





# Prognostic heterogeneity of adult B-cell precursor acute lymphoblastic leukaemia patients with t(1;19)(q23;p13)/TCF3-PBX1 treated with measurable residual disease-oriented protocols

Jordi Ribera,<sup>1</sup>  Isabel Granada,<sup>1</sup> Mireia Morgades,<sup>1</sup> Teresa González,<sup>2</sup> Juana Ciudad,<sup>3,4</sup> Esperanza Such,<sup>5</sup>  María-José Calasanz,<sup>6</sup> Santiago Mercadal,<sup>7</sup>  Rosa Coll,<sup>8</sup> José González-Campos,<sup>9</sup> Mar Tormo,<sup>10</sup> Irene García-Cadenas,<sup>11</sup> Cristina Gil,<sup>12</sup> Marta Cervera,<sup>13</sup> Pere Barba,<sup>14</sup> Dolors Costa,<sup>15</sup> Rosa Ayala,<sup>16</sup> Arancha Bermúdez,<sup>17</sup> Alberto Orfao,<sup>3,4</sup>  and Josep-Maria Ribera,<sup>1</sup> on behalf of the Programa para el Tratamiento de Hemopatías Malignas (PETHEMA) Group (Spanish Society of Hematology, SEHH)

<sup>1</sup>Josep Carreras Leukaemia Research Institute, ICO-Hospital Germans Trias i Pujol, Universitat Autònoma de Barcelona, Badalona, <sup>2</sup>Hospital Universitario de Salamanca, Universidad de Salamanca, IBMCC (CSIC/USAL), IBSAL and CIBERONC, <sup>3</sup>Cytometry Service (NUCLEUS) and Department of Medicine, Cancer Research Center (IBMCC-CSIC/USAL-IBSAL), University of Salamanca, Salamanca, <sup>4</sup>Centro de Investigación Biomédica en Red de Cáncer (CIBERONC) CB16/12/00400, Instituto de Salud Carlos III, Madrid, <sup>5</sup>Hematology Department, Hospital Universitari Politècnic La Fe, Valencia, <sup>6</sup>Centro de Investigación Clínica Aplicada (CIMA), Universidad de Navarra, Pamplona, <sup>7</sup>Hematology Department, ICO-Hospital Duran i Reynals, Hospitalet de Llobregat, <sup>8</sup>Hematology Department, ICO-Hospital Josep Trueta, Girona, <sup>9</sup>Hematology Department, Hospital Universitario Virgen del Rocío, Sevilla, <sup>10</sup>Hematology Department, Hospital Clínico Universitario, Valencia, <sup>11</sup>Hematology Department,

## Summary

The prognosis of t(1;19)(q23;p13)/transcription factor 3-pre-B-cell leukaemia homeobox 1 (*TCF3-PBX1*) in adolescent and adult patients with acute lymphoblastic leukaemia (ALL) treated with measurable residual disease (MRD)-oriented trials remains controversial. In the present study, we analysed the outcome of adolescent and adult patients with t(1;19)(q23;p13) enrolled in paediatric-inspired trials. The patients with *TCF3-PBX1* showed similar MRD clearance and did not have different survival compared with other B-cell precursor ALL patients. However, patients with *TCF3-PBX1* had a significantly higher cumulative incidence of relapse, especially among patients aged  $\geq 35$  years carrying additional cytogenetic alterations. These patients might benefit from additional/intensified therapy (e.g. immunotherapy in first complete remission with or without subsequent haematopoietic stem cell transplantation).

**Keywords:** acute lymphoblastic leukaemia, adults, t(1;19)(q23;p13)/*TCF3-PBX1*, prognosis, cytogenetic alterations.

Hospital de Sant Pau, Josep Carreras  
Leukaemia Research Institute, Barcelona,  
<sup>12</sup>Hematology Department, Hospital  
General de Alicante, Alicante,  
<sup>13</sup>Hematology Department, ICO-Hospital  
Joan XXIII, Tarragona, <sup>14</sup>Hematology  
Department, Hospital Universitari Vall  
d'Hebrón, <sup>15</sup>Haematopathology Section,  
Department of Pathology, Hospital Clínic,  
Barcelona, <sup>16</sup>Hematology Department,  
Hospital Universitario Doce de Octubre,  
Madrid, and <sup>17</sup>Hematology Department,  
Hospital Universitario Marqués de  
Valdecilla, Santander, Spain

