**Supplement Figures, 1-5, and Figure Legend**

**Supplement Figure 1.** Morphology and immunophenotype of pSTAT3+ DLBCL. **A-D.** Diffuse large B-celllymphoma (DLBCL), ABC subtype. **A.** Hematoxylin and Eosin. Diffuse sheet of large lymphoma cells with irregular nuclear contours, dispersed chromatin, 2-3 nucleoli and moderate amount of cytoplasm, consistent with centroblastic morphology. **B.** Lymphoma cells are positive for MUM1. **C.** Nuclear expression of phosphorylated STAT3 (pSTAT3) in lymphoma cells. **D.** pSTAT3+ DLBCL lymphoma cells are positive for MYC expression. **E-H.** DLBCL, GCB subtype. **E.** Hematoxylin and Eosin. Similar morphology is observed in pSTAT3+ DLBCL. **F.** Lymphoma cells are positive for CD10. **G.** Nuclear expression of pSTAT3 is not present in lymphoma cells. **H.** pSTAT3- DLBCL lymphoma cells are negative for MYC expression. All images were photographed at 400X magnification.

**Supplement Figure 2.** Relationship between *STAT3* mRNA and pSTAT3 expression and survival analysis based on *STAT3* mRNA level. **A.** Correlation between *STAT3* mRNA level and pSTAT3 expression in lymphoma cells is observed. Red bar denotes the mean value of pSTAT3 expression in lymphoma cells. low; low *STAT3* mRNA, int; intermediate *STAT3* mRNA, high; *STAT3* mRNA. Please see manuscript text for the reason of separation. **B.** Overall survival in all cases based on *STAT3* mRNA level. **C.** Overall survival in GCB DLBCL based on *STAT3* mRNA level. **D.** Overall survival in ABC DLBCL based on *STAT3* mRNA level.

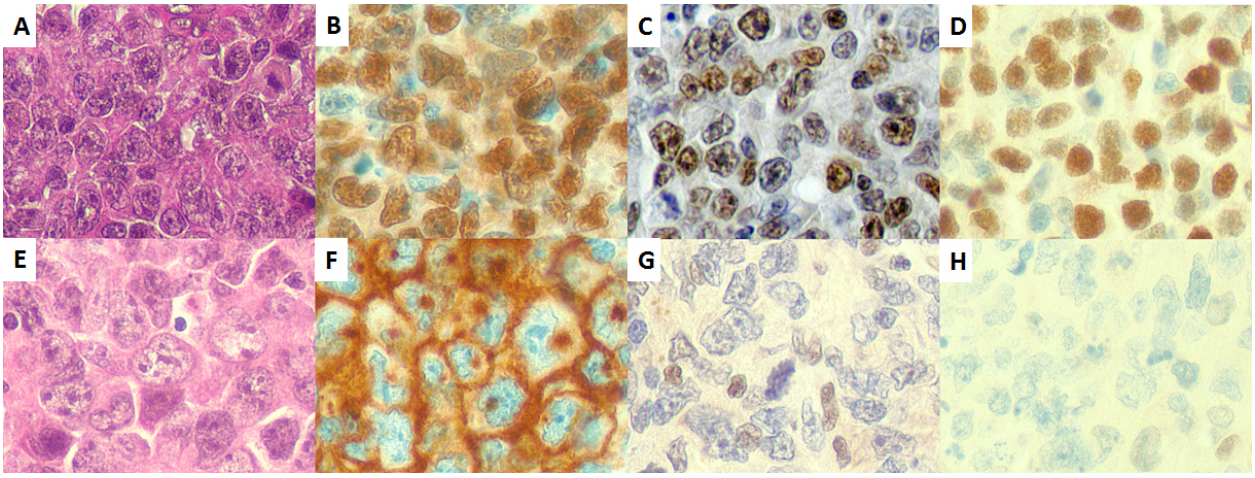
**Supplement Figure 3.** Survival analyses based on pSTAT3 expression in DLBCL with MYC/BCL2 double expression and DLBCL without MYC/BCL2 double expression after COO stratification. In all groups, statistical significances were not observed in terms of overall survival (OS).

**Supplement Figure 4.** Overall survival (OS) and progression-free survival (PFS) in all DLBCL cases, DLBCL with germinal center B-cell-like phenotype (GCB) and DLBCL with activated B-cell-like phenotype (ABC). With 30% cutoff, no differences were seen OS and PFS between pSTAT3+ DLBCL and pSTAT3- DLBCL as well as in GCB/ABC subgroups.

