

Prognostic impact of prevalent chronic lymphocytic leukemia stereotyped subsets: analysis within prospective clinical trials of the German CLL Study Group

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Supplementary tables

Table 1. Early stage CLL cohort subset #2

	u-subset #2	m-subset #2	u-IGHV3-21	m-IGHV3-21	u-IGHV	m-IGHV
TARGET ANALYSIS POPULATION	6	10	3	10	181	382
AGE AT STUDY ENTRY (YEARS), MEDIAN (RANGE)	60 (51 – 65)	64 (45 – 75)	58 (56 – 60)	63 (56 – 68)	61 (37 – 75)	60 (32 – 75)
GENDER MALE, N (%)	2 (33.3)	4 (40.0)	1 (33.3)	5 (50.0)	120 (66.3)	232 (60.7)
ECOG PERFORMANCE STATUS MEDIAN (RANGE)	0 (0 – 0)	0 (0 – 1)	0.5 (0 – 1)	0 (0 – 0)	0 (0 – 1)	0 (0 – 2)
CLL-IPI RISK GROUP	5	10	2	10	168	369
LOW, N (%)	0 (0.0)	9 (90.0)	2 (100.0)	10 (100.0)	0 (0.0)	345 (93.5)
INTERMEDIATE, N (%)	5 (100.0)	1 (10.0)	0 (0.0)	0 (0.0)	136 (81.0)	16 (4.3)
HIGH, N (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	28 (16.7)	7 (1.9)
VERY HIGH, N (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.4)	1 (0.3)
LEUKOCYTE COUNT (X 10⁹/L) MEDIAN (RANGE)	23.9 (14.2 – 59.0)	25.0 (4.7 – 94.4)	49.4 (49.4 – 49.4)	24.9 (10.7 – 51.7)	23.3 (4.6 – 184.0)	20.1 (6.3 – 184.2)
SERUM THYMIDINE KINASE (U/L) MEDIAN (RANGE)	14.1 (4.9 – 23.9)	7.5 (2.9 – 19.0)	7.8 (6.4 – 43.9)	4.4 (3.4 – 8.6)	7.7 (2.0 – 109.0)	5.1 (1.1 – 80.0)
SERUM B2-MICROGLOBULIN (mg/L) MEDIAN (RANGE)	2.7 (1.3 – 3.5)	2.8 (1.1 – 4.4)	1.9 (0.9 – 1.9)	1.5 (0.4 – 1.9)	2.0 (0.2 – 9.4)	1.7 (0.6 – 8.9)
DELETION 17p BY FISH, N (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	7 (4.1)	8 (2.1)
DELETION 11q BY FISH, N (%)	0 (0.0)	1 (10.0)	2 (66.7)	0 (0.0)	33 (19.4)	5 (1.3)
TRISOMY 12 BY FISH, N (%)	0 (0.0)	0 (0.0)	1 (33.3)	0 (0.0)	35 (20.3)	21 (5.6)
DELETION 13q BY FISH, N (%)	3 (60.0)	6 (60.0)	1 (33.3)	5 (50.0)	90 (52.0)	247 (66.8)
TP53 MUTATED N (%)	2 (40.0)	6 (60.0)	0 (0.0)	0 (0.0)	19 (12.0)	11 (3.2)
NOTCH1 MUTATED, N (%)	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	13 (8.2)	4 (1.1)
SF3B1 MUTATED, N (%)	2 (40.0)	6 (60.0)	0 (0.0)	0 (0.0)	19 (12.0)	11 (3.2)

