

Retrospective analysis of a cohort of 41 *de novo* B-cell prolymphocytic leukemia patients: impact of genetics and targeted therapies (a FILO study)

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SUPPLEMENTARY DATA

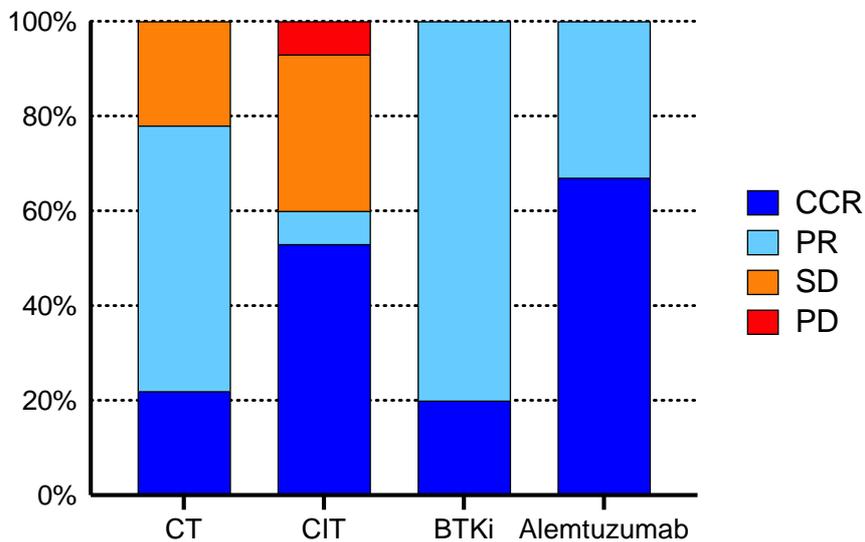
SUPPLEMENTARY TABLES

Supplementary Table S1. Characteristics at diagnosis according to the del17p status.

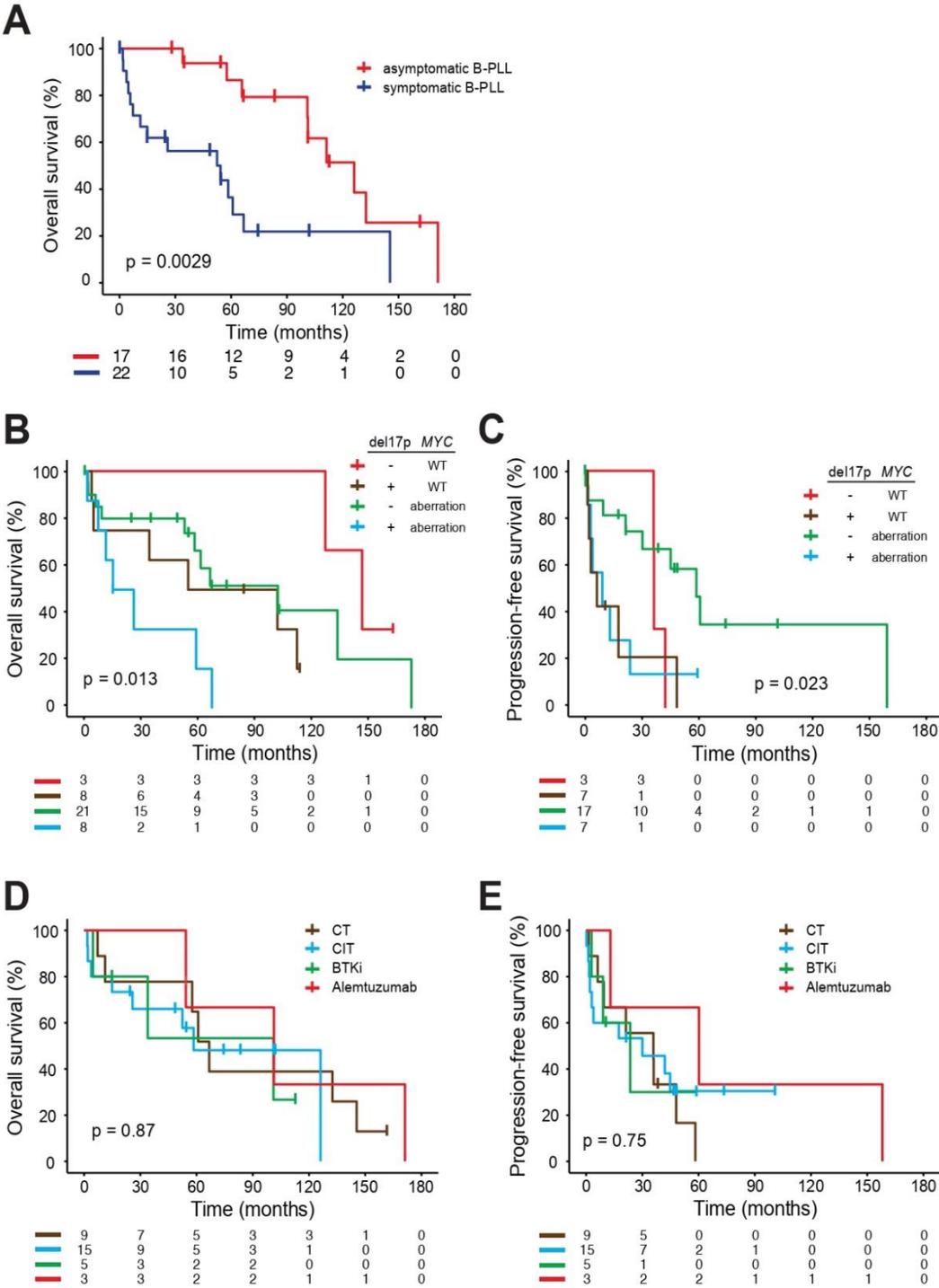
Parameter	no del17p (n=24)	del17p (n=16)	p value
Age at diagnosis, years			
Median (range)	71 (51-88)	74 (46-87)	0.5
Sex, n/N (%)			
Women	8/24 (33%)	8/16 (50%)	0.3
Constitutional symptoms, n/N (%)			
Yes	4/18 (22%)	0/10 (0%)	0.3
Splenomegaly, n/N (%)			
Present	13/22 (59%)	11/16 (69%)	0.5
Lymphadenopathy, n/N (%)			
Present	6/22 (27%)	5/16 (31%)	0.9
Extranodal disease, n/N (%)			
Present	1/18 (6%)	3/13 (23%)	0.3
Lymphocytes, 10⁹/L			
Median (range)	19 (5-137)	56 (9-227)	0.04
Prolymphocytes, % among lymphocytes			
Median (range)	83 (66-100)	80 (61-94)	0.4
Hemoglobin value, g/dL			
Median (range)	13 (8-17)	10 (8-14)	0.2
Platelets, 10⁹/L			
Median (range)	147 (72-316)	130 (25-210)	0.12
LDH, n/N %			
Increased	7/13 (54%)	8/10 (80%)	0.4
Beta-2-microglobulin, n/N (%)			
Increased	4/8 (50%)	7/8 (88%)	0.3
Complex karyotype, n/N (%)			
Present	13/24 (54%)	15/16 (94%)	0.01
Highly complex karyotype, n/N (%)			
Present	5/24 (21%)	14/16 (88%)	< 0.001
TP53 mutation, n/N (%)			
Present	2/15 (13%)	7/7 (100%)	< 0.001
MYC gain or rearrangement, n/N (%)			
Present	21/24 (88%)	8/16 (50%)	0.01