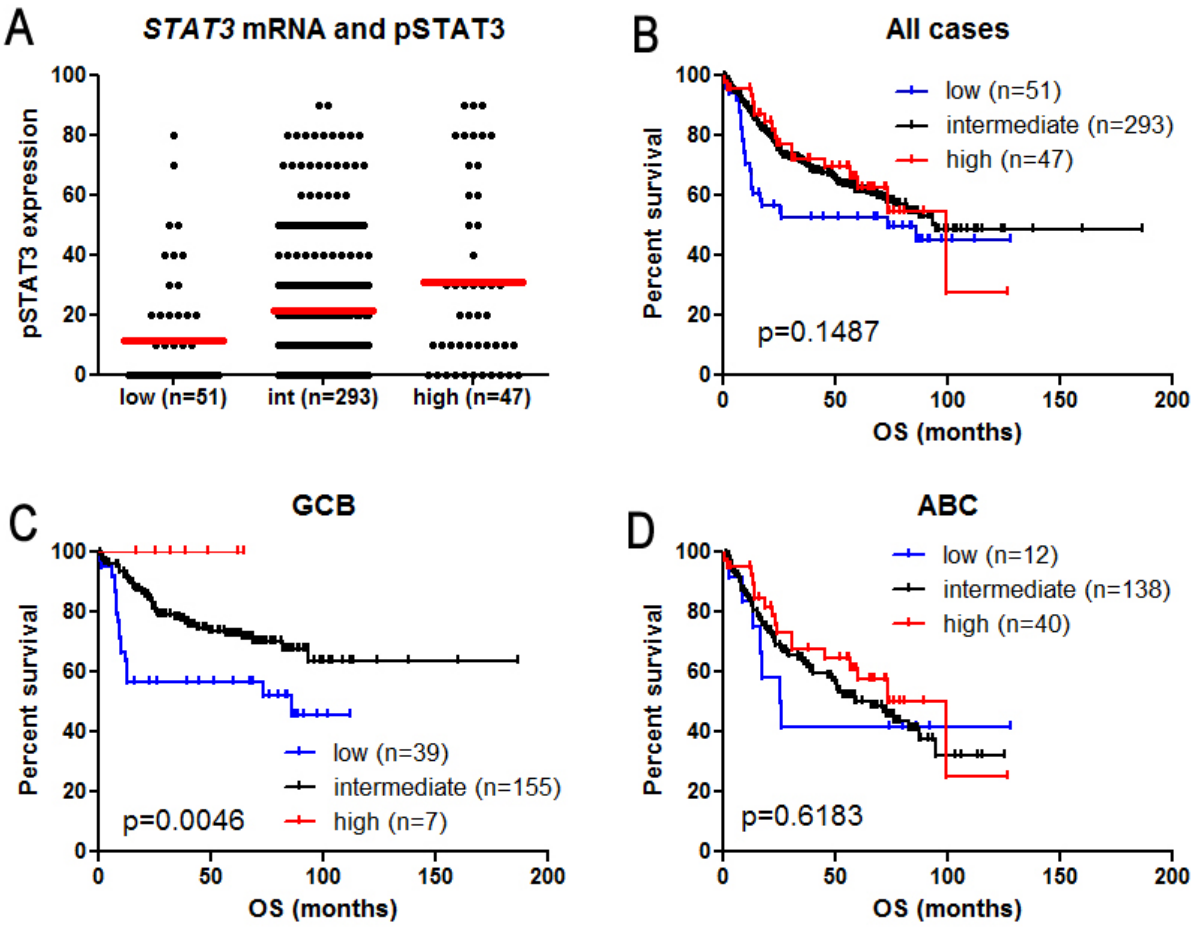
**Supplement Figure 5.** Survival analyses in 3 and 4 groups based on pSTAT3 expression in lymphoma cells. In the upper row with three groups, risk stratification is statistically significant in OS (p=0.0009) and PFS (p=0.010). In the lower row, overall risk stratification is observed in OS (p=0.024) and PFS (p=0.021). However, statistical significance was not observed between Q3 and Q4 in OS (p=0.798) and PFS (p=0.489). In the upper row, when Q3 and Q4 combined, risk stratification is becomes more powerful.

