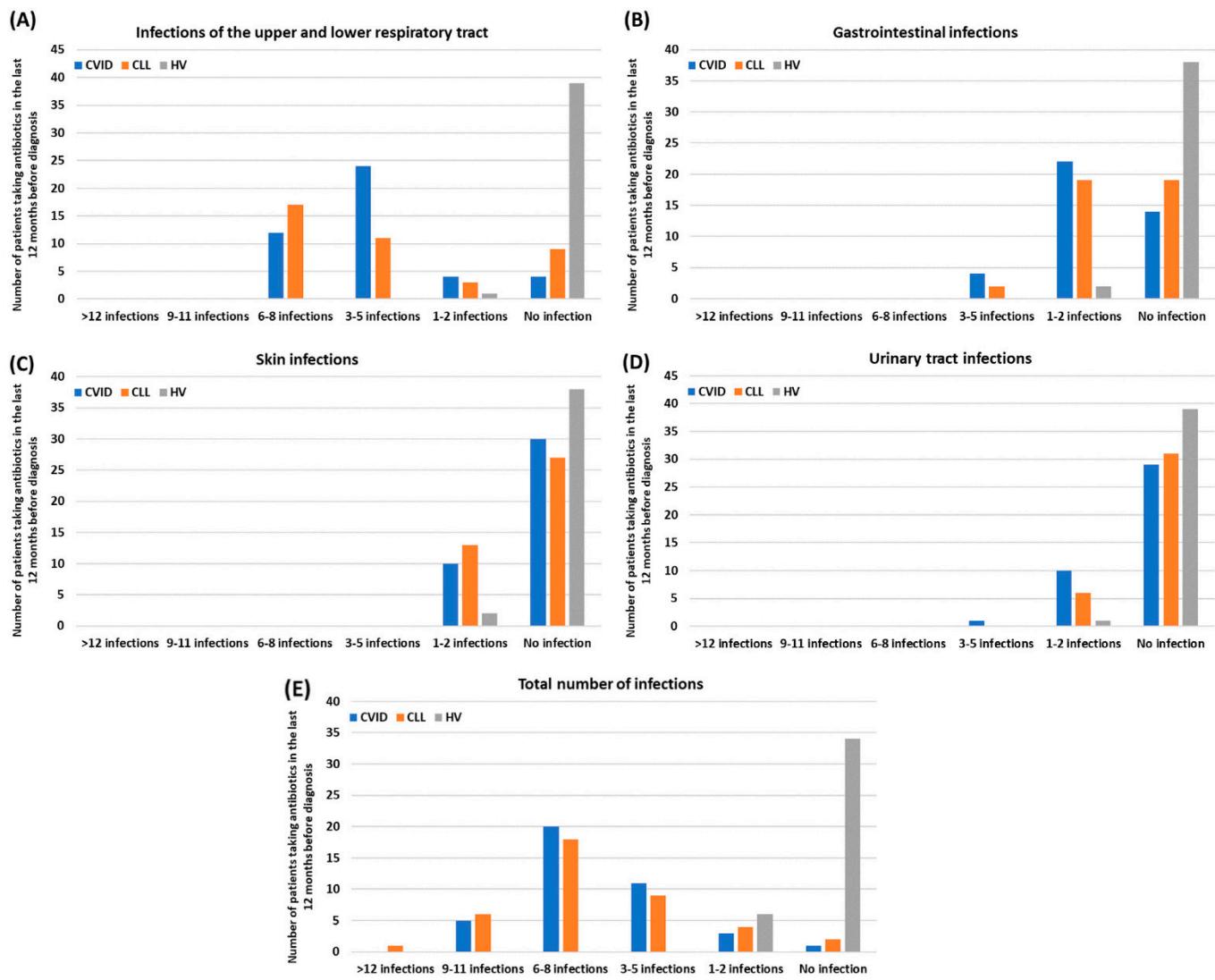


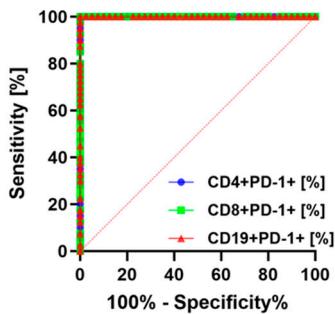
**Supplementary Figure S1.** Sample flow cytometry analysis and a gating strategy to evaluate subpopulations of T and B lymphocytes. We measured the percentage of positive events for CD4+CD3+ (green), CD8+CD3+ (blue), and CD19+CD3- (orange) cells, against molecules such as CD200, CD200R, CTLA-4, CD86, PD-1, and PD-L1. To ensure the accuracy of our findings, we included Fluorescence Minus One (FMO) controls as negative controls to establish the appropriate gating thresholds. The example analysis concerns a patient from the HV group.



**Supplementary Figure S2.** Schematic representation of the number of infections requiring antibiotic therapy in CVID and CLL patients and healthy volunteers during the last 12 months after diagnosis. (A) Number of upper and lower respiratory tract infections requiring antibiotic therapy in the last 12 months; (B) Number of gastrointestinal infections requiring antibiotic therapy in the past 12 months; (C) Number of skin infections requiring antibiotic therapy in the past 12 months; (D) Number of urinary tract infections requiring antibiotic therapy in the past 12 months; (E) total number of all infections requiring antibiotic therapy in the last 12 months.

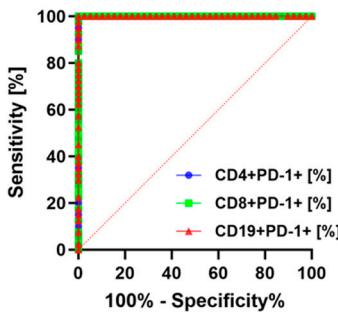
## CLL vs. HV patients

(A) ROC curve analysis of frequencies of T and B lymphocytes positive for PD-1 [%]

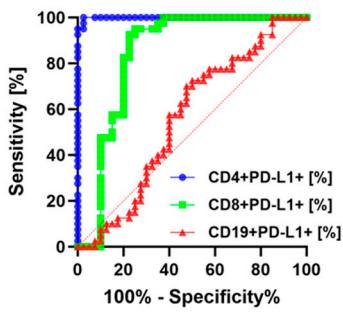


## CVID vs. HV patients

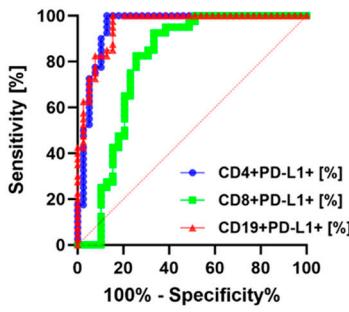
(B) ROC curve analysis of frequencies of T and B lymphocytes positive for PD-1 [%]



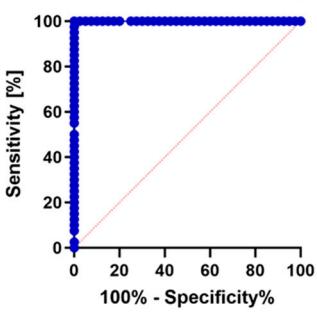
(C) ROC curve analysis of frequencies of T and B lymphocytes positive for PD-L1 [%]