Table 2. Advanced stage CLL cohort subset # 2

	u-subset #2	m-subset #2	u-IGHV3-21	m-IGHV3-21	u-IGHV	m-IGHV
TARGET ANALYSIS POPULATION	18	43	35	30	1108	627
AGE AT STUDY ENTRY (YEARS) MEDIAN (RANGE), N (%)	66 (52 – 88)	67 (48 – 86)	67 (39 – 80)	69 (49 – 89)	65 (30 – 90)	65 (36 – 88)
GENDER	18	43	35	30	1108	627
MALE, N (%)	10 (55.6)	26 (60.5)	26 (74.3)	23 (76.7)	780 (70.4)	421 (67.1)
ECOG PERFORMANCE STATUS	18	41	34	30	1081	608
MEDIAN (RANGE)	1 (0 – 2)	0 (0 – 2)	1 (0 – 2)	1 (0 – 2)	1 (0 – 3)	0 (0 – 3)
BINET STAGE	18	43	35	30	1107	627
A, N (%)	2 (11.1)	5 (11.6)	4 (11.4)	9 (30.0)	184 (16.6)	104 (16.6)
B, N (%)	10 (55.6)	23 (53.5)	18 (51.4)	10 (33.3)	582 (52.6)	238 (38.0)
C, N (%)	6 (33.3)	15 (34.9)	13 (37.1)	11 (36.7)	341 (30.8)	285 (45.5)
CLL-IPI RISK GROUP	18	39	33	28	1050	576
LOW, N (%)	0 (0.0)	18 (46.2)	0 (0.0)	11 (39.3)	0 (0.0)	249 (43.2)
INTERMEDIATE, N (%)	6 (33.3)	13 (33.3)	11 (33.3)	14 (50.0)	392 (37.3)	216 (37.5)
HIGH, N (%)	11 (61.1)	7 (17.9)	17 (51.5)	3 (10.7)	555 (52.9)	103 (17.9)
VERY HIGH, N (%)	1 (5.6)	1 (2.6)	5 (15.2)	0 (0.0)	103 (9.8)	8 (1.4)
LEUKOCYTE COUNT (X 10⁹/L) MEDIAN (RANGE)	74.8 (7.3 – 206.4)	67.5 (3.1 – 492.0)	67.4 (3.4 – 781.0)	46.2 (5.7 – 204.3)	86.3 (0.2 – 867.0)	67.6 (3.1 – 741.9)
SERUM THYMIDINE KINASE (U/L) MEDIAN (RANGE)	19.1 (1.7 – 130.0)	21.3 (0.0 – 163.0)	16.2 (0.5 – 151.0)	10.6 (0.0 – 47.8)	19.9 (0.0 – 848.0)	11.3 (0.0 – 970.0)
SERUM B2-MICROGLOBULIN (MG/L) MEDIAN (RANGE)	3.5 (0.2 – 9.8)	2.8 (0.0 – 8.4)	3.1 (0.3 – 12.4)	2.7 (0.2 – 5.2)	3.0 (0.0 – 17.8)	2.8 (0.0 – 12.2)
DELETION 17p BY FISH, N (%)	0 (0.0)	0 (0.0)	4 (12.5)	1 (3.3)	76 (7.0)	20 (3.3)
DELETION 11q BY FISH, N (%)	5 (27.8)	13 (32.5)	8 (25.0)	4 (13.3)	331 (30.5)	33 (5.5)
TRISOMY 12 BY FISH, N (%)	1 (5.6)	1 (2.5)	3 (9.4)	3 (10.0)	175 (16.2)	78 (13.1)
DELETION 13q BY FISH, N (%)	16 (88.9)	33 (82.5)	15 (46.9)	18 (60.0)	487 (45.1)	397 (66.4)
TP53 MUTATED, N (%)	1 (7.7)	1 (3.4)	6 (18.8)	0 (0.0)	98 (12.8)	30 (7.2)
NOTCH1 MUTATED, N (%)	0 (0.0)	2 (6.7)	6 (20.0)	0 (0.0)	157 (20.6)	20 (4.8)
SF3B1 MUTATED, N (%)	5 (41.7)	14 (46.7)	3 (10.0)	3 (15.0)	128 (16.8)	49 (11.8)

Table 3. TTFT cox regression in early stage cohort subsets #1, 8 and 2

COX REGRESSION TTFT	UNIVARIABLE COMPARISON	HAZARD RATIO [HR]	95% CONFIDENCE INTERVAL		P VALUE
			LOWER	UPPER	
SUBSET AND IGHV ANALYSIS					
SUBSET #1, 8	vs. Subset #2	1.586	0.645	3.904	0.315
NON SUBSET #1,2,4,8 U-CLL	vs. Subset #2	0.975	0.522	1.821	0.936
NON SUBSET #1,2,4,8 M-CLL & SUBSET #4	vs. Subset #2	0.232	0.124	0.434	< 0.001
DELETION IN 17p					
YES	vs. no	2.353	1.299	4.262	0.005
DELETION IN 11q					
YES	vs. no	1.704	1.134	2.560	0.010
LEUKOCYTE COUNT (X 10⁹/L)					
≥ 50	vs. < 50	3.200	2.252	4.548	< 0.001
LYMPHOCYTE DOUBLING TIME					
≤ 12 MONTHS	vs. > 12 months	2.185	1.637	2.916	< 0.001

Table 4. TTNT cox regression in advanced stage cohort subsets #1, 8 and 2

COX REGRESSION TTNT	UNIVARIABLE COMPARISON	HAZARD RATIO [HR]	95% CONFIDENCE INTERVAL		P VALUE
			LOWER	UPPER	
SUBSET AND IGHV ANALYSIS					
SUBSET #1, 8	vs. Subset #2	1.293	0.655	2.552	0.458
NON SUBSET #1,2,4,8 U-CLL	vs. Subset #2	1.291	0.786	2.119	0.313
NON SUBSET #1,2,4,8 M-CLL & SUBSET #4	vs. Subset #2	0.594	0.351	1.005	0.052
DELETION IN 17p					
YES	vs. no	2.543	1.724	2.741	< 0.001
DELETION IN 11q					
YES	vs. no	1.465	1.188	1.808	< 0.001
TP53 MUTATIONAL STATUS					
MUTATED	vs. unmutated/ missing	1.842	1.334	2.543	< 0.001
SF3B1 MUTATIONAL STATUS					
MUTATED	vs. unmutated/ missing	1.413	1.117	1.788	0.004
LEUKOCYTE COUNT (X 10⁹/L)					
≥ 50	vs. < 50	1.305	1.065	1.600	0.010
SERUM THYMIDINE KINASE (U/L)					
> 10	vs. ≤ 10	1.382	1.132	1.687	0.001