SUPPLEMENTARY FIGURE LEGENDS

Supplementary Figure S1. Response to different first-line therapies (CT, chemotherapy, n=9; CIT, chemoimmunotherapy, n=15; BTKi, BTK inhibitor, n=5; alemtuzumab, n=3). CCR, clinical complete response; PR, partial response; SD, stable disease; PD, progressive disease. Response to therapy was evaluated using modified criteria from those of iwCLL¹. Patients meeting iwCLL clinical and laboratory complete remission criteria were considered as in clinical complete remission (CCR) as previously described². Partial response (PR), stable (SD) and progressive disease (PD) were defined using the iwCLL criteria. Overall response rate (ORR) was defined as the addition of PR and CCR rates. CT regimens included chlorambucil (n=4), CHOP/miniCHOP (n=2), fludarabine-cyclophosphamide (n=2), intensive polychemotherapy (LMBA-02 protocol) (n=1). CIT regimens included fludarabine-rituximab (FR) (n=1), fludarabine-cyclophosphamide-rituximab (FCR) (n=4), bendamustine-rituximab (BR) (n=6), chlorambucil-rituximab (n=2), rituximab-CHOP (n=2).



Supplementary Figure S2. Outcomes of B-PLL patients in different subgroups. (A) Kaplan-Meier estimates of OS according to the asymptomatic or symptomatic presentation at diagnosis (asymptomatic B-PLL, red; symptomatic B-PLL, blue). Kaplan-Meier estimates of (B) OS and (C) PFS according to the del17p and MYC status at diagnosis (no del17p and no MYC aberration, red; del17p and no MYC aberration, brown; no del17p and MYC aberration, green; del17p and MYC aberration, blue). Kaplan-Meier estimates of (D) OS and (E) PFS according to the first-line treatment received (CT, chemotherapy, brown; CIT, chemoimmunotherapy, blue; BTKi, green; alemtuzumab, red). WT: wildtype.



REFERENCES

1. Hallek M, Cheson BD, Catovsky D, et al. iwCLL guidelines for diagnosis, indications for treatment, response assessment, and supportive management of CLL. *Blood*. 2018;131(25):2745–2760.
2. Moore J, Baran AM, Meacham PJ, et al. Initial treatment of B-cell prolymphocytic leukemia with ibrutinib. *Am J Hematol*. 2020;95(5):E108–E110.