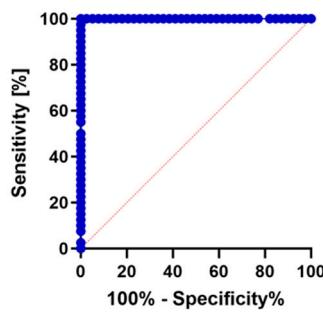
(D) ROC curve analysis of frequencies of T and B lymphocytes positive for PD-L1 [%]



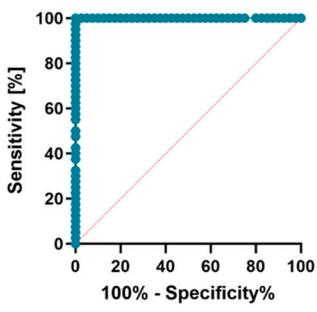
(E) ROC curve analysis of serum concentration sPD-1 [ng/ml]



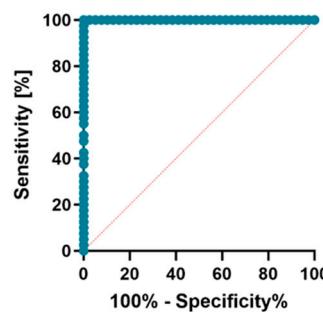
(F) ROC curve analysis of serum concentration sPD-1 [ng/ml]



(G) ROC curve analysis of serum concentration sPD-L1 [ng/ml]



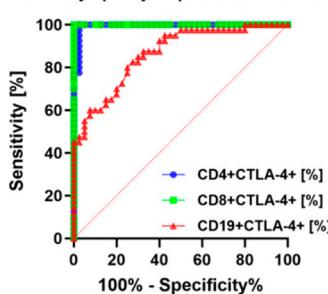
(H) ROC curve analysis of serum concentration sPD-L1 [ng/ml]



**Supplementary Figure S3** Analysis of ROC curves for the percentage of PD-1/PD-L1 occurrence on selected T and B lymphocyte subpopulations and the raw concentration of tested molecules between the tested patient groups. (A) ROC curve analysis of frequencies CD4+/CD8+ T lymphocytes and CD19+ B lymphocytes positive for PD-1 among CLL vs. HV patients [%];(B) ROC curve analysis of frequencies CD4+/CD8+ T lymphocytes and CD19+ B lymphocytes positive for PD-1 among CVID vs. HV patients [%]; (C) ROC curve analysis of frequencies CD4+/CD8+ T lymphocytes and CD19+ B lymphocytes positive for PD-L1 among CLL vs. HV patients [%];(D) ROC curve analysis of frequencies CD4+/CD8+ T lymphocytes and CD19+ B lymphocytes positive for PD-L1 among CVID vs. HV patients [%]; (E) ROC curve analysis of serum concentration sPD-1 among CLL vs. HV patients [ng/ml]; (F) ROC curve analysis of serum concentration sPD-1 among CVID vs. HV patients [ng/ml]; (G) ROC curve analysis of serum concentration sPD-L1 among CLL vs. HV patients [ng/ml]; (H) ROC curve analysis of serum concentration sPD-L1 among CVID vs. HV patients [ng/ml].

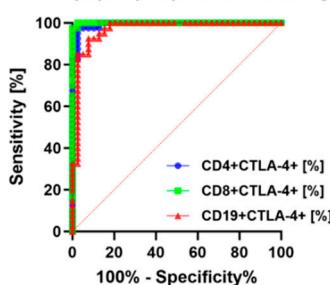
## CLL vs. HV patients

(A) ROC curve analysis of frequencies of T and B lymphocytes positive for CTLA-4 [%]

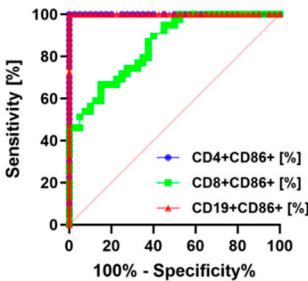


## CVID vs. HV patients

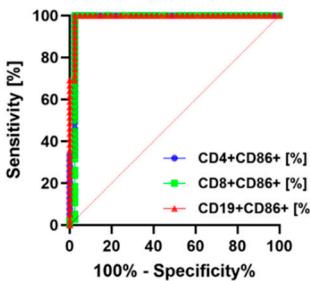
(B) ROC curve analysis of frequencies of T and B lymphocytes positive for CTLA-4 [%]



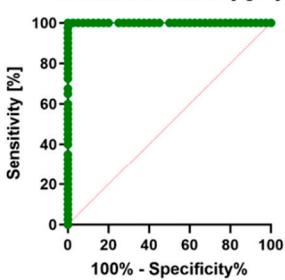
(C) ROC curve analysis of frequencies of T and B lymphocytes positive for CD86 [%]



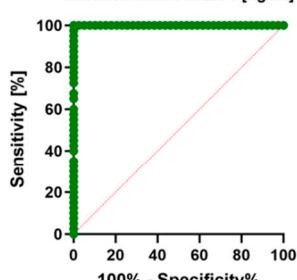
(D) ROC curve analysis of frequencies of T and B lymphocytes positive for CD86 [%]



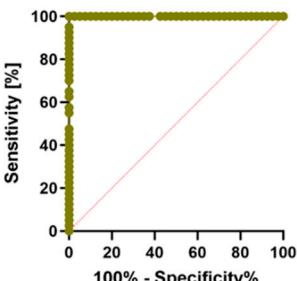
(E) ROC curve analysis of serum concentration sCTLA-4 [ng/ml]



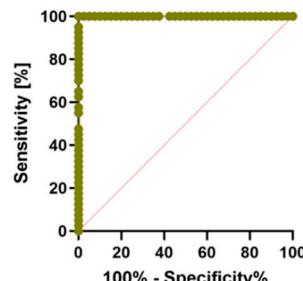
(F) ROC curve analysis of serum concentration sCTLA-4 [ng/ml]



(G) ROC curve analysis of serum concentration sCD86 [ng/ml]



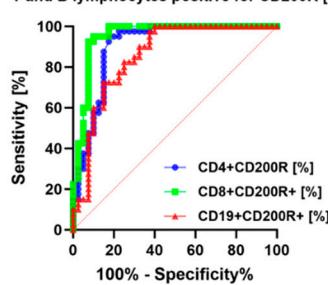
(H) ROC curve analysis of serum concentration sCD86 [ng/ml]



**Supplementary Figure S4.** Analysis of ROC curves for the percentage of CTLA-4/CD86 occurrence on selected T and B lymphocyte subpopulations and the raw concentration of tested molecules between the tested patient groups. (A) ROC curve analysis of frequencies CD4+/CD8+ T lymphocytes and CD19+ B lymphocytes positive for CTLA-4 among CLL vs. HV patients [%];(B) ROC curve analysis of frequencies CD4+/CD8+ T lymphocytes and CD19+ B lymphocytes positive for CTLA-4 among CVID vs. HV patients [%]; (C) ROC curve analysis of frequencies CD4+/CD8+ T lymphocytes and CD19+ B lymphocytes positive for CD86 among CLL vs. HV patients [%];(D) ROC curve analysis of frequencies CD4+/CD8+ T lymphocytes and CD19+ B lymphocytes positive for CD86 among CVID vs. HV patients [%]; (E) ROC curve analysis of serum concentration sCTLA-4 among CLL vs. HV patients [ng/ml]; (F) ROC curve analysis of serum concentration sCTLA-4 among CVID vs. HV patients [ng/ml]; (G) ROC curve analysis of serum concentration sCD86 among CLL vs. HV patients [ng/ml]; (H) ROC curve analysis of serum concentration sCD86 among CVID vs. HV patients [ng/ml].

