**Supplementary Appendix**

**Telomere length and telomerase levels delineate subgroups of B-cell chronic lymphocytic leukemia with different biological characteristics and clinical outcomes**

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**Online Supplementary Table S1. hTERT expression and telomere length in relation to chromosomal abnormalities.**

<table>
<thead>
<tr>
<th>Chromosomal abnormalities</th>
<th>hTERT median (IQR*)</th>
<th>P value</th>
<th>T/S ratio median (IQR)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>94 (40-250)</td>
<td>0.015</td>
<td>0.94 (0.61-1.46)</td>
<td>0.005</td>
</tr>
<tr>
<td>11q-, 17p-</td>
<td>235 (107-618)</td>
<td></td>
<td>0.44 (0.23-0.81)</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>94 (40-250)</td>
<td>0.223</td>
<td>0.94 (0.61-1.46)</td>
<td>0.762</td>
</tr>
<tr>
<td>13q-</td>
<td>56 (20-166)</td>
<td></td>
<td>0.92 (0.42-1.61)</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>94 (40-250)</td>
<td>0.222</td>
<td>0.94 (0.61-1.46)</td>
<td>0.008</td>
</tr>
<tr>
<td>+12</td>
<td>159 (87-359)</td>
<td></td>
<td>0.39 (0.24-0.71)</td>
<td></td>
</tr>
<tr>
<td>11q-, 17p-</td>
<td>235 (107-618)</td>
<td>0.001</td>
<td>0.44 (0.23-0.81)</td>
<td>0.023</td>
</tr>
<tr>
<td>13q-</td>
<td>56 (20-166)</td>
<td></td>
<td>0.92 (0.42-1.61)</td>
<td></td>
</tr>
<tr>
<td>+12</td>
<td>159 (87-359)</td>
<td></td>
<td>0.39 (0.24-0.71)</td>
<td></td>
</tr>
<tr>
<td>11q-, 17p-</td>
<td>235 (107-618)</td>
<td>0.640</td>
<td>0.44 (0.23-0.81)</td>
<td>0.590</td>
</tr>
<tr>
<td>13q-</td>
<td>56 (20-166)</td>
<td>0.065</td>
<td>0.92 (0.42-1.61)</td>
<td>0.030</td>
</tr>
<tr>
<td>+12</td>
<td>159 (87-359)</td>
<td></td>
<td>0.39 (0.24-0.71)</td>
<td></td>
</tr>
</tbody>
</table>

*IQR: interquartile.

**Online Supplementary Table S2. hTERT expression and telomere length in relation to lymphocyte doubling time.**

<table>
<thead>
<tr>
<th>Lymphocyte doubling time (LDT)</th>
<th>hTERT median (IQR*)</th>
<th>P value</th>
<th>T/S ratio median (IQR)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDT&lt; 6 months</td>
<td>150 (101-438)</td>
<td>0.069</td>
<td>0.36 (0.27-0.67)</td>
<td>0.034</td>
</tr>
<tr>
<td>6&lt; LDT&lt; 12 months</td>
<td>87 (25-250)</td>
<td></td>
<td>0.81 (0.39-1.31)</td>
<td></td>
</tr>
<tr>
<td>LDT&lt; 6 months</td>
<td>150 (101-438)</td>
<td>0.158</td>
<td>0.36 (0.27-0.67)</td>
<td>0.007</td>
</tr>
<tr>
<td>LDT stable</td>
<td>128 (45-237)</td>
<td></td>
<td>0.88 (0.49-1.32)</td>
<td></td>
</tr>
<tr>
<td>6&lt; LDT&lt; 12 months</td>
<td>87 (25-250)</td>
<td>0.456</td>
<td>0.81 (0.39-1.31)</td>
<td>0.424</td>
</tr>
<tr>
<td>LDT stable</td>
<td>128 (45-237)</td>
<td></td>
<td>0.88 (0.49-1.32)</td>
<td></td>
</tr>
</tbody>
</table>

*IQR: interquartile.
Online Supplementary Table S3. Time and hazard ratio of different factors for their effects on disease progression.

