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

B-cell prolymphocytic leukemia (B-PLL) is a very rare lymphoid neoplasm accounting for less than 0.5% of low-grade mature B-cell lymphomas.[1-3] B-PLL is a poor-prognosis disease with a historical median overall survival (OS) of 3 years.[3] B symptoms, marked lymphocytosis, cytopenia and massive splenomegaly are hallmarks of B-PLL patients at diagnosis.[1-3] A minority of patients present with an indolent phase, not requiring immediate therapy. The characterization of B-PLL genetic landscape has led to the identification of recurrent abnormalities including complex karyotype (CK), *MYC* translocations/gains (*MYC* aberration), 17p deletion (del17p) and *TP53* mutations (*TP53* abnormalities [*TP53*abn]).[1,4-6]

Due to the rarity of the disease, the absence of international guidelines and randomized clinical trial data, most therapeutic approaches used chemoimmunotherapy (CIT) or are executed according to chronic lymphocytic leukemia (CLL) guidelines. A watch and wait strategy is proposed to asymptomatic B-PLL patients while, for symptomatic B-PLL, rituximab-based CIT, alemtuzumab and more recently BCR inhibitors (BCRi) have been used for frontline therapy. Recent case reports and small series have indeed described the efficacy of Bruton tyrosine kinase inhibitor (BTKi)[7-10] and phosphoinositide 3-kinase inhibitor (P13Ki),[11] notably in frontline and relapse *TP53*abn B-PLL population. Allogeneic stem cell transplantation (allo-SCT) is still considered as the only curative therapy for eligible and responsive B-PLL patients.

Our group has recently shown in a retrospective cohort of 34 patients with rigorous diagnostic criteria for B-PLL that three distinct cytogenetic risk groups could be identified: low (no *MYC* aberration), intermediate (*MYC* aberration but no del17p), and high-risk (*MYC* aberration and del17p), with profound impact on OS[5].

Despite these advances, several questions remain unanswered in B-PLL. Factors associated with initial asymptomatic disease and those predicting time to first treatment (TFT) are still unknown as the impact of CIT or BCRi in different genetic subgroups. Based on our previous biological work,[5] we describe here the clinical outcomes and associated prognostic factors of initially asymptomatic or symptomatic diseases, and the impact of different therapies in an extended and homogenously defined cohort of 41 *de novo* B-PLL patients.

We conducted a retrospective analysis of French adult patients with a diagnosis of *de novo* B-PLL, according to the 2016 World Health Organization classification criteria[1] after thorough exclusion of potential differential diagnoses as described previously.[5] While the 2022 World Health Organization classification included it in “splenic B-cell lymphoma/leukemia with prominent nucleoli”[12] that also includes “hairy cell leukemia variant” (HCL-v), B-PLL is still recognized as a specific entity by the International Consensus Classification of mature lymphoid neoplasms.[13] Forty-one patients diagnosed between 1992 and 2020 in 17 French centers were included after the reviewing of blood smears by three independent expert cytologists. In addition to the 2016 classification criteria (i.e., prolymphocytes accounting for at least 55% of the lymphoid cells in peripheral blood), inclusion cytological criteria included round nucleus and prominent central nucleolus while presence of hybrid features overlapping HCL, such as hairy projections was a strict exclusion criterion. Although we cannot exclude that some cases previously defined as HCL-v may be present in our cohort, it should be noted that only one case harbored usage of the *IGHV4-34* gene family (n=1/25) and no *MAP2K1* mutation was observed in the 20 cases explored by next-generation sequencing. Patients with a history of another B-cell malignancy (CLL or marginal zone lymphoma [MZL]) were excluded and diagnosis of MCL was ruled out according to karyotype and fluorescence *in situ* hybridization (FISH) assays looking for *CCND1* rearrangements or translocations involving *CCND2* or *CCND3*. Cytogenetic and molecular analyses for detection of MYC aberration and *TP53*abn were performed as described previously.[5] All cases were analyzed for del17p by FISH and 23 of 41 had DNA available for evaluation of *TP53* mutations by molecular analyses. CK and high CK (HCK) were defined by the presence of ≥3 and ≥5 chromosomal abnormalities respectively. The study was performed in accordance with the Declaration of Helsinki and was approved by the local Investigational Review Board (CPP Ile-de-France VI, Paris, France, 05/21/2014). The primary endpoints were overall survival (OS) defined as time from diagnosis to death from any cause or last follow-up, and progression-free survival (PFS) defined as time from first treatment initiation to progression, death, or last follow-up. TFT was defined as time from diagnosis to first therapy in asymptomatic B-PLL. Response to therapy was evaluated using modified criteria from those of iwCLL.[9,14] Baseline characteristics are described as median and range for continuous variables and frequency and percen-