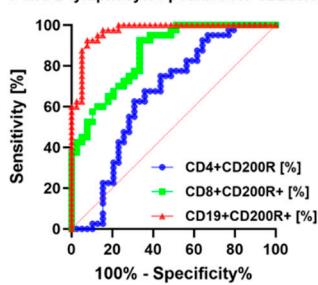
### CLL vs. HV patients

(A) ROC curve analysis of frequencies of T and B lymphocytes positive for CD200R [%]

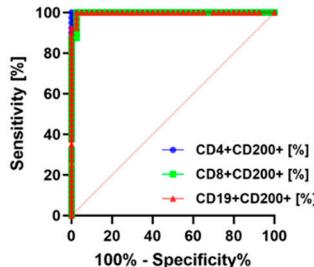


### CVID vs. HV patients

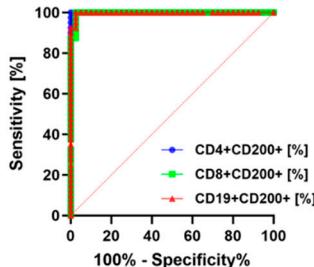
(B) ROC curve analysis of frequencies of T and B lymphocytes positive for CD200R [%]



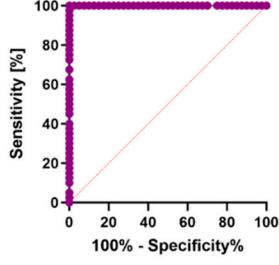
(C) ROC curve analysis of frequencies of T and B lymphocytes positive for CD200 [%]



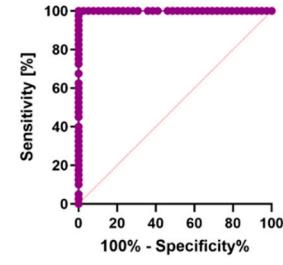
(D) ROC curve analysis of frequencies of T and B lymphocytes positive for CD200 [%]



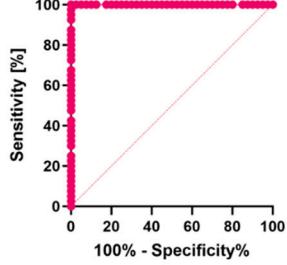
(E) ROC curve analysis of serum concentration sCD200R [ng/ml]



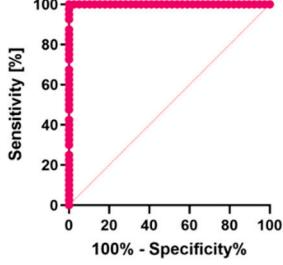
(F) ROC curve analysis of serum concentration sCD200R [ng/ml]



(G) ROC curve analysis of serum concentration sCD200 [ng/ml]



(H) ROC curve analysis of serum concentration sCD200 [ng/ml]



**Supplementary Figure S5.** Analysis of ROC curves for the percentage of CD200R/CD200 occurrence on selected T and B lymphocyte subpopulations and the raw concentration of tested molecules between the tested patient groups. (A) ROC curve analysis of frequencies CD4+/CD8+ T lymphocytes and CD19+ B lymphocytes positive for CD200R among CLL vs. HV patients [%];(B) ROC curve analysis of frequencies CD4+/CD8+ T lymphocytes and CD19+ B lymphocytes positive for CD200R among CVID vs. HV patients [%]; (C) ROC curve analysis of frequencies CD4+/CD8+ T lymphocytes and CD19+ B lymphocytes positive for CD200 among CLL vs. HV patients [%];(D) ROC curve analysis of frequencies CD4+/CD8+ T lymphocytes and CD19+ B lymphocytes positive for CD200 among CVID vs. HV patients [%]; (E) ROC curve analysis of serum concentration sCD200R among CLL vs. HV patients [ng/ml]; (F) ROC curve analysis of serum concentration sCD200R among CVID vs. HV patients [ng/ml]; (G) ROC curve analysis of serum concentration sCD200 among CLL vs. HV patients [ng/ml]; (H) ROC curve analysis of serum concentration sCD200 among CVID vs. HV patients [ng/ml].

**Supplementary Table S1.** Selected parameters of morphology and biochemistry of peripheral blood

| Parameter | CVID (n = 40)                   |                | CLL (n = 40)                  |                         | HV (n = 40)                    |                           | p-value | p-value      |             |            |
|-----------|---------------------------------|----------------|-------------------------------|-------------------------|--------------------------------|---------------------------|---------|--------------|-------------|------------|
|           | Mean ± SD                       | Median (Range) | Mean ± SD                     | Median (Range)          | Mean ± SD                      | Median (Range)            |         | CVID vs. CLL | CVID vs. HV | CLL vs. HV |
| WBC       | 6.92 ± 1.63<br>(4.78-9.99)      | 6.7            | 31.95± 11.35<br>(10.34-47.85) | 34.19<br>(5.54- 35.60)  | 5.66 ± 1.39<br>(3.40-7.78)     | 6.03<br>(0.76-2.85)       | 0.000*  | 0.000*       | 0.000*      | 0.005*     |
| LYM       | 0.96± 0.54<br>(0.08-1.99)       | 0.92           | 12.16± 5.21                   | 11.26<br>(0.09-1.71)    | 1.56 ± 0.49                    | 1.49<br>(0.20-0.81)       | 0.000*  | 0.000*       | 0.000*      | 0.000*     |
| MON       | 0.47± 0.15<br>(0.20-0.79)       | 0.47           | 0.57± 0.45<br>(0.09-1.71)     | 0.42<br>(0.61-7.40)     | 0.48± 0.15<br>(3.35± 1.27)     | 0.48<br>(0.91-5.52)       | 0.8394  | 0.601        | 0.524       | 0.629      |
| NEU       | 1.03± 0.56<br>(0.03-1.92)       | 1.14           | 3.31± 1.44                    | 3.15<br>(2.34-5.21)     | 3.35± 1.27<br>(4.51± 0.32)     | 3.50<br>(3.81-5.19)       | 0.000*  | 0.000*       | 0.6288      | 0.000*     |
| EOS       | 0.08± 0.03<br>(0.03-0.19)       | 0.08           | 0.12± 0.10<br>(0.01-0.51)     | 0.10<br>(0.10± 0.04)    | 0.09<br>(0.03-0.22)            | 0.09                      | 0.1510  | 0.169        | 0.698       | 0.047      |
| BAS       | 0.03± 0.02<br>(0.00-0.08)       | 0.03           | 0.08± 0.05<br>(0.01-0.21)     | 0.07<br>(0.04± 0.02)    | 0.03<br>(0.00-0.09)            | 0.03                      | 0.000*  | 0.000*       | 0.000*      | 0.1136     |
| RBC       | 3.39± 0.24<br>(2.86-3.89)       | 3.39           | 4.21± 0.70                    | 4.18<br>(8.20-14.40)    | 4.51± 0.32<br>(13.30± 0.90)    | 4.53<br>(11.10-15.50)     | 0.000*  | 0.000*       | 0.038*      | 0.000*     |
| HGB       | 9.98± 0.67<br>(8.33-11.63)      | 9.98           | 12.27± 1.71                   | 12.50<br>(34.00-198.00) | 13.30± 0.90<br>(244,50± 64.11) | 13.30<br>(233.50-152-404) | 0.000*  | 0.000*       | 0.0044*     | 0.000*     |
| PLT       | 115.43± 18.24<br>(86.36-148,42) | 114.09         | 122.85± 41.52                 | 116.00<br>(0.31-12.93)  | 244,50± 64.11<br>(12.40± 2.11) | 233.50<br>(7.23-16.06)    | 0.000*  | 0.3459       | 0.000*      | 0.000*     |
| IgG       | 5.08± 0.86<br>(2.96-6.58)       | 5.19           | 5.37± 3.51                    | 5.32<br>(0.05-3.38)     | 12.40± 2.11<br>(1.47± 0.57)    | 12.65<br>(0.40-2.52)      | 0.000*  | 0.7661       | 0.000*      | 0.000*     |
| IgM       | 1.37± 0.53<br>(0.37-2.38)       | 1.38           | 0.58± 0.79                    | 0.32<br>(0.23-4.37)     | 1.47± 0.57<br>(2.07± 0.76)     | 1.49<br>(0.70-4.00)       | 0.000*  | 0.000*       | 0.000*      | 0.392      |
| IgA       | 0.62± 0.23<br>(0.11-1.09)       | 0.64           | 1.79± 1.10                    | 1.44<br>(0.23-4.37)     | 1.95<br>(0.000*                | 0.000*                    | 0.000*  | 0.048        | 0.000*      |            |

