Table1. Baseline clinicopathological information between DCB and DNB groups.

| Variables | DCB (n=72) | NDB (n=47) |
|---|---|---|
| Age (years) | 65.54±7.37 | 68.68±8.63 |
| Gender | | |
| Female | 25 (34.7%) | 18 (38.3%) |
| Male | 47 (65.3%) | 29 (61.7%) |
| Pathology | | |
| Adenocarcinoma | 42 (58.3%) | 21 (44.7%) |
| Squamous cell carcinoma | 26 (36.1%) | 18 (38.3%) |
| Sarcomatoid carcinoma | 4 (5.6%) | 5 (10.6%) |
| Poor differentiated carcinoma | 0 (0.0%) | 3 (6.4%) |
| Multiple primary carcinoma | | |
| Yes | 11 | 14 |
| No | 61 | 33 |
| Smoking history | | |
| Yes | 59 | 31 |
| No | 13 | 16 |
| Family history of cancer | | |
| Yes | 19 | 17 |
| No | 53 | 30 |
| ECOG PS | | |
| 0-1 | 72 (100%) | 38 (80.9%) |
| 2 | 0 (0.0%) | 9 (19.1%) |
| TMB | | |
| <10/MB | 23 (31.9%) | 31 (66.0%) |
| 10-19/MB | 29 (40.3%) | 11 (23.4%) |
| ≥20/MB | 20 (27.8%) | 5 (10.6%) |
| PD-L1 | | |
| 50-74% | 40 (55.6%) | 28 (59.6%) |
| 75-100% | 32 (44.4%) | 19 (40.4%) |
| Treatment | | |
| ICI | 11 (15.3%) | 14 (29.8%) |
| Chemotherapy+ICI | 54 (75.0%) | 31 (66.0%) |
| Chemotherapy+ICI+antiangiogenesis | 7 (9.7%) | 2 (4.2%) |
| Best overall response | | |
| CR | 25 (34.7%) | 0 (0.0%) |
| PR | 31 (43.1%) | 6 (12.8%) |
| SD | 16 (22.2%) | 19 (40.4%) |
| PD | 0 (0.0%) | 16 (34.0%) |
| ED | 0 (0.0%) | 6 (12.8%) |
| Tumor response rate | | |
| ORR | 56 (77.8%) | 6 (12.8%) |
| DCR | 72 (100%) | 25 (53.2%) |

DCB: durable clinical benefit; NDB: no durable benefit; ECOG: eastern cooperative oncology

group; PS: performance status score; TMB: tumor mutation burden; PD-L1, programmed cell death ligand 1; ICI：immune checkpoint inhibitor; CR: complete response; PR: partial response; SD: stable disease; PD: progressive disease; ED: early death; ORR, overall response rate; DCR, diseased control rate; ORR=(CR+PR)/(CR+PR+SD+PD)*100(%); DCR=(CR+PR+SD)/(CR+PR+SD+PD)*100(%); TH: helper T cells; TS: suppressor T cells.

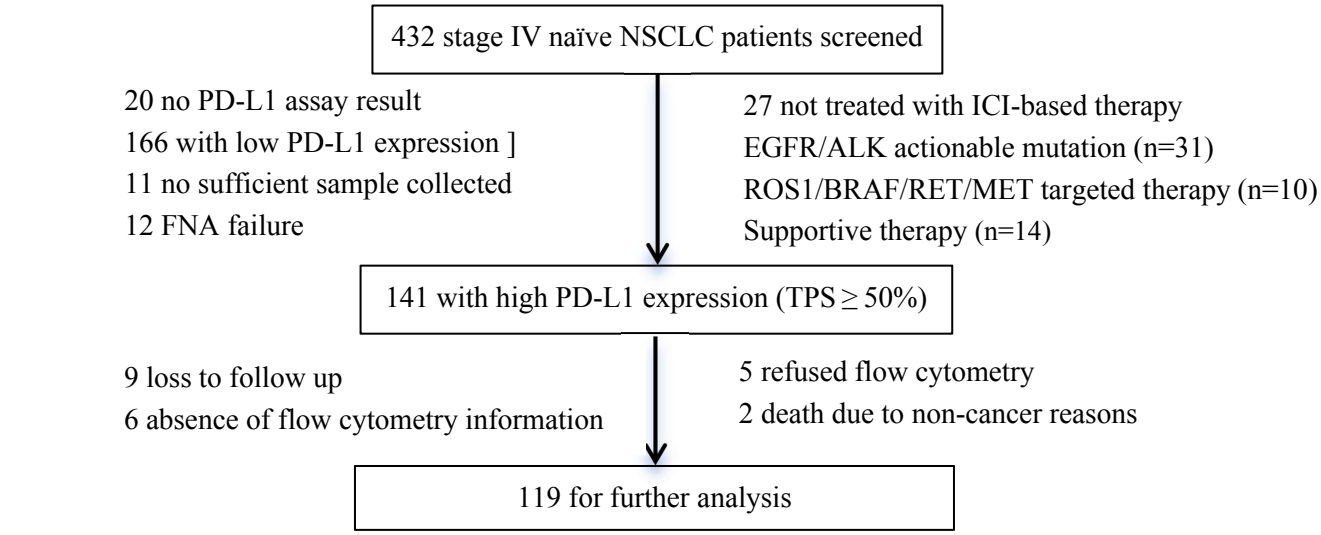
Table 2. Counts of baseline lymphocyte subsets in DCB and NDB groups.