tage for categorical variables. Comparisons between categorical variables were performed by χ^2 or Fisher's exact test, as appropriate. Comparisons between continuous variables were performed by Wilcoxon-Mann-Whitney non-parametric test. Median follow-up was calculated using the reverse Kaplan-Meier method. Survival curves were calculated by using the Kaplan-Meier method, and the log-rank test was used for comparisons between groups. Univariate analyses were performed using the Cox proportional hazards model. All tests of statistical significance were two-sided, and a *P* value <0.05 was considered statistically significant. All statistical analyses were performed using the R statistical package (version 4.1.0, R Core Team, 2021) and the RStudio software (versions 1.2.5033).

The main characteristics of the whole cohort at diagnosis are detailed in Table 1 and correspond to those previously reported in the literature.[3] Median age at B-PLL diagnosis was 72 years old (range, 46-88 years) and most patients were male (25/41, 61%). Splenomegaly was present in 62%

Table 1. Characteristics at diagnosis and their prognostic impact on overall and progression-free survivals in the whole B-cell prolymphocytic leukemia cohort. Univariate analysis was performed using log-rank tests. Complex karyotype and high complex karyotype were defined by the presence of ≥3 and ≥5 chromosomal abnormalities respectively.

Parameter	Whole cohort (N=41)	OS		PFS	
		HR [95% CI]	*P* value	HR [95% CI]	*P* value
Age in years at diagnosis Median (range)	72 (46-88)	1.03 [0.99-1.07]	0.16	1.02 [0.98-1.06]	0.4
Sex, N (%) Male	25/41 (61)	0.92 [0.66-3.21]	0.92	1.36 [0.59-3.15]	0.47
Constitutional symptoms, N (%) Yes	4/29 (14)	2.05 [0.44-9.51]	0.36	na	na
Splenomegaly, N (%) Present	24/39 (62)	1.25 [0.56-2.81]	0.59	0.63 [0.28-1.45]	0.28
Lymphadenopathy, N (%) Present	11/39 (28)	2.31 [0.9-5.89]	0.08	1.11 [0.43-2.85]	0.83
Extranodal disease, N (%) Present	4/32 (12)	**5.71 [1.34-24.4]**	**0.02**	2.97 [0.79-11.1]	0.11
Lymphocytes, x10^9/L Median (range)	32 (5-227)	1 [0.99-1.01]	0.86	1 [0.99-1.01]	0.78
Prolymphocytes, % among lymphocytes Median (range)	83 (61-100)	0.96 [0.92-1.01]	0.1	0.97 [0.93-1.02]	0.2
Hemoglobin value, g/dL Median (range)	12 (8-17)	0.87 [0.74-1.03]	0.11	0.94 [0.79-1.11]	0.44
Platelets, x10^9/L Median (range)	135 (25-316)	**0.99 [0.98-0.99]**	**0.02**	0.99 [0.99-1]	0.41
LDH, N % Increased	15/24 (62)	1.44 [0.41-5.03]	0.57	1.45 [0.38-5.51]	0.58
β-2-microglobulin, N (%) Increased	11/17 (65)	1.71 [0.42-7.04]	0.46	1.07 [0.21-5.56]	0.94
Complex karyotype, N (%) Present	28/41 (68)	1.08 [0.45-2.6]	0.86	2.03 [0.75-5.53]	0.17
High complex karyotype, N (%) Present	19/41 (46)	1.39 [0.63-3.1]	0.41	2.39 [0.99-5.71]	0.05
del17p, N (%) Present	16/40 (40)	**2.8 [1.19-6.59]**	**0.02**	**3.38 [1.42-8.07]**	**0.006**
TP53 mutation, N (%) Present	9/23 (39)	2.41 [0.76-7.65]	0.14	1.72 [0.52-5.72]	0.38
del17p or *TP53* mutation, N (%) Present	18/31 (58)	2.78 [0.99-7.78]	0.05	**2.9 [1.05-7.97]**	**0.04**
MYC gain or rearrangement, N (%) Present	30/41 (73)	1.4 [0.59-3.35]	0.45	0.5 [0.21-1.19]	0.12
MYC / del17p status, N (%) *MYC* WT / no del17p *MYC* WT / del17p *MYC* aberration / no del17p *MYC* aberration / del17p	 3/40 (7.5) 8/40 (20) 21/40 (52) 8/40 (25)	 4.59 [0.79-26.6] 2.76 [0.56-13.7] 11 [1.84-65.9]	 0.09 0.23 0.009	 1.6 [0.38-6.65] 0.42 [0.11-1.68] 1.89 [0.45-7.9]	 0.52 0.22 0.38