\* Statistically significant results; Abbreviations: BAS- basophil; EOS- eosinophil; HGB- hemoglobin; IgA- immunoglobulin A; IgG- immunoglobulin G; IgM- immunoglobulin M; LYM- lymphocyte; MON- monocyte; NEU-neutrophil; PLT- platelet; RBC- red blood cell; WBC-white blood cell.

**Supplementary Table S2.** The peripheral blood immunophenotype of patients with CVID and CLL in comparison to that of HV.

| Parameter                                 | CVID (n = 40) |                        | CLL (n = 40) |                        | HV (n = 40) |                        | <i>p</i> -value |              |             |            |
|---|---------------|------------------------|--------------|------------------------|-------------|------------------------|-----------------|--------------|-------------|------------|
|   | Mean ± SD     | Median (Range)         | Mean ± SD    | Median (Range)         | Mean ± SD   | Median (Range)         |                 | CVID vs. CLL | CVID vs. HV | CLL vs. HV |
| Frequencies of CD45+ leukocytes [%]       | 92.88± 5.76   | 92.07<br>(88.75-98.79) | 96.05± 8.28  | 95.50<br>(84.83-98.42) | 97.28± 2.75 | 97.88<br>(89.14-99.37) | 0.000*          | 0.000*       | 0.000*      | 0.000*     |
| Frequencies of CD3+ T lymphocytes [%]     | 67.23± 9.66   | 66.40<br>(44.85-89.85) | 14.20± 7.54  | 12.24<br>(3.47-33.41)  | 74.83± 6.31 | 71.94<br>(65.09-96.34) | 0.000*          | 0.000*       | 0.000*      | 0.003*     |
| Frequencies of CD19+ B lymphocytes [%]    | 9.74± 5.37    | 8.71<br>(2.81-24.17)   | 82.01± 10.54 | 83.52<br>(53.66-97.02) | 12.59± 2.25 | 12.46<br>(7.91-16.83)  | 0.000*          | 0.000*       | 0.000*      | 0.000*     |
| Frequencies of CD4+CD3+ T lymphocytes [%] | 31.30± 12.22  | 28.98<br>(14.49-67.23) | 6.43± 3.23   | 5.92<br>(1.52-26.57)   | 47.53± 4.76 | 46.76<br>(42.19-65.51) | 0.000*          | 0.000*       | 0.000*      | 0.000*     |
| Frequencies of CD8+CD3+ T lymphocytes [%] | 31.30±13.23   | 28.13<br>(12.25-57.20) | 5.03±3.16    | 4.26<br>(0.58-13.08)   | 26.39± 2.98 | 26.91<br>(20.18-31.07) | 0.000*          | 0.000*       | 0.000*      | 0.387      |
| CD4+CD3+/CD8+CD3+ lymphocyte ratio        | 1.49± 1.50    | 1.07<br>(0.26-3.16)    | 1.43± 0.74   | 1.28<br>(0.34-3.95)    | 1.80±1.39   | 1.74<br>(1.09-3.19)    | 0.000*          | 0.000*       | 0.000*      | 0.001*     |

\* Statistically significant results; Abbreviations: CD- cluster of differentiation

**Supplementary Table S3.** Analysis of the percentage of selected subpopulations of peripheral blood lymphocytes showing positive expression of the tested immunological checkpoints and their ligands