| Lymphocyte subsets (cells/μL) | DCB (n=72) | NDB (n=47) | *p* value |
|---|---|---|---|
| Total lymphocyte | 1638±739.19 | 1356±634.03 | 0.3803 |
| Total T cell | 1167±577.02 | 978±480.61 | 0.2962 |
| CD4+ T cell | 768±415.26 | 468±223.31 | 0.0006 |
| CD8+ T cell | 359±195.48 | 470±324.18 | 0.0043 |
| Total B cell | 122±77.84 | 110±67.20 | 0.4008 |
| NK cell | 312±180.95 | 254±175.81 | 0.8698 |
| TH/TS ratio | 2.24±0.75 | 1.17±0.43 | 0.0018 |

Table 3. Comparison of circulating lymphocyte subpopulations after disease progression in DCB and NDB groups

| Lymphocyte subsets | DCB(55) | | NDB(41) | |
|---|---|---|---|---|
| | Count(cells/μL) | *p* value | Count(cells/μL) | *p* value |
| Total lymphocyte ($1^{st}$ vs PD) | 1633 ± 764.14 vs 1655±770.43 | 0.8831 | 1378±631.51 vs 1606± 868.17 | 0.1246 |
| Total T cell ($1^{st}$ vs PD) | 1176 ± 601.38 vs 1172±559.44 | 0.9755 | 993±484.08 vs 1125± 591.26 | 0.1942 |
| CD4+ T cell ($1^{st}$ vs PD) | 770 ± 435.75 vs 721±341.18 | 0.5626 | 464 ± 201.12 vs 454 ± 264.06 | 0.7446 |
| CD8+ T cell ($1^{st}$ vs PD) | 364 ± 204.19 vs 403±205.04 | 0.3300 | 485 ± 339.01 vs 607 ± 358.10 | 0.1160 |
| Total B cell ($1^{st}$ vs PD) | 125±81.80 vs 113 ±91.42 | 0.4921 | 108 ± 65.11 vs 125 ± 150.15 | 0.5940 |
| NK cell ($1^{st}$ vs PD) | 295 ± 164.03 vs 336±246.82 | 0.3354 | 262 ± 181.51 vs 279 ± 167.69 | 0.6532 |
| TH/TS ratio ($1^{st}$ vs PD) | 2.21±0.78 vs 1.88 ±0.60 | 0.0006 | 1.15 ± 0.40 vs 0.86 ± 0.44 | <0.0001 |