HR: hazard ratio; 95% CI: 95% confidence interval; NA: not assessed; PFS: progression-free survival; OS: overall survival; LDH: lactate dehydrogenase; del: deletion.

of patients (24/39) while lymphadenopathy (11/39, 28%) and extranodal disease (4/32, 12%) were rarer. The distribution of cytogenetic abnormalities was as follows: *MYC* aberrations (30/41, 73%), CK (28/41, 68%), high CK (HCK, 19/41, 46%) and del17p (16/40, 40%). *TP53abn* (mutation or del17p) was detected in 18 0f 31 patients (58%). Del17p was significantly associated with lymphocytosis, CK, HCK and *TP53* mutations, while *MYC* aberration was enriched in patients lacking del17p (*Online Supplementary Table S1*). Median follow-up for the whole cohort was 102 months (range, 0.2-171 months). B-PLL was symptomatic at diagnosis in 22 of 39 (56%) patients. Main differences observed between asymptomatic and symptomatic B-PLL patients are summarized in Table 2. As expected, the proportion of patients with cytopenia and/or tumoral disease was higher in the symptomatic B-PLL subgroup. Interestingly, significantly more symptomatic B-PLL patients harbored both *MYC* aberrations and del17p (7/22, 32%) than asymptomatic B-PLL patients (0/16, 0%; *P*=0.04). Among the 17 asymptomatic B-PLL patients, 13 (76%) progressed with a median TFT of 46.9 months. Of note, the four patients who did not progress harbored either *MYC* aberration (n=3) or del17p (n=1) but no HCK (0/4 compared to 8/13 asymptomatic B-PLL who progressed; *P*=0.08).

During follow-up, 34 of 41 (83%) B-PLL patients required therapy. The median number of therapeutic lines was two (range, 1-4). Frontline therapies consisted of chemotherapy (CT) (9/34, 26%), CIT (15/34, 44%), BTKi (5/34, 15%), alemtuzumab (3/34, 9%) and rituximab monotherapy (1/34, 3%). Only two patients received allo-SCT. Overall-

Table 2. Characteristics at diagnosis according to the asymptomatic (asymptomatic B-cell prolymphocytic leukemia, N=17) or symptomatic (symptomatic B-cell prolymphocytic leukemia, N=22) presentation.