OS; overall survival, PFS; progression-free survival, **Upper row**, T1; pSTAT3 expression ≤20% of lymphoma cells, T2; pSTAT3 expression ≥30% and <50% of lymphoma cells, T3; pSTAT3 expression ≥50% lymphoma cells. **Lower row**, Q1; pSTAT3 expression <30% of lymphoma cells, Q2; pSTAT3 expression ≥30% and <50% of lymphoma cells, Q3; pSTAT3 expression ≥50% and <70% of lymphoma cells, Q4; pSTAT3 expression ≥70% of lymphoma cells,

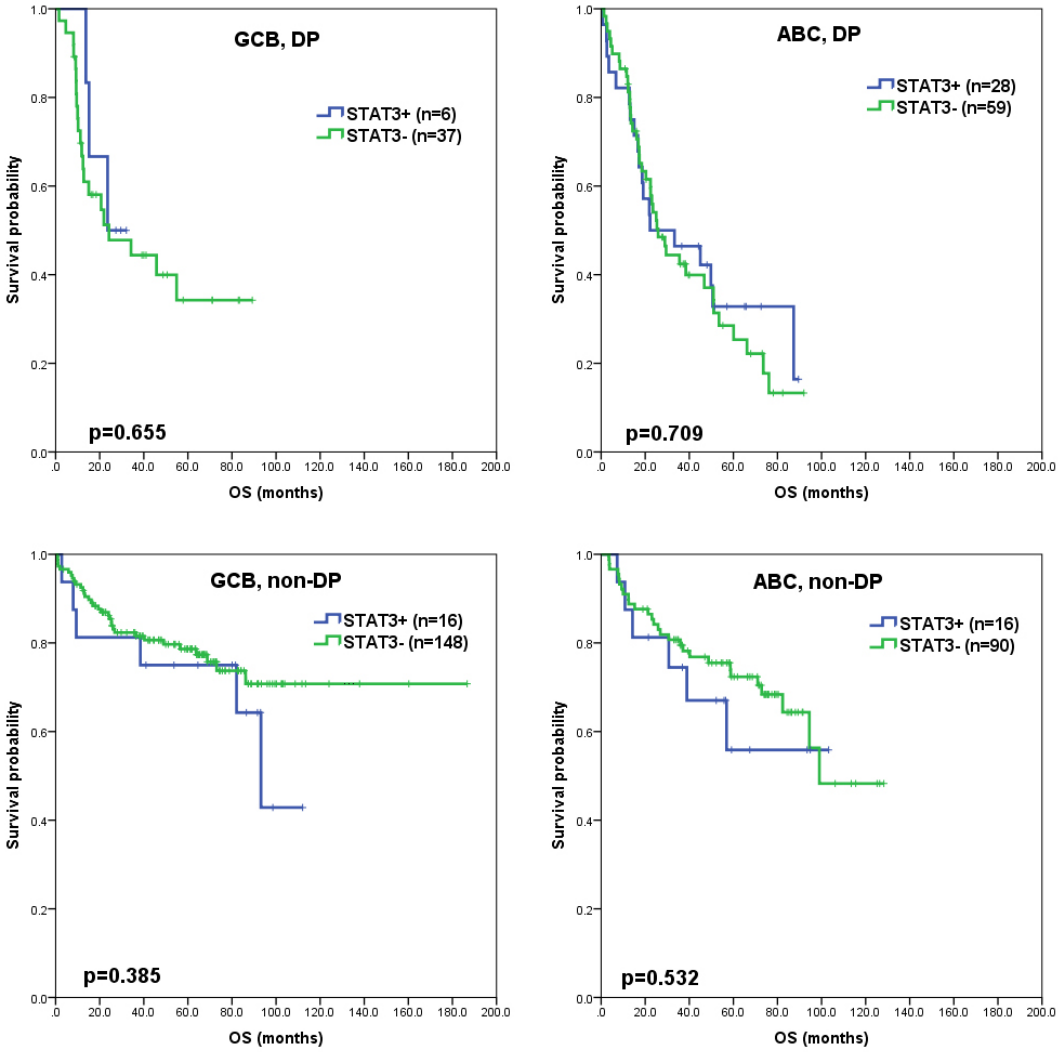
**Supplement Figure 1.**



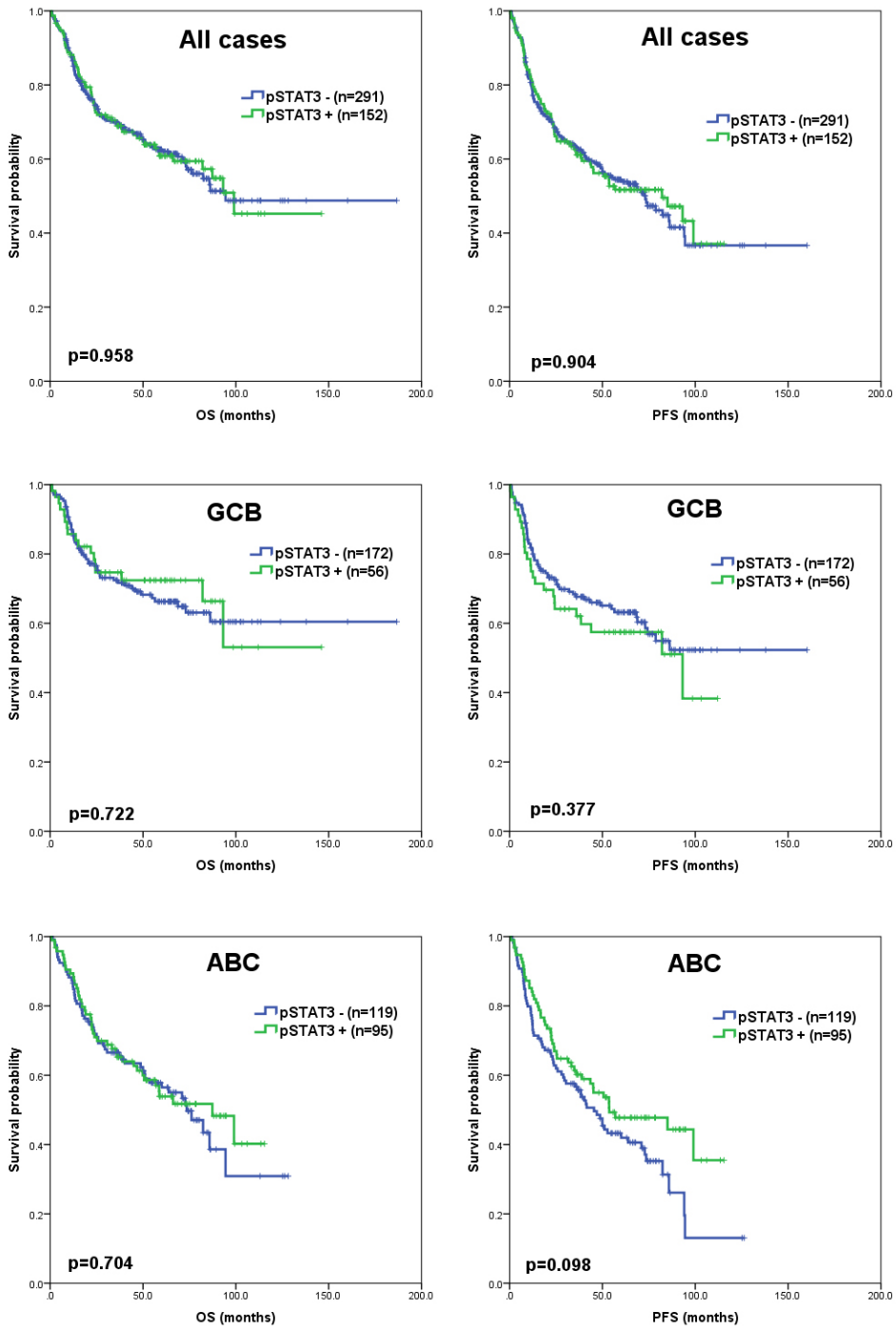