Figure 1. Flowchart of patient selection



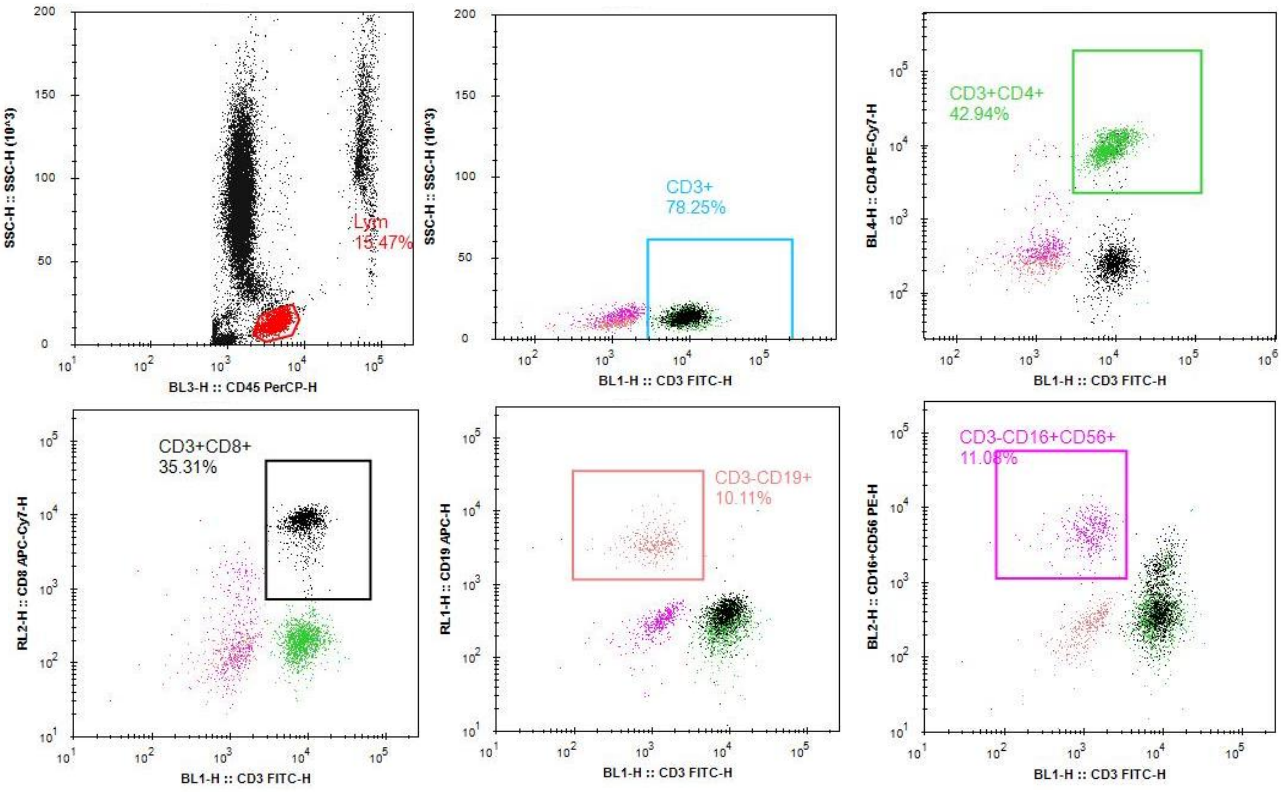
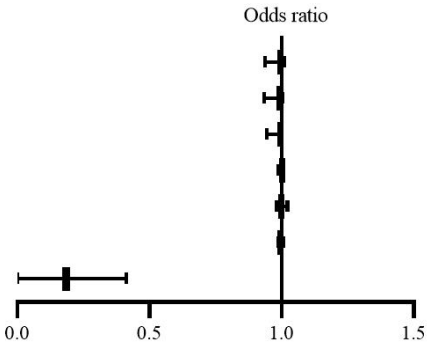




Figure 2. The circulating lymphocyte subsets determined using six-color flow cytometry, including T lymphocytes (CD3+), CD4+ T cells (CD3+CD4+), CD8+ T cells (CD3+CD8+), B lymphocytes (CD3-CD19+), natural killer cells (NK cells, CD3-CD16+CD56+).




| | p value | Odds ratio |
|---|---|---|
| Total lymphocyte | 0.3803 | 0.9943(0.9387-1.0112) |
| Total T cell | 0.2962 | 0.9932(0.9353-1.0032) |
| CD4+ T cell | 0.0006 | 0.9961(0.9443-0.9887) |
| CD8+ T cell | 0.0043 | 1.0021(0.9871-1.0053) |
| Total B cell | 0.4008 | 0.9977(0.9808-1.0220) |
| NK cell | 0.8698 | 0.9881(0.9953-1.0049) |
| TH/TS ratio | 0.0018 | 0.1855(0.0002-0.4125) |

Figure 3. The logistic regression of baseline circulating lymphocyte subsets to predict objective response.