Parameter	Asymptomatic B-PLL (N=17)	Symptomatic B-PLL (N=22)	*P value*
Age in years at diagnosis Median (range)	72 (51-87)	70 (46-88)	0.9
Sex, N (%) Female	5/17 (29)	9/22 (41%)	0.5
Constitutional symptoms, N (%) Yes	0/15 (0)	3/13 (23%)	0.09
Splenomegaly, N (%) Present	6/16 (38)	16/21 (76%)	0.02
Lymphadenopathy, N (%) Present	0/16 (0)	10/21 (48%)	0.002
Extranodal disease, N (%) Present	0/14 (0)	4/17 (24%)	0.11
Lymphocytes, x10^9/L Median (range)	20 (5-175)	41 (5-227)	0.2
Prolymphocytes, % among lymphocytes Median (range)	78 (66-94)	83 (61-100)	0.4
Hemoglobin value, g/dL Median (range)	14 (8-17)	11 (8-14)	0.02
Platelets, x10^9/L Median (range)	162 (91-316)	128 (25-206)	0.02
LDH, N % Increased	6/12 (50)	9/12 (75%)	0.4
β-2-microglobulin, N (%) Increased	4/10 (40)	7/7 (100%)	0.04
Complex karyotype, N (%) Present	14/17 (82)	13/22 (59%)	0.12
Highly complex karyotype, N (%) Present	8/17 (47)	10/22 (45%)	0.9
del17p, N (%) Present	5/16 (31)	10/22 (45%)	0.4
TP53 mutation, N (%) Present	3/8 (38)	5/14 (36%)	0.9
MYC gain or rearrangement, N (%) Present	10/17 (59)	18/22 (82%)	0.2
MYC / del17p status, N (%) *MYC* WT/no del17p *MYC* WT/del17p *MYC* aberration/no del17p *MYC* aberration/del17p	 2/16 (12) 5/16 (31) 9/16 (56) 0/16 (0)	 1/22 (4.5%) 3/22 (14%) 11/22 (50%) 7/22 (32%)	0.04

B-PLL: B-cell prolymphocytic leukemia; LDH: lactate dehydrogenase; del: deletion.

response rates (ORR) for frontline CT (78%), CIT (60%), BTKi (100%) and alemtuzumab (100%) were not significantly different (*P*=0.3) (*Online Supplementary Figure S1*). In the whole cohort, median PFS of patients receiving frontline therapy was 30 months and median OS was 67 months (Figure 1A, B). Twenty-six of 41 patients (63%) have died due to B-PLL progression (38%), therapy-related toxicity (23%), other causes (27%) and of unknown origin (12%). Main clinical and biological factors associated with PFS and OS in univariate analyses are summarized in Table 1. Median OS was significantly longer in asymptomatic B-PLL compared to symptomatic B-PLL (126 *vs*. 54