| Parameter | CVID (n = 40)                  |                | CLL (n = 40)           |                | HV (n = 40)            |                | <i>p</i> -value        | <i>p</i> -value |             |               |
|-----------|--------------------------------|----------------|------------------------|----------------|------------------------|----------------|------------------------|-----------------|-------------|---------------|
|           | Mean ± SD                      | Median (Range) | Mean ± SD              | Median (Range) | Mean ± SD              | Median (Range) |                        | CVID vs. CLL    | CVID vs. HV | CLL vs. HV    |
| PD-1      | CD4+PD-1+ T lymphocytes [%]    | 14.36± 4.70    | 14.41<br>(6.52-24.72)  | 18.34± 9.84    | 14.85<br>(4.55-44.00)  | 3.09± 1.14     | 3.00<br>(1.04-5.68)    | 0.000*          | 0.657       | 0.000* 0.000* |
|           | CD8+PD-1+ T lymphocytes [%]    | 14.58± 7.20    | 13.39<br>(5.17-37.47)  | 14.72± 6.49    | 14.57<br>(3.27-29.16)  | 2.35± 0.98     | 2.26<br>(0.79-4.28)    | 0.000*          | 0.135       | 0.000* 0.000* |
|           | CD19+PD-1+ B lymphocytes [%]   | 6.07± 2.98     | 6.01<br>(2.01-17.59)   | 19.86± 6.78    | 19.72<br>(5.33-35.65)  | 3.88± 1.38     | 3.73<br>(1.46-6.82)    | 0.000*          | 0.000*      | 0.000* 0.000* |
| PD-L1     | CD4+PD-L1+ T lymphocytes [%]   | 7.80± 2.79     | 7.86<br>(2.55-13.92)   | 8.91± 3.30     | 8.99<br>(2.96-16.15)   | 0.78± 0.30     | 0.81<br>(0.21-1.33)    | 0.000*          | 0.166       | 0.000* 0.000* |
|           | CD8+PD-L1+ T lymphocytes [%]   | 5.99± 3.49     | 5.09<br>(1.06-17.00)   | 6.90± 4.01     | 5.86<br>(1.23-19.72)   | 0.58± 0.25     | 0.57<br>(0.01-1.01)    | 0.000*          | 0.284       | 0.000* 0.000* |
|           | CD19+PD-L1+ B lymphocytes [%]  | 7.21± 4.13     | 5.93<br>(1.62-17.87)   | 8.47± 4.77     | 6.97<br>(1.88-20.73)   | 0.22± 0.14     | 0.23<br>(0.00-0.48)    | 0.000*          | 0.201       | 0.000* 0.000* |
| CTLA-4    | CD4+CTLA-4+ T lymphocytes [%]  | 10.34± 4.75    | 9.60<br>(4.17-23.55)   | 12.35± 5.54    | 10.33<br>(4.03-31.14)  | 3.20± 0.68     | 3.23<br>(1.91-4.41)    | 0.000*          | 0.0657      | 0.000* 0.000* |
|           | CD8+CTLA-4+ T lymphocytes [%]  | 13.12± 7.86    | 11.28<br>(4.16-36.89)  | 15.91± 3.91    | 15.35<br>(8.36-26.69)  | 3.21± 0.82     | 3.01<br>(2.09-5.12)    | 0.000*          | 0.0014*     | 0.000* 0.000* |
|           | CD19+CTLA-4+ B lymphocytes [%] | 5.92± 2.66     | 6.22<br>(1.15-10.89)   | 13.58± 6.20    | 13.57<br>(3.12-29.42)  | 1.75± 0.65     | 1.75<br>(0.59-3.17)    | 0.000*          | 0.000*      | 0.000* 0.000* |
| CD86      | CD4+CD86+ T lymphocytes [%]    | 4.84± 0.58     | 4.69<br>(4.02-5.99)    | 5.53±0.79      | 5.44<br>(4.16-6.97)    | 2.89± 0.62     | 2.80<br>(2.04-3.98)    | 0.000*          | 0.000*      | 0.000* 0.000* |
|           | CD8+CD86+ T lymphocytes [%]    | 2.96± 0.59     | 2.95<br>(2.03-3.98)    | 4.00± 0.56     | 3.92<br>(3.01-4.95)    | 2.11± 0.51     | 2.05<br>(1.17-2.99)    | 0.000*          | 0.000*      | 0.000* 0.000* |
|           | CD19+CD86+ B lymphocytes [%]   | 25.21±1.89     | 25.15<br>(22.18-28.00) | 39.20±6.51     | 39.61<br>(27.24-48.52) | 11.20± 1.84    | 11.61<br>(8.27-13.97)  | 0.000*          | 0.000*      | 0.000* 0.000* |
| CD200R    | CD4+CD200R+ T lymphocytes [%]  | 4.50± 2.97     | 3.59<br>(1.13-11.52)   | 10.84± 4.10    | 10.23<br>(3.23-20.39)  | 5.48± 1.90     | 5.64<br>(1.89-9.31)    | 0.000*          | 0.000*      | 0.000* 0.016* |
|           | CD8+CD200R+ T lymphocytes [%]  | 7.64± 4.330    | 6.63<br>(2.46-21.02)   | 10.51± 4.76    | 9.66<br>(2.09-25.33)   | 3.20± 1.36     | 3.15<br>(0.74-7.10)    | 0.000*          | 0.0022*     | 0.000* 0.000* |
|           | CD19+CD200R+ B lymphocytes [%] | 9.58± 3.88     | 9.27<br>(3.51-18.41)   | 13.05± 5.28    | 10.80<br>(6.18-27.33)  | 20.42± 4.82    | 19.11<br>(12.55-33.00) | 0.000*          | 0.0022*     | 0.000* 0.000* |
| CD200     | CD4+CD200+ T lymphocytes [%]   | 13.72± 5.69    | 11.47<br>(6.36-27.10)  | 19.39± 9.87    | 18.50<br>(5.32-43.59)  | 2.21± 0.57     | 2.15<br>(1.20-3.30)    | 0.000*          | 0.0103*     | 0.000* 0.000* |
|           | CD8+CD200+ T lymphocytes [%]   | 12.50± 7.41    | 10.55<br>(3.01-33.61)  | 14.46± 6.58    | 14.15<br>(4.59-30.69)  | 3.11± 1.07     | 3.14<br>(1.40-5.81)    | 0.000*          | 0.008*      | 0.000* 0.000* |
|           | CD19+CD200+ B lymphocytes [%]  | 67.22± 18.68   | 68.25<br>(23.01-96.27) | 93.69± 8.00    | 96.91<br>(62.39-99.99) | 40.87± 12.59   | 40.68<br>(18.15-71.33) | 0.000*          | 0.000*      | 0.000* 0.000* |

\* Statistically significant results; Abbreviations: CVID - common variable immunodeficiency; CLL- chronic lymphocytic leukemia; CD- cell differentiation antigen; CTLA-4- cytotoxic T-lymphocyte-associated antigen 4; PD-1-Programmed Cell Death Protein 1; PD-L1 - Programmed Cell Death Ligand 1; HV- healthy volunteers.

**Supplementary Table S4.** The concentration of soluble forms of the tested immunological checkpoints and their ligands in the serum of immunodeficient patients about healthy volunteers.

| Serum concentration<br>(ng/ml) | CVID ( <i>n</i> = 40) |                        | CLL ( <i>n</i> = 40) |                        | HV ( <i>n</i> = 40) |                     | <i>p</i> -value | <i>p</i> -value |             |            |
|--------------------------------|-----------------------|------------------------|----------------------|------------------------|---------------------|---------------------|-----------------|-----------------|-------------|------------|
|                                | Mean ± SD             | Median (Range)         | Mean ± SD            | Median (Range)         | Mean ± SD           | Median (Range)      |                 | CVID vs. CLL    | CVID vs. HV | CLL vs. HV |
| sPD-1                          | 19.20± 3.48           | 19.66<br>(13.19-26.49) | 50.57± 9.91          | 51.20<br>(30.17-64.69) | 2.10± 1.19          | 1.98<br>(0.52-5.42) | 0.000*          | 0.000*          | 0.000*      | 0.000*     |
| sPD-L1                         | 7.44± 1.61            | 7.31<br>(4.46-10.89)   | 30.22± 5.45          | 29.97<br>(20.50-37.97) | 0.77± 0.50          | 0.72<br>(0.04-2.25) | 0.000*          | 0.000*          | 0.000*      | 0.000*     |
| sCTLA-4                        | 14.50± 3.56           | 14.66<br>(6.75-19.96)  | 21.60± 4.06          | 20.46<br>(15.56-28.84) | 1.54± 0.88          | 1.45<br>(0.40-4.74) | 0.000*          | 0.000*          | 0.000*      | 0.000*     |
| sCD86                          | 12.92± 1.06           | 12.85<br>(11.23-14.95) | 20.12±3.38           | 20.39<br>(15.03-25.42) | 2.05± 0.62          | 2.21<br>(1.03-2.95) | 0.000*          | 0.000*          | 0.000*      | 0.000*     |
| sCD200R                        | 18.77± 3.96           | 19.09<br>(10.37-26.22) | 35.85± 5.22          | 35.20<br>(25.39-43.96) | 2.09± 1.19          | 1.76<br>(0.96-6.29) | 0.000*          | 0.000*          | 0.000*      | 0.000*     |
| sCD200                         | 40.73± 8.82           | 38.75<br>(22.79-55.46) | 41.79± 8.13          | 38.90<br>(30.65-59.25) | 2.22± 1.34          | 2.17<br>(0.11-4.87) | 0.000*          | 0.622           | 0.000*      | 0.000*     |

