

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.

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

*IQR: interquartile.

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

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

*IQR: interquartile.

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

	TTF† months (95% CI)†	P value log-rank	Hazard ratio (95% CI)†	P value
<i>IGVH</i> status				
<i>IGVH</i> mutated	107 (63;-)	< 0.0001	1	< 0.0001
<i>IGVH</i> unmutated	19 (8;33)		4.43 (2.56;7.67)	
Chromosomal abnormalities				
normal	68 (35;151)	< 0.0001	1	
11q-, 17p-	3 (2;13)		4.73 (2.32;9.64)	< 0.0001
13q-	- (77;-)		0.46 (0.19;1.14)	0.0940
+12	40 (4;75)		2.45 (1.10;5.70)	0.0370
normal, 13q-	107 (53;-)	< 0.0001	1	
11q-, 17p-, +12	5 (3;24)		5.02 (2.82;8.96)	< 0.0001
hTERT levels*				
hTERT low	104 (66;-)	< 0.0001	1	
hTERT high	31 (19;50)		3.50 (2.01;6.08)	< 0.0001
Telomere length**				
T/S long	104 (63;-)	< 0.0001	1	
T/S short	35 (15;54)		2.97 (1.74;5.09)	< 0.0001
hTERT level; T/S length				
hTERT low & T/S long	104 (66;-)	< 0.0001	1	
hTERT high & T/S short	15 (4;40)		6.18 (3.07;12.42)	< 0.0001
hTERT low & T/S short	77 (33;107)		2.28 (1.25;4.15)	0.0072
hTERT high & T/S long	51 (28;-)		2.71 (1.52;4.84)	0.0007

†TTF: 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.

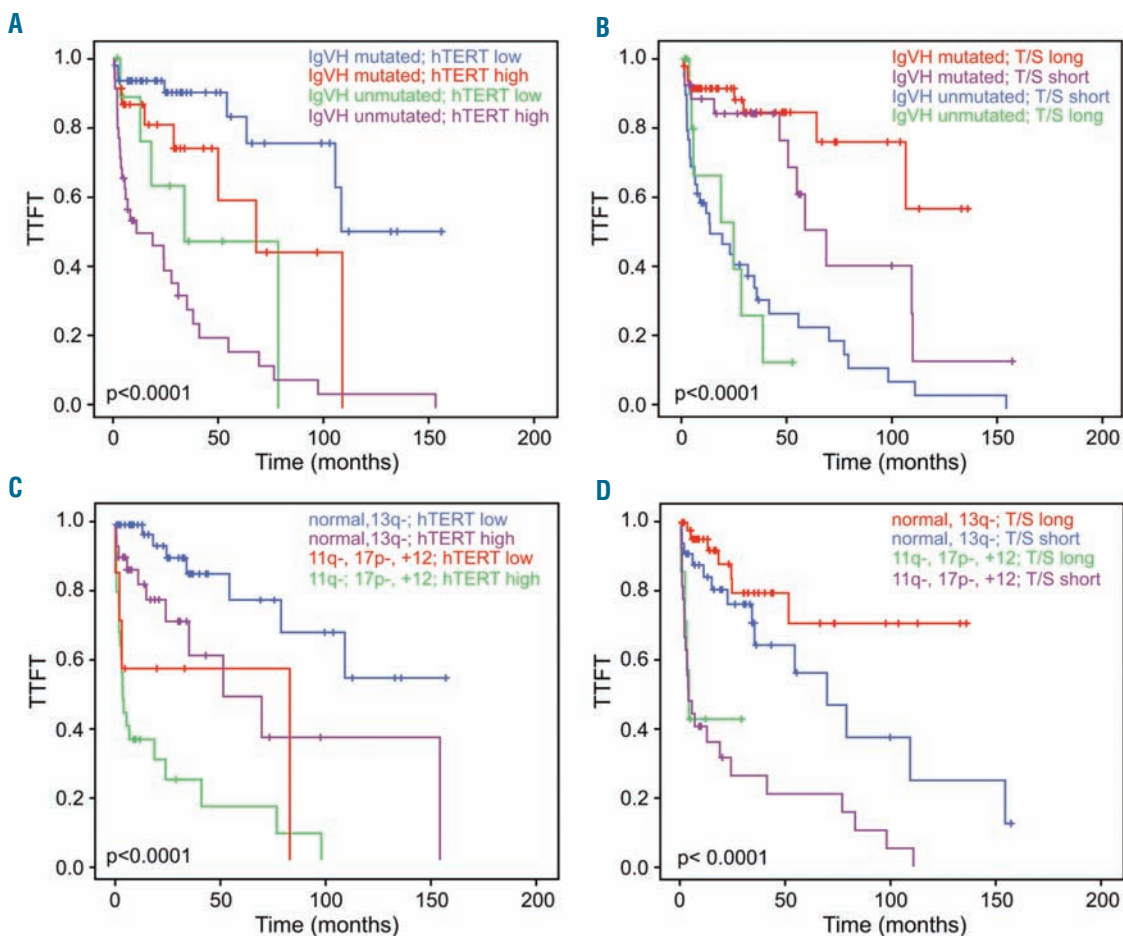
	TTF† months (95% CI)†	P value log-rank	Hazard ratio (95% CI)†	P value
hTERT and <i>IGVH</i> status*				
hTERT low; <i>IGVH</i> mutated	- (104;-)	< 0.0001	1	
hTERT high; <i>IGVH</i> mutated	67 (49;108)		2.21 (1.09;4.47)	0.0277
hTERT low; <i>IGVH</i> unmutated	33 (13;77)		3.46 (1.78;6.74)	0.0003
hTERT high; <i>IGVH</i> unmutated	11 (4;31)		7.65 (3.70;15.80)	< 0.0001
T/S and <i>IGVH</i> status**				
T/S long; <i>IGVH</i> mutated	- (104;-)	< 0.0001	1	
T/S short; <i>IGVH</i> mutated	67 (50;108)		1.40 (0.73;2.71)	0.3136
T/S long; <i>IGVH</i> unmutated	24 (5;37)		3.82 (2.07;7.05)	< 0.0001
T/S short; <i>IGVH</i> unmutated	13 (6;35)		5.36 (2.74;10.49)	< 0.0001
hTERT & T/S and <i>IGVH</i> status				
hTERT low & T/S long; <i>IGVH</i> mutated	- (104;-)	< 0.0001	1	
hTERT high & T/S short; <i>IGVH</i> mutated	49 (4;108)		2.62 (1.01;6.84)	0.0486
other hTERT & T/S; <i>IGVH</i> mutated	107 (107;-)		1.42 (0.54;3.74)	0.4764
hTERT low & T/S long; <i>IGVH</i> unmutated	- (18;-)		3.04 (1.49;6.22)	0.0061
hTERT high & T/S short; <i>IGVH</i> unmutated	11 (4;35)		7.99 (3.41;18.68)	< 0.0001
other hTERT & T/S; <i>IGVH</i> unmutated	27 (13;37)		4.33 (1.52;12.32)	0.0061

†TTF: 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.

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

*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, (B) 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).