<table>
<thead>
<tr>
<th>Factor</th>
<th>TTFT* months (95% CI)*</th>
<th>P value log-rank</th>
<th>Hazard ratio (95% CI)*</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IGVH status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IGVH mutated</td>
<td>107 (63; 151)</td>
<td>&lt; 0.0001</td>
<td>1</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>IGVH unmutated</td>
<td>19 (8; 33)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Chromosomal abnormalities</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>normal</td>
<td>68 (35; 151)</td>
<td>&lt; 0.0001</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>11q- , 17p-</td>
<td>3 (2; 13)</td>
<td></td>
<td>4.73 (2.32; 9.64)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>13q-</td>
<td>77 (27; 151)</td>
<td></td>
<td>0.46 (0.19; 1.14)</td>
<td>0.0540</td>
</tr>
<tr>
<td>+12</td>
<td>40 (4; 75)</td>
<td></td>
<td>2.45 (1.10; 5.70)</td>
<td>0.0370</td>
</tr>
<tr>
<td>normal , 13q-</td>
<td>107 (53; 151)</td>
<td>&lt; 0.0001</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>11q- , 17p-, +12</td>
<td>5 (3; 24)</td>
<td></td>
<td>5.02 (2.82; 8.96)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td><strong>hTERT levels</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hTERT low</td>
<td>104 (66; 151)</td>
<td>&lt; 0.0001</td>
<td>1</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>hTERT high</td>
<td>31 (19; 50)</td>
<td></td>
<td>3.50 (2.01; 6.08)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td><strong>Telomere length</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T/S long</td>
<td>104 (63; 151)</td>
<td>&lt; 0.0001</td>
<td>1</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>T/S short</td>
<td>35 (15; 54)</td>
<td></td>
<td>2.97 (1.74; 5.09)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td><strong>hTERT and IGVH status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hTERT low &amp; IGVH mutated</td>
<td>- (104; -)</td>
<td>&lt; 0.0001</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>hTERT high &amp; IGVH mutated</td>
<td>67 (49; 108)</td>
<td></td>
<td>2.21 (1.09; 4.47)</td>
<td>0.0277</td>
</tr>
<tr>
<td>hTERT low &amp; IGVH unmutated</td>
<td>33 (13; 77)</td>
<td></td>
<td>3.46 (1.78; 6.74)</td>
<td>0.0003</td>
</tr>
<tr>
<td>hTERT high &amp; IGVH unmutated</td>
<td>11 (4; 31)</td>
<td></td>
<td>7.65 (3.70; 15.80)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td><strong>T/S and IGVH status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T/S long &amp; IGVH mutated</td>
<td>- (104; -)</td>
<td>&lt; 0.0001</td>
<td>1</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>T/S short &amp; IGVH mutated</td>
<td>67 (50; 108)</td>
<td></td>
<td>1.40 (0.73; 2.71)</td>
<td>0.3136</td>
</tr>
<tr>
<td>T/S long &amp; IGVH unmutated</td>
<td>24 (5; 57)</td>
<td></td>
<td>3.82 (2.07; 7.05)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>T/S short &amp; IGVH unmutated</td>
<td>13 (6; 35)</td>
<td></td>
<td>5.36 (2.74; 10.49)</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

TTFT: time to first treatment; CI: confidence interval; hTERT low: hTERT ≤ median, hTERT high: hTERT > median; T/S short: T/S ≤ median, T/S long: T/S > median.

Online Supplementary Table S4. Time and hazard ratio of hTERT level, telomere length, and IGVH status for their effects on disease progression.

