62 ± 0.61                  | 0.6888 |  |          |
| Th17 (%) <sup>3</sup>                                        | 3.42 ± 0.39                        | 3.18 ± 0.54                   | 3.88 ± 0.51                  | 0.2198      | 3.71 ± 0.47        | 3.39 ± 0.52                        | 4.28 ± 0.96                  | 0.4081 |  |          |
| Treg (%) <sup>3</sup>                                        | 4.43 ± 0.46                        | 4.71 ± 0.59                   | 3.91 ± 0.74                  | 0.5251      | 4.10 ± 0.35        | 4.12 ± 0.41                        | 4.08 ± 0.68                  | 0.8322 |  |          |
| CD8+ (%) <sup>3</sup>                                        | 26.87 ± 2.48                       | 17.60 ± 1.95                  | 31.50 ± 3.06                 | 0.0533      | 25.47 ± 1.86       | 19.06 ± 1.48                       | 29.03 ± 2.40                 | 0.0025 |  |          |
| CTLs                                                         |                                    |                               |                              |             |                    |                                    |                              |        |  |          |
| GrB+Perf+ (%) <sup>3</sup>                                   | 37.54 ± 3.91                       | 25.29 ± 3.76                  | 43.66 ± 5.01                 | 0.072       | 38.39 ± 3.98       | 2625.34 ± 6.49                     | 45.64 ± 4.                   | 0.0085 |  |          |

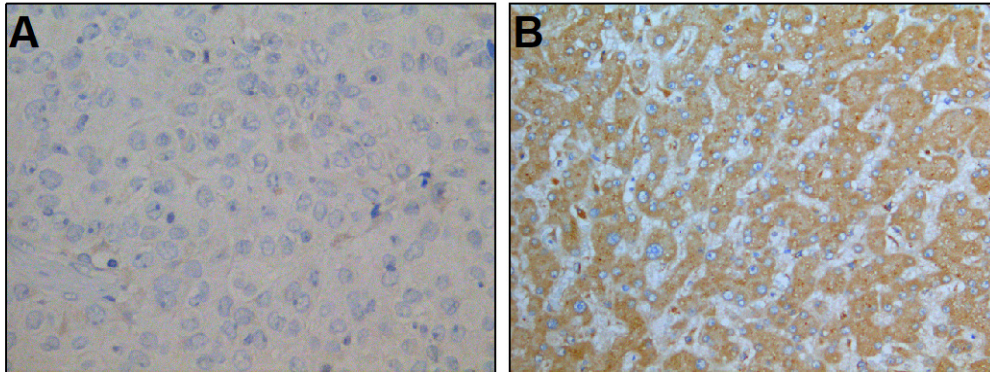
<sup>1</sup> Patients were categorized according to median OS. <sup>2</sup> Median (interquartile range). <sup>3</sup> Mean ± SEM. NLR = Neutrophil-lymphocyte ratio. SII = Systemic immune-inflammatory index. GrB = Granzyme B. Perf = Perforin.



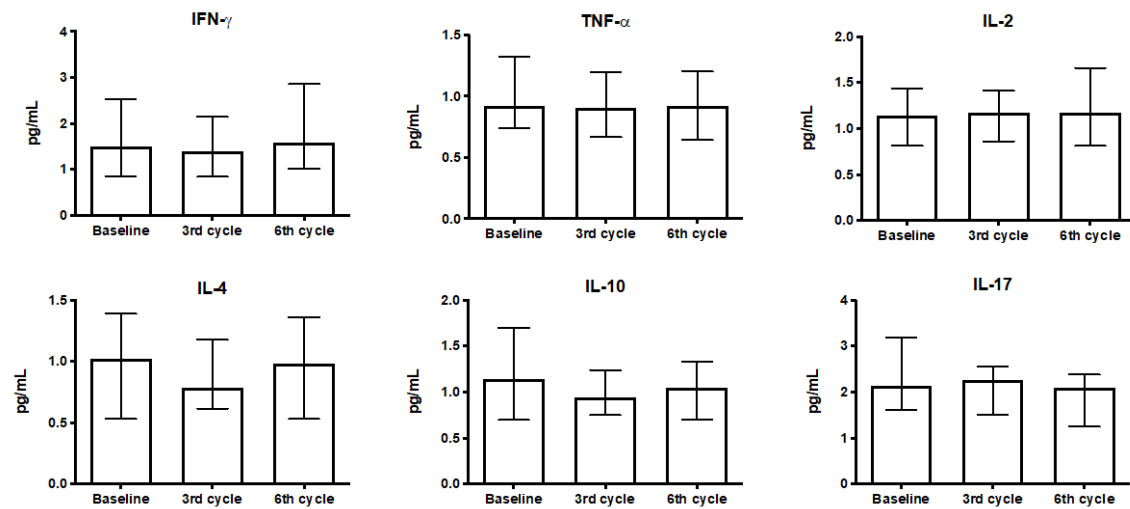
**Supplementary Figure S1.** Schematic representation of lung adenocarcinoma patient's treatment. The first, third, and sixth cycle of treatment is indicated. Also, the blood sample collection is shown. Created with BioRender.com.



**Supplementary Figure S2.** Kaplan-Meier overall survival (OS) analysis. Total patients ( $n = 53$ ), patients with shorter ( $< 12$  months,  $n = 22$ ) and longer ( $> 12$  months,  $n = 31$ ) OS are shown.



**Supplementary Figure S3.** Negative and positive controls for IL-6 staining. (A) Tumor tissue without primary antibody (Negative control) and (B) IL-6 staining in liver biopsy (Positive control) are shown. Magnification 200X.



**Supplementary Figure S4.** IFN- $\gamma$ , TNF- $\alpha$ , IL-2, IL-4, IL-10 and IL-17 plasma concentrations in patients throughout treatment cycles.  $n = 53$ . Median and interquartile ranges are shown.