\* Statistically significant results; Abbreviations: CVID - common variable immunodeficiency; CLL- chronic lymphocytic leukemia; CD- cell differentiation antigen; sCD86- soluble form of CD86; sCD200R- soluble form of CD200R; sCD200- soluble form of CD200; sCTLA-4- soluble form of cytotoxic T-lymphocyte-associated antigen 4; sPD-1- soluble form of Programmed Cell Death Protein 1; sPD-L1 - soluble form of Programmed Cell Death Ligand 1; HV- healthy volunteers.

**Supplementary Table S5.** Correlation analysis of the tested parameters of the immune system and peripheral blood morphology and biochemistry in patients with CVID

| A pair of variables                 | R Spearman | t(N-2) | p-value |
|-------------------------------------|------------|--------|---------|
| CD8+PD-1+ [%] & sCD200 [ng/ml]      | -0.462     | -3.165 | 0.003*  |
| sCD200R [ng/ml] & WBC               | -0.439     | -2.969 | 0.005*  |
| CD19+PD-1+ [%] & BAS                | -0.419     | -2.809 | 0.008*  |
| CD4+CTLA-4+ [%] & WBC               | -0.410     | -2.735 | 0.010*  |
| CD4+CD200+ [%] & sPD-1 [ng/ml]      | -0.381     | -2.509 | 0.017*  |
| CD19+PD-L1+ [%] & MON               | -0.376     | -2.470 | 0.018*  |
| CD4+CD200R+ [%] & sPD-L1 [ng/ml]    | -0.367     | -2.401 | 0.022*  |
| CD19+CD86 [%] & sCD200R [ng/ml]     | -0.363     | -2.368 | 0.023*  |
| CD19+CD200+ [%] & CD8+PD-L1+ [%]    | -0.339     | -2.191 | 0.035*  |
| CD19+CD200R+ [%] & CD8+ CTLA-4+ [%] | -0.331     | -2.132 | 0.040*  |
| CD4+CD86+ [%] & EOS                 | -0.324     | -2.084 | 0.044*  |
| sPD-1 [ng/ml] & RBC                 | -0.322     | -2.070 | 0.046*  |
| CD4+CD200R+ [%] & sPD-1 [ng/ml]     | -0.317     | -2.030 | 0.050*  |
| CD8+CD200+ [%] & CD8+ CTLA-4+ [%]   | 0.328      | 2.113  | 0.041*  |
| CD4+ PD-L1+ [%] & PLT               | 0.329      | 2.117  | 0.041*  |
| CD4+PD-1+ [%] & PLT                 | 0.332      | 2.139  | 0.039*  |
| CD19+CTLA-4+ [%] & MON              | 0.333      | 2.148  | 0.038*  |
| CD4+PD-1+ [%] & IgG                 | 0.338      | 2.187  | 0.035*  |
| sCTLA-4 [ng/ml] & PLT               | 0.348      | 2.255  | 0.030*  |
| CD8+ PD-1+ [%] & sCD86 [ng/ml]      | 0.348      | 2.258  | 0.030*  |
| CD8+CD200R+ [%] & CD8+ PD-L1+ [%]   | 0.350      | 2.273  | 0.029*  |
| CD4+PD-1+ [%] & CD8+PD-1+ [%]       | 0.361      | 2.356  | 0.024*  |
| CD4+PD-1+ [%] & sCD86 [ng/ml]       | 0.363      | 2.372  | 0.023*  |
| CD19+CTLA-4+ [%] & sPD-1 [ng/ml]    | 0.364      | 2.375  | 0.023*  |
| CD4+CD200R+ [%] & HGB               | 0.370      | 2.422  | 0.020*  |
| CD19+CD86 [%] & NEU                 | 0.373      | 2.444  | 0.019*  |
| sPD-L1 [ng/ml] & sCTLA-4[ng/ml]     | 0.378      | 2.480  | 0.018*  |
| sCD200 [ng/ml] & sCTLA-4 [ng/ml]    | 0.381      | 2.506  | 0.017*  |
| CD8+ CD200R+ [%] & CD8+ CTLA-4+ [%] | 0.389      | 2.569  | 0.014*  |
| sPD-L1 [ng/ml] & PLT                | 0.396      | 2.626  | 0.012*  |
| CD19+PD-1+ [%] & CD19+PD-L1+ [%]    | 0.399      | 2.646  | 0.012*  |
| CD4+ PD-L1+ [%] & IgA               | 0.412      | 2.747  | 0.009*  |
| sCD200R [ng/ml] & sCTLA-4 [ng/ml]   | 0.420      | 2.815  | 0.008*  |
| CD8+CD200R+ [%] & RBC               | 0.423      | 2.840  | 0.007*  |
| CD4+CD200R+ [%] & RBC               | 0.462      | 3.171  | 0.003*  |
| sCD200R [ng/ml] & sPD-1 [ng/ml]     | 0.484      | 3.361  | 0.002*  |
| sCD200R [ng/ml] & EOS               | 0.498      | 3.495  | 0.001*  |

|                                 |       |       |        |
|---------------------------------|-------|-------|--------|
| sPD-L1 [ng/ml] & sPD-1 [ng/ml]  | 0.498 | 3.495 | 0.001* |
| CD4+CD200+ [%] & LYM            | 0.553 | 4.035 | 0.000* |
| sCTLA-4 [ng/ml] & sPD-1 [ng/ml] | 0.669 | 5.468 | 0.000* |