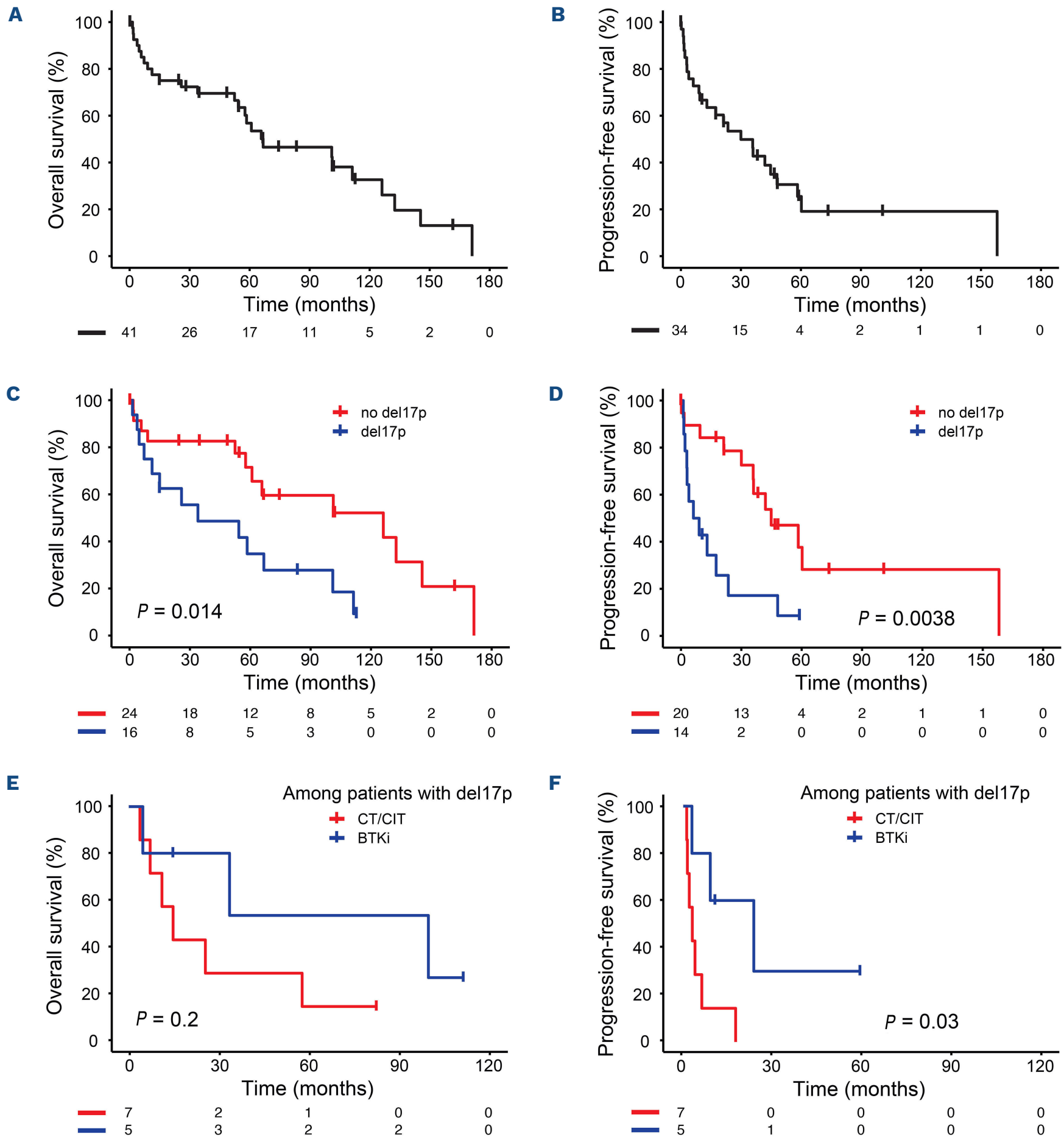

Figure 1. Outcomes of B-cell prolymphocytic leukemia patients. Kaplan-Meier estimates of (A) overall survival (OS) (n=41) and (B) progression-free survival (PFS) (n=34) in the whole cohort. Kaplan-Meier estimates of (C) OS and (D) PFS according to the presence of del17p (no del17p, red; del17p, blue). Kaplan-Meier estimates of (E) OS and (F) PFS according to the treatment received (blue: Bruton tyrosine kinase inhibitor [BTKi]; red: chemotherapy or chemoimmunotherapy [CT/CIT]) among del17p patients.