Received 2 July 2021; accepted for publication  
6 September 2021

Correspondence: Jordi Ribera, Josep Carreras  
Leukaemia Research Institute, ICO-Hospital  
Germans Trias i Pujol, Universitat Autònoma  
de Barcelona, Carretera de Canyet s/n, Camí  
de les Escoles s/n, 08916 Badalona, Spain.  
E-mail: jribera@carrerasresearch.org

## Introduction

The t(1;19)(q23;p13)/transcription factor 3-pre-B-cell leukaemia homeobox 1 (*TCF3-PBX1*) is a subtype of B-cell precursor acute lymphoblastic leukaemia (BCP ALL) with an incidence of around 5–7%.<sup>1</sup> In paediatric ALL, therapy intensification has improved the outcome, moving from poor to intermediate–good prognosis. In adults the scenario is less clear, with reports showing favourable,<sup>2</sup> intermediate<sup>3–5</sup> and poor prognosis.<sup>6–8</sup> The low incidence of this alteration limits the prognosis assessment in homogeneously treated patients, and differences within chemotherapy schedules and in the indication of allogeneic haematopoietic stem cell transplantation (alloHSCT) may explain these controversial results. However, the prognostic significance of *TCF3-PBX1* in paediatric-inspired, measurable residual disease (MRD)-based trials has not been extensively evaluated in adolescents and adults with ALL.

## Patients and methods

The outcomes of adolescent and adults (aged 15–60 years) with Philadelphia (Ph) chromosome-negative BCP ALL and *TCF3-PBX1* rearrangement diagnosed between 2003 and 2017 and treated with MRD-oriented protocols from the Programa Español de Tratamientos en Hematología (PETHEMA) Group (high-risk protocols ALL AR03 and ALL HR11, and standard-risk protocol ALL RE08) were retrospectively analysed.<sup>9–11</sup> Patients were re-classified into cytogenetic subtypes according to the World Health Organization (WHO) 2017 classification.

When possible, patients with normal karyotype or no metaphases were screened for the most recurrent BCP ALL subtypes, including *TCF3-PBX1*, by fluorescence *in situ* hybridisation (FISH) and by reverse transcription polymerase chain reaction to a lesser extent. Among patients with Ph-negative ALL, high-risk was defined by age of >30 years, white blood cell (WBC) count of >30 × 10<sup>9</sup>/l or the presence of 11q23/Lysine Methyltransferase 2A (*KMT2A*) rearrangements. Therapeutic decisions were based on MRD levels in the two high-risk protocols. A good MRD response was considered when the MRD level was <0.1% at the end of induction and <0.01% at the end of consolidation. Patients with end-consolidation MRD levels of ≥0.01% received alloHSCT, while patients with good MRD clearance received delayed consolidation and maintenance therapy. MRD was centrally assessed by multiparametric flow cytometry in a EuroFlow laboratory. Comparisons between groups were performed with the chi-square test, Fisher's exact test and the median test as appropriate. Overall survival (OS) was estimated using the Kaplan–Meier method and curves were compared by the log-rank test. The cumulative incidence of relapse (CIR) was calculated using cumulative incidence functions considering non-relapse mortality (NRM) as a competing risk and was compared by Gray's test. Two-sided *P* < 0.05 were considered statistically significant.

## Results

Of 539 patients with BCP ALL, 154 were excluded for uninformative cytogenetics. From 385 patients with Ph-negative

## Short Report

BCP ALL with informative cytogenetics, 26 (7%) were classified as *TCF3-PBX1*. Of them, 22 had t(1;19)(q23;p13) or der(19)t(1;19) by G-banding and four cases with normal karyotype (two) or no metaphases (two) showed *TCF3-PBX1* rearrangement by FISH. Patients with t(1;19) were classified according to the type of rearrangement [balanced translocation *versus* der(19)t(1;19)] and the karyotype complexity [isolated t(1;19)/der(19)t(1;19) *versus* t(1;19)/der(19)t(1;19) with additional chromosomal alterations (ACA)]. In all, 10/22 (45%) patients with *TCF3-PBX1* had t(1;19) balanced rearrangements, while 12/22 (55%) had der(19)t(1;19). In turn, nine of the 22 (41%) cases had a t(1;19) or der(19)t(1;19) as an isolated aberration, while 13/22 (59%) had ACA [median (range) 2 (1–10)]. The most recurrent ACA were trisomy 1/1q (four), –6/del(6q) [MYB Proto-Oncogene (*C-MYB*); three], del(9p) [cyclin-dependent kinase inhibitor 2A/B (*CDKN2A/B*), paired box 5 (*PAX5*); five] and –13/del(13q) [retinoblastoma 1 (*RBI*); four]. Although der(19)t(1;19) was preferentially seen in association with ACA, there was no statistically significant relationship between both classifications (balanced/derivative *versus* isolated/ACA). Four patients (15%) were treated within the ALL RE08 protocol, while 10 and 12 patients were treated according to the ALL AR03 and ALL HR11 trials respectively.