**Supplement Figure 2.**



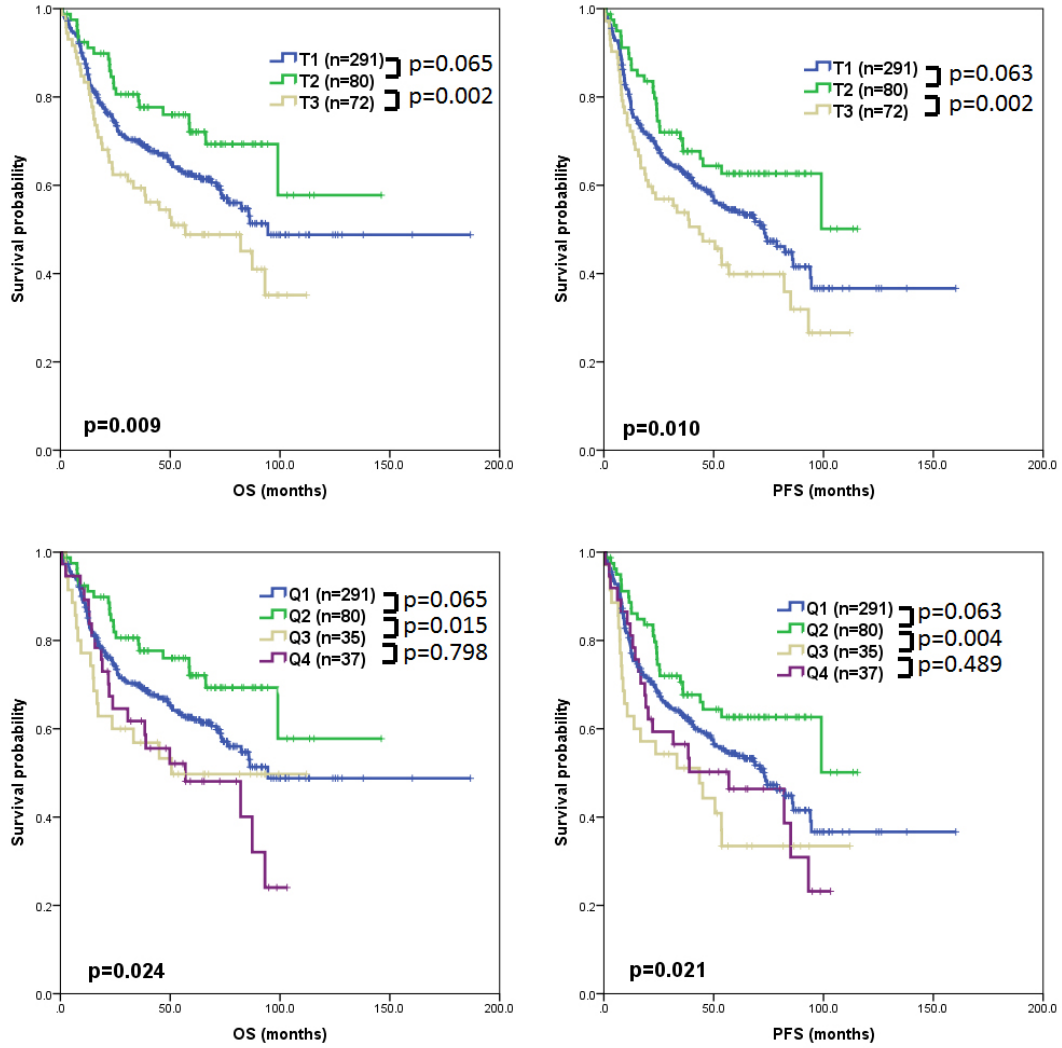
**Supplement Figure 3.**



**Supplement Figure 4.**



**Supplement Figure 5.**



## Supplement Tables

**Supplement Table 1.** Number of cases based on pSTAT3 expression, MYC/BCL2 double expression and COO classification

| | MYC/BCL2 double positive (DP) | | | MYC/BCL2 non-double positive (non-DP) | | |
|---|---|---|---|---|---|---|
| | GCB | ABC | not-classifiable | GCB | ABC | not-classifiable |
| pSTAT3+ | 6 | 28 | 0 | 16 | 16 | 0 |
| pSTAT3- | 37 | 59 | 0 | 148 | 90 | 0 |

*COO; cell-of-origin, GCB; germinal center B-cell-like phenotype, ABC; activated B-cell-like phenotype

**Supplement Table 2.** The numbers and percentages of pSTAT3 positive DLBCL with each cutoff

| pSTAT3 cutoff | 10% | 20% | 30% | 40% | **50%** | 60% | 70% | 80% | 90% |
|---|---|---|---|---|---|---|---|---|---|
| n | 298 | 227 | 152 | 103 | **72** | 48 | 37 | 24 | 5 |
| % | 67% | 51% | 34% | 23% | **16%** | 11% | 8% | 5% | 1% |