months; *P*=0.003; *Online Supplementary Figure S2A*). The presence of del17p pejoratively influenced both PFS (median 8 *vs*. 45 months; *P*=0.004) and OS (median 34 *vs*. 126 months; *P*=0.02) (Figure 1C, D) while low platelet count (hazard ratio [HR]=0.99, 95% confidence interval [CI]: 0.98-0.99) and extranodal disease (HR=5.71, 95% CI: 1.34-24.4) were associated with shorter OS (Table 1). The poorest median OS and PFS were observed in *MYC* aberration / del17p patients (20 and 6 months, respectively) (Table 1; *Online Supplementary Figure S2B, C*) while patients with either *MYC* aberration (101 and 58 months, respectively) or del17p (78 and 9 months, respectively) harbored comparable intermediate prognosis inferior to those without any of these abnormalities (145 and 36 months, respectively). The presence of *TP53* mutation was highly correlated to the presence of del17p (*Online Supplementary Table S1*). Although the presence of *TP53* mutation did not significantly affect OS (HR=2.41, 95% CI: 0.76-7.65; *P*=0.14) or PFS (HR=1.72, 95% CI: 0.52-5.72; *P*=0.38), the statistical analysis is limited by the reduced number of patients with available *TP53* mutation status. The specific prognostic impact of *TP53* mutation was not possible due to the very few cases (n=2) of *TP53* mutation without del17p.

We eventually interrogated the impact of different frontline therapies on outcomes (*Online Supplementary Figure S2D, E*). The type of frontline therapies did not significantly modify PFS or OS but was not randomly distributed among genetic subgroups as patients that received BTKi all harbored del17p. Looking specifically in the del17p subgroup, patients receiving BTKi (n=5) displayed better outcomes compared to those receiving CT/CIT (n=7) (respective median PFS and OS of 24 and 101 *vs*. 3 and 15 months; *P*=0.03 and *P*=0.2) (Figure 1E, F).

Although definitive conclusions are limited by its retrospective nature, the small numbers of patients in specific subgroups and lack of available DNA for *TP53* mutation analysis in all samples, our study of the largest B-PLL cohort to date provides meaningful insights in this very rare disease. We identified that asymptomatic B-PLL represents around 40% of patients at diagnosis, do not harbor both *MYC* aberration and del17p, and displays a significant better OS. We highlight the pejorative impact of del17p and confirm that the subgroup presenting with both *MYC* aberration and del17p has the worst outcome with a median OS shorter than 2 years. Finally, albeit on a small number of patients, we confirm the efficacy of frontline BTKi in del17p B-PLL.[7,8,9]

Authors

Caroline Algrin,[1*] Louis Pérol,[2*] Elise Chapiro,[3,4*] Lucile Baseggio,[5] Karim Maloum,[6] Catherine Settegrana,[7] Jean-François Lesesve,[8] Justine Siavellis,[9] Alain Delmer,[10] Anne-Sophie Michallet,[11] Emmanuelle Ferrant,[12] Pierre Feugier,[13] Cécile Tomowiak,[14] Annie Brion,[15] David Ghez,[16] Luc-Matthieu Fornecker,[17] Sarah Ivanoff,[9] Stéphanie Struski,[18] Laurent Sutton,[19] Isabelle Radford-Weiss,[20] Virginie Eclache,[21] Christine Lefebvre,[22] Véronique Leblond,[2] Florence Nguyen-Khac,[3,4#] and Damien Roos-Weil[2,4#] for the FILO (French Innovative Leukemia Organization) group, see Appendix below.