The main clinical and biological characteristics of the 26 patients with *TCF3-PBX1* were compared with those of the 359 patients with Ph-negative BCP ALL with informative cytogenetics (Table 1). The patients with *TCF3-PBX1* showed

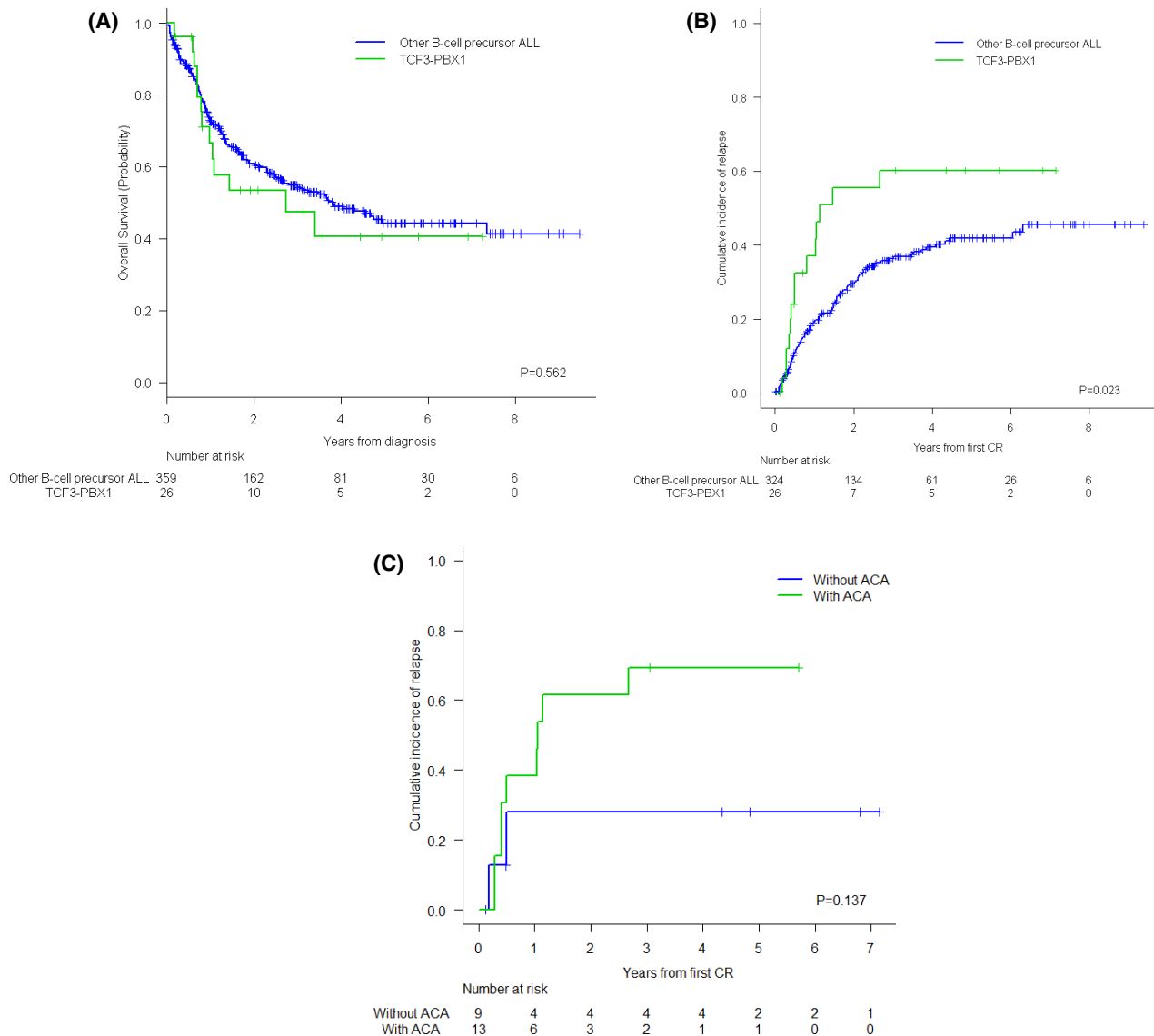
higher female gender, more frequent pre-B phenotype and a trend towards higher WBC counts. There were no significant differences in age and WBC count between patients with balanced translocation, der(19)t(1;19), isolated t(1;19)/der(19)t(1;19) and t(1;19)/der(19)t(1;19) with ACA. All the patients with *TCF3-PBX1* achieved complete remission (CR). End-induction MRD response (available for 23/26 *TCF3-PBX1* and 277/359 patients) was not significantly different between the two groups of patients [MRD <0.01% *TCF3-PBX1*: 16/23 (70%) vs. 169/277 (61%) respectively,  $P = 0.417$ ]. There were no significant differences according to good MRD response (MRD <0.01%) between patients with isolated t(1;19)/der(19)t(1;19) and those with t(1;19)/der(19)t(1;19) with ACA, as well as between patients with balanced rearrangements and der(19)t(1;19). Only two patients with *TCF3-PBX1* received an alloHSCT due to an end-consolidation MRD level of 0.05% and to poor response to the first induction cycle respectively. One of them is alive in third CR after chimeric antigen receptor T cells targeting CD19 (CART19) therapy and the second died due to a concomitant melanoma, with ALL in CR. The remaining patients with *TCF3-PBX1* completed delayed consolidation and maintenance (16 patients), relapsed during consolidation (five), died in consolidation (one), withdrew from the protocol (one) or were under consolidation (one).