\* Statistically significant results

**Supplementary Table S6.** Correlation analysis of the tested parameters of the immune system and peripheral blood morphology and biochemistry in patients with CLL

| A pair of variables                 | R Spearman | t(N-2) | p-value |
|-------------------------------------|------------|--------|---------|
| CD8+ PD-1+ [%] & IgG                | -0.513     | -3.684 | 0.001*  |
| CD4+CD200+ [%] & HGB                | -0.499     | -3.546 | 0.001*  |
| CD19+CD200+ [%] & CD19+CTLA-4+ [%]  | -0.466     | -3.244 | 0.002*  |
| CD19+CD200+ [%] & CD8+CD200R+ [%]   | -0.429     | -2.925 | 0.006*  |
| CD4+CD200+ [%] & RBC                | -0.427     | -2.914 | 0.006*  |
| CD19+CTLA-4+ [%] & LYM              | -0.422     | -2.873 | 0.007*  |
| CD4+ PD-L1+ [%] & sCD200R [ng/ml]   | -0.422     | -2.867 | 0.007*  |
| CD4+PD-L1+ [%] & sCD86 [ng/ml]      | -0.390     | -2.615 | 0.013*  |
| CD19+CTLA-4+ [%] & CD4+CTLA-4+ [%]  | -0.389     | -2.605 | 0.013*  |
| CD8+PD-1+ & sCD200 [ng/ml]          | -0.384     | -2.564 | 0.014*  |
| CD8+ PD-1+ [%] & WBC                | -0.379     | -2.527 | 0.016*  |
| CD19+PD-L1+ [%] & PLT               | -0.376     | -2.498 | 0.017*  |
| CD8+CD200+ [%] & WBC                | -0.374     | -2.487 | 0.017*  |
| CD4+CTLA-4+ [%] & IgA               | -0.361     | -2.383 | 0.022*  |
| CD8+ PDL-1+ [%] & sCD200R [ng/ml]   | -0.357     | -2.356 | 0.024*  |
| sCTLA-4 [ng/ml] & sCD86 [ng/ml]     | -0.356     | -2.347 | 0.024*  |
| CD19+CD86 [%] & sCD86 [ng/ml]       | -0.331     | -2.164 | 0.037*  |
| CD8+CD200R+ [%] & CD4+ CTLA-4+ [%]  | -0.320     | -2.080 | 0.044*  |
| CD8+PD-1+ [%] & sPD-L1 [ng/ml]      | -0.315     | -2.049 | 0.047*  |
| CD19+CTLA-4+[%] & IgM               | 0.314      | 2.037  | 0.049*  |
| CD8+CD200R+ [%] & IgA               | 0.319      | 2.078  | 0.045*  |
| CD4+CD86+ [%] & sCD86 [ng/ml]       | 0.325      | 2.120  | 0.041*  |
| sCD200R [ng/ml] & WBC               | 0.327      | 2.130  | 0.040*  |
| CD4+ CD200R+ [%] & CD8+ CD200R+ [%] | 0.328      | 2.142  | 0.039*  |
| CD19+CD200+ [%] & sCD200R [ng/ml]   | 0.329      | 2.144  | 0.038*  |
| sPD-L1 [ng/ml] & sCD86 [ng/ml]      | 0.345      | 2.266  | 0.029*  |
| CD8+CD200+ [%] & CD8+CD86+ [%]      | 0.355      | 2.343  | 0.024*  |
| CD8+ CD200+ [%] & CD8+CTLA-4+ [%]   | 0.360      | 2.382  | 0.022*  |
| CD19+CD200+ [%] & LYM               | 0.375      | 2.493  | 0.017*  |
| CD19+CD200+[%] & CD4+ CTLA-4+ [%]   | 0.376      | 2.504  | 0.017*  |
| sCD200R [ng/ml] & EOS               | 0.390      | 2.611  | 0.013*  |
| sCD86 [ng/ml] & sCD200R [ng/ml]     | 0.397      | 2.663  | 0.011*  |
| CD4+CD86+ [%] & HGB                 | 0.397      | 2.669  | 0.011*  |

|                                  |       |       |        |
|----------------------------------|-------|-------|--------|
| CD19+CD200R+ [%] & IgM           | 0.402 | 2.707 | 0.010* |
| CD4+CD86+ [%] & RBC              | 0.421 | 2.863 | 0.007* |
| CD8+CTLA-4+ [%] & BAS            | 0.426 | 2.899 | 0.006* |
| CD19+CD200R+ [%] & MON           | 0.426 | 2.900 | 0.006* |
| CD4+CD200+ [%] & sCD200R [ng/ml] | 0.434 | 2.969 | 0.005* |
| CD4+PD-1+ [%] & CD8+PD-1+ [%]    | 0.441 | 3.029 | 0.004* |
| CD4+CD200+ [%] & sPD-1 [ng/ml]   | 0.442 | 3.039 | 0.004* |

\* Statistically significant results

**Supplementary Materials Table S7.** ROC curve analysis

| Parameter      | CLL vs. HV  | CVID vs. HV | CLL vs. CVID |
|----------------|-------------|-------------|--------------|
| CD4+PD-1+[%]   | AUC         | 1,000       | 0,598        |
|                | SE          | 0,000       | 0,064        |
|                | -95%        | 1,000       | 0,472        |
|                | +95%        | 1,000       | 0,724        |
|                | z statistic | -           | 1,522        |
|                | p value     | 0,000       | 0,128        |
| CD8+PD-1+[%]   | AUC         | 1,000       | 0,529        |
|                | SE          | 0,000       | 0,066        |
|                | -95%        | 0,000       | 0,401        |
|                | +95%        | 0,000       | 0,658        |
|                | z statistic | -           | 0,445        |
|                | p value     | 0,000       | 0,656        |
| CD19+PD-1+[%]  | AUC         | 1,000       | 0,969        |
|                | SE          | 0,000       | 0,018        |
|                | -95%        | 1,000       | 0,933        |
|                | +95%        | 1,000       | 1,000        |
|                | z statistic | -           | 25,905       |
|                | p value     | 0,000       | 0,000        |
| CD4+PD-L1+[%]  | AUC         | 0,97        | 0,591        |
|                | SE          | 0,018       | 0,026        |
|                | -95%        | 0,934       | 0,901        |
|                | +95%        | 1,000       | 0,717        |
|                | z statistic | 25,812      | 17,352       |
|                | p value     | 0,000       | 457,495      |
| CD8+PD-L1+[%]  | AUC         | 0,841       | 0,571        |
|                | SE          | 0,051       | 0,056        |
|                | -95%        | 0,741       | 0,684        |
|                | +95%        | 0,941       | 0,903        |
|                | z statistic | 6,688       | 5,260        |
|                | p value     | 0,000       | 0,000        |
| CD19+PD-L1+[%] | AUC         | 0,976       | 0,584        |
|                | SE          | 0,014       | 0,021        |
|                | -95%        | 0,947       | 0,914        |