[1]Groupe Hospitalier Mutualiste de Grenoble, Service d'Onco-Hématologie, Grenoble; [2]Sorbonne Université, Service d'Hématologie Clinique, Hôpital Pitié-Salpêtrière, AP-HP, Paris; [3]Sorbonne Université, Unité de Cytogénétique Hématologique, Hôpital Pitié-Salpêtrière, AP-HP, Paris; [4]Centre de Recherche des Cordeliers, INSERM, Drug Resistance in Hematological Malignancies (DRIHM) Team, Sorbonne Université, Université Sorbonne Paris Cité, Université Paris Descartes, Université Paris Diderot, Paris; [5]Hôpital Lyon Sud, Laboratoire d'Hématologie, Hospices Civils de Lyon, Pierre-Bénite; [6]Sorbonne Université, Service d'Hématologie Biologique, Hôpital Pitié-Salpêtrière, AP-HP, Paris; [7]Hôpital Ambroise Paré, Laboratoire d'Hématologie, AP-HP, Boulogne-Billancourt; [8]CHRU Nancy, Service d'Hématologie Biologique, INSERM 1256 NGERE, Nancy; [9]Hôpital Avicenne, Service d'Hématologie Clinique, AP-HP, Bobigny; [10]CHU Reims, Service d'Hématologie Clinique, Reims; [11]Centre Léon Bérard, Service d'Hématologie Clinique, Lyon; [12]Hôpital Lyon Sud, Service d'Hématologie Clinique, Hospices Civils de Lyon, Pierre-Bénite; [13]CHU Nancy, Service d'Hématologie Clinique, Vandœuvre-lès-Nancy; [14]CHU Poitiers, Service d'Hématologie Clinique, Poitiers; [15]CHU J Minjoz, Service d'Hématologie Clinique, Besançon; [16]Institut Gustave Roussy, Service d'Hématologie Clinique, Villejuif; [17]Service d'Hématologie, Institut de Cancérologie Strasbourg Europe (ICANS), Strasbourg; [18]IUCT Oncopole - Toulouse, Laboratoire d'hématologie/Plateau Technique Hématologie-Oncologie, Toulouse; [19]CHU Tours, Service d'Hématologie Clinique, Tours; [20]CHU Necker-Enfants Malades, Laboratoire de Cytogénétique, APHP, Paris; [21]Hôpital Avicenne, Service d'Hématologie Biologique, AP-HP, Bobigny and [22]CHU Grenoble Alpes, Laboratoire de Cytogénétique des Hémopathies, Grenoble, France

CA, LP and EC contributed equally as co-first authors.

#FNK and DRW contributed equally as co-senior authors.*

Correspondence:
C. ALGRIN - caroline.algrin@avec.fr
D. ROOS-WEIL - damien.roosweil@aphp.fr

https://doi.org/10.3324/haematol.2022.282162

Received: September 26, 2022.
Accepted: December 14, 2022.
Early view: December 22, 2022.

Disclosures

No conflicts of interest to disclose.

Contributions

CA, EC, VL, FNK and DRW designed the study; CA, LP, EC, VL, FNK and DRW analyzed data; CA, LP and DRW wrote the manuscript; CA, LP, EC, LB, KM, CS, JFL, JS, AD, ASM, EM, PF, CT, AB, DG, LMF, SI, SS, IRW, VE, CL, LS, VL, FNK and DRW recruited patients. All authors critically reviewed and approved the manuscript.

Acknowlegments

We thank Mohamad Sabbah for his assistance in data collection.

Funding

This study was supported in part by grants from INCA-DGOS-INSERM 12560 (SiRIC CURAMUS is financially supported by the French National Cancer Institute, the French Ministry of Solidarity and Health and INSERM with financial support from ITMO Cancer AVIESAN).

Data-sharing statement

The data that support the findings of this study are available on request from the corresponding author.