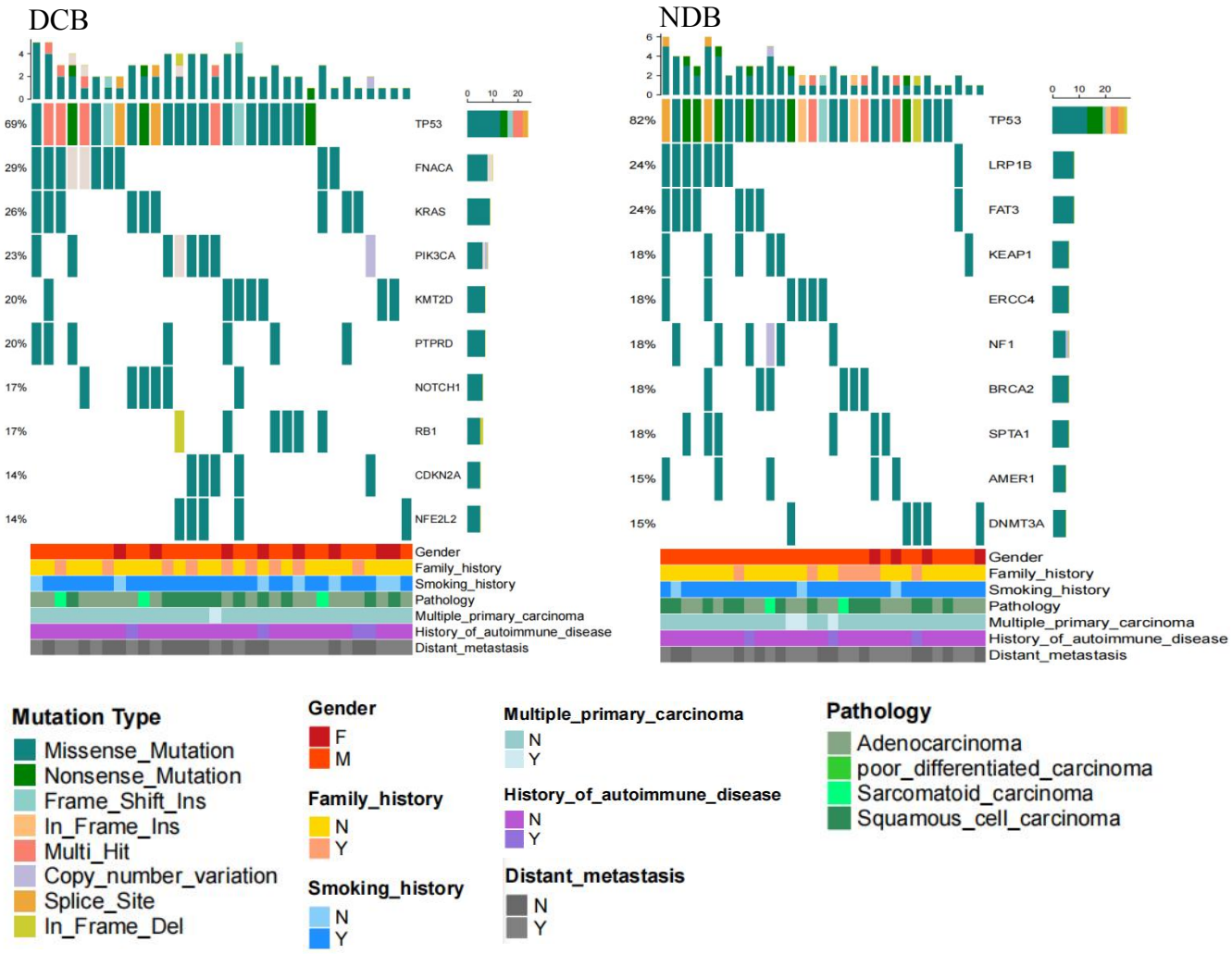



Figure 4. The top 10 genes detected by pre-treated NGS in both DCB and NDB groups. The prevalence of alterations were listed on the right; mutation counts were exhibited at the top; medical records of patients were shown on the bottom.