Table 5. PFS cox regression in advanced stage CLL subsets #1, 2 and 8

COX REGRESSION PFS	UNIVARIABLE COMPARISON	HAZARD RATIO [HR]	95% CONFIDENCE INTERVAL		P VALUE
			LOWER	UPPER	
SUBSET AND IGHV ANALYSIS GROUP					
U-CLL	vs. Subset #1,2,8	1.302	1.028	1.650	0.028
M-CLL & SUBSET #4	vs. Subset #1,2,8	0.670	0.516	0.868	0.002
GENDER					
MALE	vs. female	1.180	1.037	1.342	0.012
DELETION IN 17p					
YES	vs. no	2.432	1.777	3.330	< 0.001
DELETION IN 11q					
YES	vs. no	1.479	1.287	1.700	< 0.001
TP53 MUTATIONAL STATUS					
MUTATED	vs. unmutated	1.798	1.374	2.353	< 0.001
SF3B1 MUTATIONAL STATUS					
MUTATED	vs. unmutated	1.269	1.058	1.521	0.010
LEUKOCYTE COUNT (X 10⁹/L)					
≥ 50	vs. < 50	1.230	1.081	1.398	0.002
SERUM THYMIDINE KINASE (U/L)					
> 10	vs. ≤ 10	1.250	1.097	1.425	0.001

Table 6. PFS cox regression in advanced stage cohort subsets #1, 8 and 2

COX REGRESSION PFS	UNIVARIABLE COMPARISON	HAZARD RATIO [HR]	95% CONFIDENCE INTERVAL		P VALUE
			Lower	Upper	
SUBSET AND IGHV ANALYSIS					
SUBSET #1, 8	vs. Subset #2	1.322	0.767	2.314	0.308
NON SUBSET #1,2,4,8 U-CLL	vs. Subset #2	1.513	1.012	2.262	0.044
NON SUBSET #1,2,4,8 M-CLL & SUBSET #4	vs. Subset #2	0.802	0.527	1.222	0.305
GENDER					
MALE	vs. female	1.167	1.004	1.357	0.044
DELETION IN 17p					
Yes	vs. no	2.539	1.842	3.500	< 0.001
DELETION IN 11q					
YES	vs. no	1.392	1.176	1.647	< 0.001
TP53 MUTATIONAL STATUS					
MUTATED	vs. unmutated/missing	1.748	1.329	2.299	< 0.001
SF3B1 MUTATIONAL STATUS					
MUTATED	vs. unmutated/missing	1.297	1.077	1.562	0.006
SERUM THYMIDINE KINASE (U/L)					
> 10	vs. ≤ 10	1.205	1.037	1.400	0.015
LEUKOCYTE COUNT (X 10⁹/L)					
≥ 50	vs. < 50	1.190	1.025	1.381	0.022

Table 7. TTNT cox regression in advanced stage CLL subset # 2

COX REGRESSION TTNT	UNIVARIABLE COMPARISON	HAZARD RATIO [HR]	95% CONFIDENCE INTERVAL		P VALUE
			LOWER	UPPER	
IGHV ANALYSIS GROUP					
M-IGHV3-21	vs. m-IGHV	0.548	0.202	1.483	0.236
M-SUBSET #2	vs. m-IGHV	2.012	1.234	3.283	0.005
U-IGHV	vs. m-IGHV	2.062	1.692	2.513	< 0.001
AGE AT STUDY ENTRY					
> 65	vs. ≤ 65	0.810	0.675	0.973	0.025
DELETION IN 17p					
YES	vs. no	2.443	1.691	3.528	< 0.001
DELETION IN 11q					
YES	vs. no	1.636	1.374	1.949	< 0.001
TP53 MUTATIONAL STATUS					
MUTATED	vs. unmutated	1.928	1.404	2.649	< 0.001
SF3B1 MUTATIONAL STATUS					
MUTATED	vs. unmutated	1.383	1.096	1.746	0.006
LEUKOCYTE COUNT (X 10⁹/L)					
≥ 50	vs. < 50	1.278	1.075	1.519	0.005
SERUM THYMIDINE KINASE (U/L)					
> 10	vs. ≤ 10	1.436	1.206	1.709	< 0.001