Appendix

FILO group members: Caroline Algrin (Grenoble), Thérèse Aurran (Marseille), Marie Christine Béné (Nantes), Fontanet Bijou (Bordeaux), Annie Brion (Besançon), Julien Broséus (Nancy), Guillaume Cartron (Montpellier), Aline Clavert (Angers), Florence Cymbalista (Bobigny), Frédéric Davi (Paris), Caroline Dartigeas (Tours), Sophie De Guibert (Rennes), Alain Delmer (Reims), Marie Sarah Dilhuydy (Bordeaux), Bernard Drenou (Mulhouse), Jehan Dupuis (Créteil), Emmanuelle Ferrant (Lyon), Pierre Feugier (Nancy), Luc Matthieu Fornecker (Strasbourg), David Ghez (Villejuif), Romain Guièze (Clermont-Ferrand), Charles Herbaux (Lille), Bénédicte Hivert (Lille), Luca Inchiappa (Marseille), Kamel Laribi (Le Mans), Katel Le Dû (Le Mans), Magali Le Garff-Tavernier (Paris), Marielle Le Goff (Le Mans), Véronique Leblond (Paris), Stéphane Leprêtre (Rouen), Rémi Letestu (Bobigny), Vincent Lévy (Bobigny), Béatrice Mahé (Nantes), Fatiha Merabet (Versailles), Anne Sophie Michallet (Lyon), Lysiane Molina (Grenoble), Pierre Morel (Amiens), Florence Nguyen-Khac (Paris), Bertrand Pollet (Boulogne), Stéphanie Poulain (Lille), Anne Quinquenel (Reims), Daniel Ré (Antibes), Damien Roos-Weil (Paris), Laurence Simon (Corbeil Essonnes), Cécile Tomowiak (Poitiers), Olivier Tournilhac (Clermont-Ferrand), Xavier Troussard (Caen), Malgorzata Truchan-Graczyk (Saumur), Maud Voldoire (La Roche sur Yon), Lise Willems (Paris), Loïc Ysebaert (Toulouse), and Jean Marc Zini (Paris)

FILO Recherche Clinique members: Laetitia Auvray, Alexandra Fayault, Lamya Haddaoui, Delphine Nollet and Valérie Rouille

References

1. Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood. 2016;127(20):2375-2390.
2. Dearden C. Management of prolymphocytic leukemia. Hematol Am Soc Hematol Educ Program. 2015;2015:361-367.
3. Cross M, Dearden C. B and T cell prolymphocytic leukaemia. Best Pract Res Clin Haematol. 2019;32(3):217-228.
4. Hercher C, Robain M, Davi F, et al. A multicentric study of 41 cases of B-prolymphocytic leukemia: two evolutive forms. Leuk Lymphoma. 2001;42(5):981-987.
5. Chapiro E, Pramil E, Diop M, et al. Genetic characterization of B-cell prolymphocytic leukemia: a prognostic model involving MYC and TP53. Blood. 2019;134(21):1821-1831.
6. Lens D, De Schouwer PJ, Hamoudi RA, et al. p53 abnormalities in B-cell prolymphocytic leukemia. Blood. 1997;89(6):2015-2023.
7. Damlaj M, Al Balwi M, Al Mugairi AM. Ibrutinib therapy is effective in B-cell prolymphocytic leukemia exhibiting MYC aberrations. Leuk Lymphoma. 2018;59(3):739-742.
8. Gordon MJ, Raess PW, Young K, Spurgeon SEF, Danilov AV. Ibrutinib is an effective treatment for B-cell prolymphocytic leukaemia. Br J Haematol. 2017;179(3):501-503.
9. Moore J, Baran AM, Meacham PJ, Evans AG, Barr PM, Zent CS. Initial treatment of B-cell prolymphocytic leukemia with ibrutinib. Am J Hematol. 2020;95(5):E108-E110.
10. Xing L, He Q, Xie L, Wang H, Li Z. Zanubrutinib, rituximab and lenalidomide induces deep and durable remission in TP53-mutated B-cell prolymphocytic leukemia: a case report and literature review. Haematologica. 2022;107(5):1226-1228.
11. Eyre TA, Fox CP, Shankara P, Went R, Schuh AH. Idelalisib-rituximab induces clinical remissions in patients with TP53 disrupted B cell prolymphocytic leukaemia. Br J Haematol. 2017;177(3):486-491.
12. Alaggio R, Amador C, Anagnostopoulos I, et al. The 5th edition of the World Health Organization Classification of haematolymphoid tumours: lymphoid neoplasms. Leukemia. 2022;36(7):1720-1748.
13. Campo E, Jaffe ES, Cook JR, et al. The International Consensus Classification of mature lymphoid neoplasms: a report from the clinical advisory committee. Blood. 2022;140(11):1229-1253.
14. 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.