<table>
<thead>
<tr>
<th>Factor</th>
<th>TTFT* months (95% CI)*</th>
<th>P value log-rank</th>
<th>Hazard ratio (95% CI)*</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>hTERT and IGVH status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hTERT low &amp; IGVH mutated</td>
<td>- (104; -)</td>
<td>&lt; 0.0001</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>hTERT high &amp; IGVH mutated</td>
<td>67 (49; 108)</td>
<td></td>
<td>2.21 (1.09; 4.47)</td>
<td>0.0277</td>
</tr>
<tr>
<td>hTERT low &amp; IGVH unmutated</td>
<td>33 (13; 77)</td>
<td></td>
<td>3.46 (1.78; 6.74)</td>
<td>0.0003</td>
</tr>
<tr>
<td>hTERT high &amp; IGVH unmutated</td>
<td>11 (4; 31)</td>
<td></td>
<td>7.65 (3.70; 15.80)</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

TTFT: time to first treatment; CI: confidence interval; *hTERT low: hTERT ≤ median, hTERT high: hTERT > median; **T/S short: T/S ≤ median, **T/S long: T/S > median.
Online Supplementary Table S5. Time and hazard ratio of hTERT level, telomere length and chromosomal abnormalities for their effects on disease progression.

<table>
<thead>
<tr>
<th></th>
<th>TTFT months (95% CI)</th>
<th>P value</th>
<th>Hazard ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>hTERT and chromosomal abnormalities*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hTERT low; normal, 13q-</td>
<td>- (77;6)</td>
<td>&lt; 0.0001</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>hTERT high; normal, 13q+</td>
<td>20 (35;151)</td>
<td>2.61 (1.24;5.48)</td>
<td>0.0113</td>
<td></td>
</tr>
<tr>
<td>hTERT low; 11q-, 17p-, +12</td>
<td>81 (2;81)</td>
<td>4.56 (2.32;8.93)</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>hTERT high; 11q-, 17p-, +12</td>
<td>4 (2;19)</td>
<td>11.90 (5.26;26.93)</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>T/S and chromosomal abnormalities**</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T/S long; normal, 13q-</td>
<td>- (50;1)</td>
<td>&lt; 0.0001</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>T/S short; normal, 13q-</td>
<td>68 (35;151)</td>
<td>1.73 (0.83;3.62)</td>
<td>0.1444</td>
<td></td>
</tr>
<tr>
<td>T/S long; 11q-, 17p-, +12</td>
<td>4 (2;2)</td>
<td>4.33 (2.30;8.14)</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>T/S short; 11q-, 17p-, +12</td>
<td>4 (7;81)</td>
<td>7.49 (3.52;15.96)</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>hTERT &amp; T/S and chromosomal abnormalities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hTERT low &amp; T/S long;normal, 13q-</td>
<td>- (2;2)</td>
<td>&lt; 0.0001</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>hTERT high &amp; T/S short;normal,13q-</td>
<td>35 (11;151)</td>
<td>3.56 (1.22;10.36)</td>
<td>0.0198</td>
<td></td>
</tr>
<tr>
<td>other hTERT &amp; T/S;normal, 13q-</td>
<td>107 (50;1)</td>
<td>1.42 (0.47;4.29)</td>
<td>0.5326</td>
<td></td>
</tr>
<tr>
<td>hTERT low &amp; T/S long;11q-,17p-,+12</td>
<td>2 (1;1)</td>
<td>3.77 (1.84;7.75)</td>
<td>0.0003</td>
<td></td>
</tr>
<tr>
<td>hTERT high &amp; T/S short;11q-,17p,-12</td>
<td>4 (2;19)</td>
<td>13.44 (4.98;36.25)</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>other hTERT &amp; T/S;11q-, 17p-, +12</td>
<td>81 (3;81)</td>
<td>5.36 (1.65;17.48)</td>
<td>0.0053</td>
<td></td>
</tr>
</tbody>
</table>

TTFT: time to first treatment; CI: confidence interval; *hTERT low: hTERT ≤ median, hTERT high: hTERT > median. **T/S short: T/S ≤ median, T/S long: T/S > median.

Online Supplementary Figure S1. Curves of treatment-free survival [time from diagnosis to first treatment (TTFT)], according to (A) IGVH mutational status and hTERT level, (C) IGVH mutational status and telomere length, (C) chromosomal categories and hTERT level, and (D) chromosomal categories and telomere length. hTERT low ≤ median value; hTERT high: > median value; T/S short: ≤ median value; T/S long: > median value. The median (95% CI) of TTFT and hazard ratio are provided in Online Supplementary Tables S4 (panel A, B) and S5 (panel C, D).