**Supplement Table 3.** Clinical characteristics and cell-of-origin differentiation with 30% cutoff for pSTAT3 expression

| | | **pSTAT3+ (cutoff 30%)** | **pSTAT3- (cutoff 30%)** | |
|---|---|---|---|---|
| | | N(%) | N(%) | p value |
| **patients** | | 152 (34.3) | 291 (65.7) | |
| **Gender** | | | | |
| | male | 95 (63) | 165 (57) | |
| | female | 57 (37) | 126 (43) | 0.264 |
| **Age** | | | | |
| | <60 | 59 (39) | 126 (43) | |
| | ≥60 | 93 (61) | 165 (56) | 0.417 |
| **B symptoms** | | | | |
| | Absent | 85 (60) | 177 (70) | |

| | | | | |
|---|---|---|---|---|
| | Present | 56 (40) | 77 (30) | 0.060 |
| **ECOG** | | | | |
| | <2 | 113 (85) | 207 (84) | |
| | ≥2 | 20 (15) | 39 (16) | 0.883 |
| **Stage** | | | | |
| | I/II | 59 (40) | 137 (49) | |
| | III/IV | 90 (60) | 141 (51) | 0.067 |
| **Extranodal site** | | | | |
| | <2 | 112 (76) | 218 (79) | |
| | ≥2 | 35 (24) | 58 (21) | 0.538 |
| **LDH** | | | | |
| | Normal | 56 (40) | 85 (33) | |
| | Elevated | 84 (60) | 174 (67) | 0.156 |
| **IPI** | | | | |
| | 0-2 | 78 (52) | 164 (57) | |
| | 3-5 | 72 (48) | 122 (43) | 0.311 |
| **Tumor size, cm** | | | | |
| | <6 | 77 (66) | 151 (68) | |
| | ≥6 | 40 (34) | 72 (32) | 0.718 |
| **Treatment response** | | | | |
| | CR/PR | 138 (91) | 257 (88) | |
| | No response | 14 (9) | 34 (12) | 0.52 |
| **COO classification** | | | | |
| | GCB | 56 (37) | 172 (59) | |
| | ABC | 95 (63) | 119 (41) | <0.001 |

*pSTAT3, phosphorylated STAT3; ECOG, Eastern Cooperative Oncology Group; LDH, lactic dehydrogenase; IPI, International Prognostic Index; CR, complete remission; PR, partial remission; COO, cell-of-origin; GCB, germinal center B-cell-like; ABC, activated B-cell-like

**Supplement Table 4.** Distribution of cell-of-origin classification based on 4 groups of pSTAT3 expression in lymphoma cells.

| | Q1, N(%) | Q2, N(%) | Q3, N(%) | Q4, N(%) | P value |
|---|---|---|---|---|---|
| **GCB** | 172 (59) | 32 (40) | 15 (43) | 9 (24) | |
| **ABC** | 119 (41) | 47 (60) | 20 (57) | 28 (76) | <0.001 |

*Q1: pSTAT3 expression ≤20% of lymphoma cells, Q2: pSTAT3 expression ≥30% and <50% of lymphoma cells, Q3: pSTAT3 expression ≥50% and <70% of lymphoma cells, Q4: pSTAT3 expression ≥70% of lymphoma cells, GCB, germinal center B-cell-like; ABC, activated B-cell-like

**Supplement Table 5.** Distribution of cell-of-origin classification based on 3 groups of pSTAT3 expression in lymphoma cells.

| | T1, N(%) | T2, N(%) | T3, N(%) | P value |
|---|---|---|---|---|
| **GCB** | 172 (59) | 32 (40) | 24 (33) | |
| **ABC** | 119 (41) | 47 (60) | 48 (67) | <0.001 |

*T1: pSTAT3 expression ≤20% of lymphoma cells, T2: pSTAT3 expression ≥30% and <50% of lymphoma cells, T3: pSTAT3 expression ≥50% lymphoma cells, GCB, germinal center B-cell-like; ABC, activated B-cell-like

**Supplement Table 6.** Bivariate analyses of pSTAT3 with each variable and pSTAT3.

| | HR | 95% CI | p value |
|---|---|---|---|
| **pSTAT3** | 1.066 | 0.717 to 1.585 | 0.753 |
| **MYC** | 2.573 | 1.721 to 3.848 | <0.001 |
| | | | |
| **pSTAT3** | 1.462 | 1.015 to 2.106 | 0.041 |
| **ABC subtype** | 1.424 | 1.047 to 1.937 | 0.024 |
| | | | |
| **pSTAT3** | 1.347 | 0.927 to 1.958 | 0.118 |
| **≥2 Extranodal site involvement** | 2.342 | 1.680 to 3.267 | <0.001 |
| | | | |
| **pSTAT3** | 1.346 | 0.931 to 1.946 | 0.115 |
| **stage III/IV** | 2.506 | 1.789 to 3.510 | <0.001 |

*ABC, activated B-cell-like