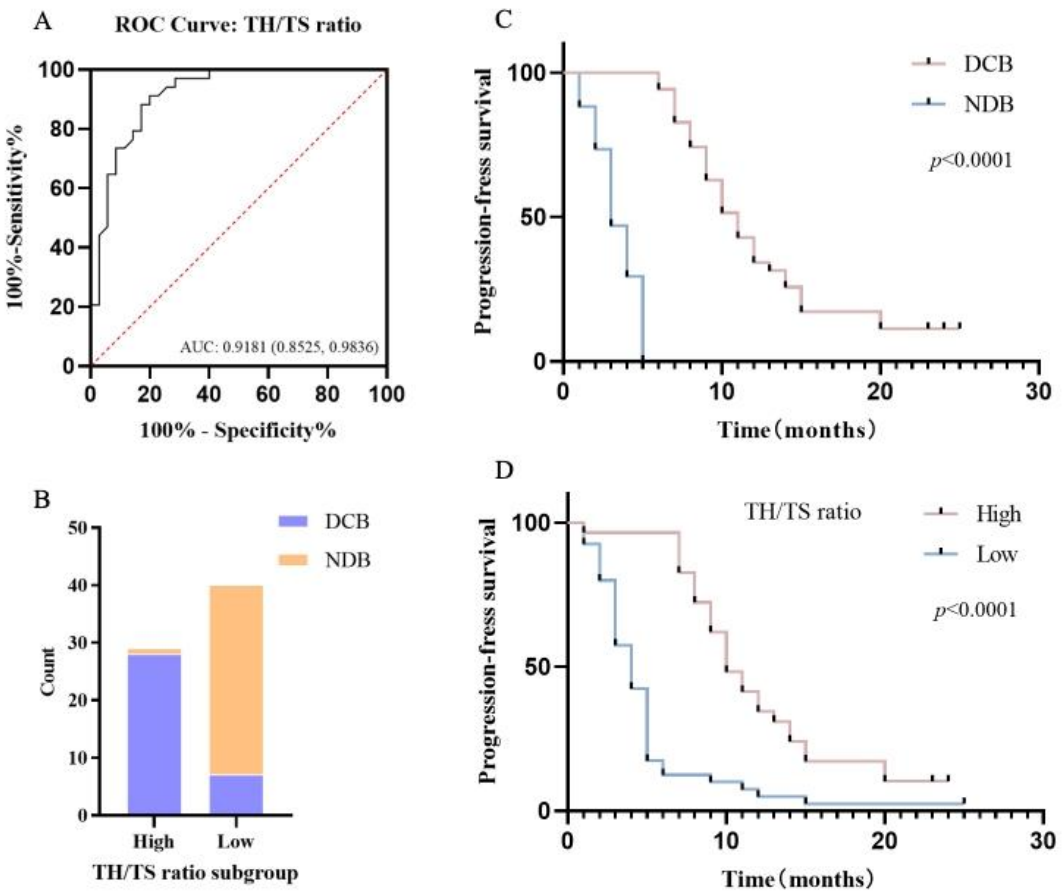



Figure 5. The ROC curve of baseline TH/TS ratio to predict therapeutic efficacy (A). The value of TH/TS cut-off-point to distinguish patients between DCB and NDB groups (B). Kaplan-Meier survival curve for PFS in DCB and NDB groups (C). Kaplan-Meier survival curve for PFS between different value of TH/TS subgroups (High: TH/TS≥1.735; Low: TH/TS<1.735) (D).

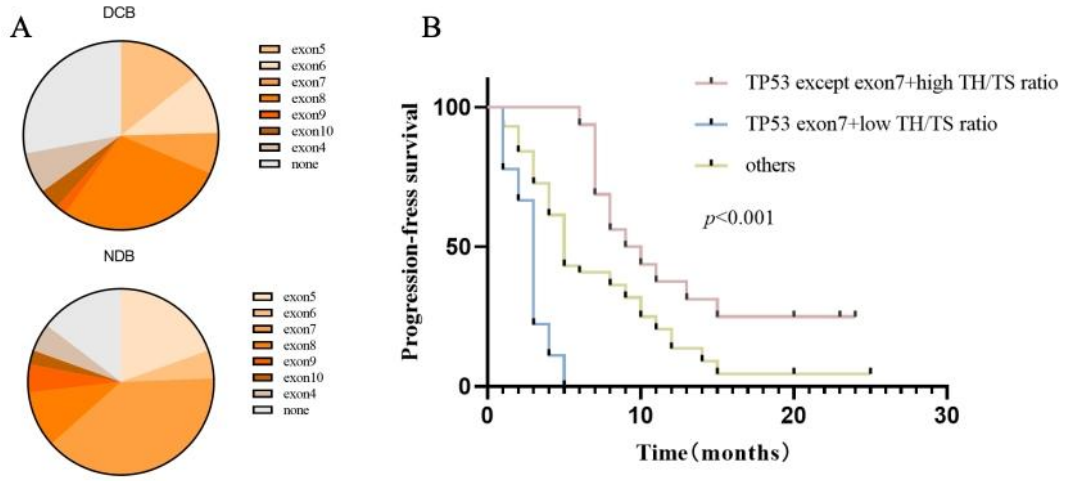



Figure 6. The distribution of TP53 variants in DCB and NDB groups (A). Kaplan-Meier survival curve for PFS between different TP53 mutations and TH/TS subgroups (B).