|                 |             |        |         |         |
|-----------------|-------------|--------|---------|---------|
|                 | +95%        | 1,000  | 0,998   | 0,710   |
|                 | z statistic | 33,136 | 21,36   | 1,304   |
|                 | p value     | 0,000  | 0,000   | 0,192   |
|                 | AUC         | 0,994  | 0,993   | 0,621   |
|                 | SE          | 0,006  | 0,006   | 0,064   |
| CD4+CTLA-4+[%]  | -95%        | 0,983  | 0,981   | 0,496   |
|                 | +95%        | 1      | 1,000   | 0,745   |
|                 | z statistic | 82,133 | 82,526  | 1,892   |
|                 | p value     | 0,000  | 0,000   | 0,058   |
|                 | AUC         | 1      | 0,999   | 0,706   |
|                 | SE          | 0      | 0,001   | 0,061   |
| CD8+CTLA-4+[%]  | -95%        | 1      | 0,997   | 0,586   |
|                 | +95%        | 1      | 1,000   | 0,825   |
|                 | z statistic | -      | 457,495 | 3,371   |
|                 | p value     | 0      | 0,000   | 0,001   |
|                 | AUC         | 0,728  | 0,969   | 0,124   |
|                 | SE          | 0,059  | 0,019   | 0,040   |
| CD19+CTLA-4+[%] | -95%        | 0,613  | 0,932   | 0,046   |
|                 | +95%        | 0,843  | 1,000   | 0,202   |
|                 | z statistic | 3,893  | 24,535  | -9,446  |
|                 | p value     | 0,000  | 0,000   | 0,000   |
|                 | AUC         | 1,000  | 0,999   | 0,473   |
|                 | SE          | 0,000  | 0,001   | 0,066   |
| CD4+CD86+[%]    | -95%        | 1,000  | 0,997   | 0,344   |
|                 | +95%        | 1,000  | 1,000   | 0,602   |
|                 | z statistic | -      | 457,495 | -0,414  |
|                 | p value     | 0,000  | 0,000   | 0,067   |
|                 | AUC         | 0,855  | 0,995   | 0,552   |
|                 | SE          | 0,040  | 0,005   | 0,066   |
| CD8+CD86+[%]    | -95%        | 0,776  | 0,985   | 0,421   |
|                 | +95%        | 0,934  | 1,000   | 0,682   |
|                 | z statistic | 8,817  | 46,648  | 0,777   |
|                 | p value     | 0,000  | 0,000   | 0,4374  |
|                 | AUC         | 1,000  | 0,990   | 0,013   |
|                 | SE          | 0,000  | 0,010   | 0,009   |
| CD19+CD86+[%]   | -95%        | 1,000  | 0,969   | -0,004  |
|                 | +95%        | 1,000  | 1,000   | 0,031   |
|                 | z statistic | -      | 46,648  | -53,185 |
|                 | p value     | 0,000  | 0,000   | 0,000   |
|                 | AUC         | 0,904  | 0,344   | 0,888   |
|                 | SE          | 0,036  | 0,064   | 0,037   |
| CD4+CD200R+[%]  | -95%        | 0,832  | 0,219   | 0,816   |
|                 | +95%        | 0,975  | 0,469   | 0,961   |
|                 | z statistic | 11,098 | -2,452  | 10,487  |
|                 | p value     | 0,000  | 0,014   | 0,000   |
|                 | AUC         | 0,951  | 0,859   | 0,697   |
|                 | SE          | 0,026  | 0,040   | 0,060   |
| CD8+CD200R+[%]  | -95%        | 0,9    | 0,780   | 0,579   |
|                 | +95%        | 1      | 0,937   | 0,815   |
|                 | z statistic | 17,362 | 8,948   | 3,279   |
|                 | p value     | 0,000  | 0,000   | 0,001   |
|                 | AUC         | 0,143  | 0,030   | 0,697   |
| CD19+CD200R+[%] | SE          | 0,043  | 0,016   | 0,059   |
|                 | -95%        | 0,058  | -0,002  | 0,583   |

|                             |             |         |         |         |
|-----------------------------|-------------|---------|---------|---------|
|                             | +95%        | 0,227   | 0,062   | 0,812   |
|                             | z statistic | -8,253  | -28,886 | 3,369   |
|                             | p value     | 0,000   | 0,000   | 0,001   |
|                             | AUC         | 1,000   | 1,000   | 0,666   |
|                             | SE          | 0,000   | 0,000   | 0,063   |
| CD4+CD200+[%]               | -95%        | 1,000   | 1,000   | 0,544   |
|                             | +95%        | 1,000   | 1,000   | 0,789   |
|                             | z statistic | -       | -       | 2,657   |
|                             | p value     | 0,000   | 0,000   | 0,008   |
|                             | AUC         | 0,997   | 0,958   | 0,613   |
|                             | SE          | 0,004   | 0,021   | 0,064   |
| CD8+CD200+[%]               | -95%        | 0,990   | 0,917   | 0,487   |
|                             | +95%        | 1,000   | 1,000   | 0,740   |
|                             | z statistic | 138,359 | 21,736  | 1,764   |
|                             | p value     | 0,000   | 0,000   | 0,077   |
|                             | AUC         | 0,998   | 0,868   | 0,935   |
|                             | SE          | 0,002   | 0,043   | 0,027   |
| CD19+CD200+[%]              | -95%        | 0,993   | 0,784   | 0,882   |
|                             | +95%        | 1,000   | 0,952   | 0,987   |
|                             | z statistic | 211,089 | 8,571   | 16,225  |
|                             | p value     | 0,000   | 0,000   | 0,000   |
|                             | AUC         | 1,000   | 1,000   | 1,000   |
|                             | SE          | 0,000   | 0,000   | 0,000   |
| Serum concentration sPD-1   | -95%        | 1,000   | 1,000   | 1,000   |
|                             | +95%        | 1,000   | 1,000   | 1,000   |
|                             | z statistic | -       | -       | -       |
|                             | p value     | 0,000   | 0,000   | 0,000   |
|                             | AUC         | 1,000   | 1,000   | 1,000   |
|                             | SE          | 0,000   | 0,000   | 0,000   |
| Serum concentration sPD-L1  | -95%        | 1,000   | 1,000   | 1,000   |
|                             | +95%        | 1,000   | 1,000   | 1,000   |
|                             | z statistic | -       | -       | -       |
|                             | p value     | 0,000   | 0,000   | 0,000   |
|                             | AUC         | 1,000   | 1,000   | 0,907   |
|                             | SE          | 0,000   | 0,000   | 0,031   |
| Serum concentration sCTLA-4 | -95%        | 1,000   | 1,000   | 0,846   |
|                             | +95%        | 1,000   | 1,000   | 0,968   |
|                             | z statistic | -       | -       | 13,054  |
|                             | p value     | 0,000   | 0,000   | 0,000   |
|                             | AUC         | 1,000   | 0,999   | 0,000   |
|                             | SE          | 0,000   | 0,002   | 0,000   |
| Serum concentration sCD86   | -95%        | 1,000   | 0,995   | 0,000   |
|                             | +95%        | 1,000   | 1,000   | 0,000   |
|                             | z statistic | -       | 281,334 | 0,000   |
|                             | p value     | 0,000   | 0,000   | 0,000   |
|                             | AUC         | 1,000   | 1,000   | 0,998   |
|                             | SE          | 0,000   | 0,000   | 0,002   |
| Serum concentration sCD200R | -95%        | 1,000   | 1,000   | 0,993   |
|                             | +95%        | 1,000   | 1,000   | 1,000   |
|                             | z statistic | -       | -       | 205,874 |
|                             | p value     | 0,000   | 0,000   | 0,000   |
|                             | AUC         | 1,000   | 1,000   | 0,532   |
|                             | SE          | 0,000   | 0,000   | 0,066   |
| Serum concentration sCD200  | -95%        | 1,000   | 1,000   | 0,404   |

|             |       |       |       |
|-------------|-------|-------|-------|
| +95%        | 1,000 | 1,000 | 0,661 |
| z statistic | -     | -     | 0,492 |
| p value     | 0,000 | 0,000 | 0,622 |