The median follow-up of alive patients using the reverse Kaplan–Meier method was 3.59 years [95% confidence interval (CI) 2.10–5.80, range 0.20–7.25] for the patients

**Table 1.** Comparison of the main characteristics of patients with *TCF3-PBX1* and patients with other B-cell precursor acute lymphoblastic leukaemia with evaluable cytogenetics.

	<i>TCF3-PBX1</i> ( $n = 26$ )	Remaining B-cell precursor ALL ( $n = 359$ )	$P$
Age, years			
Median (range)	36 (17–60)	35 (15–60)	0.675
Gender, $n$ (%)			
Male	7 (27)	197 (55)	0.006
Female	19 (73)	162 (45)	
ECOG PS score, $n/N$ (%)			
0	5/22 (23)	109/339 (32)	0.623
1	14/22 (64)	177/339 (52)	
$\geq 2$	3/22 (14)	53/339 (16)	
WBC count, $\times 10^9/l$			
Median (range)	16.2 (0–199.5)	12 (0.2–638)	0.144
Mediastinal mass, $n/N$ (%)			
No	22/22 (100)	339/346 (98)	1.000
Yes	0	7/346 (2)	
CNS involvement, $n/N$ (%)			
No	21/24 (88)	311/336 (93)	0.417
Yes	3/24 (12)	25/336 (7)	
Phenotype, $n/N$ (%)			
Pro-B	0	67 (19)	<0.001
Common B	9/24 (37)	231 (64)	
Pre-B	15/24 (63)	61 (17)	

ALL, acute lymphoblastic leukaemia; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group Performance Status; *TCF3-PBX1*, transcription factor 3-pre-B-cell leukaemia homeobox 1; WBC, white blood cell.



**Fig 1.** (A) Probability of overall survival for patients with transcription factor 3-pre-B-cell leukaemia homeobox 1 (*TCF3-PBX1*) rearrangement and the other B-cell precursor acute lymphoblastic leukaemia (ALL) patients with evaluable cytogenetics. (B) Cumulative incidence of relapse for patients with *TCF3-PBX1* rearrangement and the other B-cell precursor ALL patients with evaluable cytogenetics. (C) Cumulative incidence of relapse among patients with *TCF3-PBX1* rearrangement depending on the presence *versus* absence of additional cytogenetic alterations (ACA). [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

with *TCF3-PBX1* and 3.71 (95% CI 3.27–4.20, range 0.13–9.47) for the other patients with BCP ALL. The probability of OS for patients with *TCF3-PBX1* was similar among the three protocols and was not significantly different from that of the remaining patients with BCP ALL [5-year OS 41% (95% CI 19–63%) vs. 44% (95% CI 38–50%),  $P = 0.562$ ] (Fig 1A). The OS was better for patients with isolated t(1;19)/der(19)t(1;19) than for those with t(1;19)/der(19)t(1;19) with ACA [5-year OS 59% (95% CI 23–95%) vs. 31% (95% CI 0–62%),  $P = 0.558$ ]. Patients aged <35 years had a significantly better OS than those  $\geq 35$  years [3-years OS 77% (95% CI 49–100%) vs. 25% (95% CI 1–49%),  $P = 0.002$ ].

Patients with *TCF3-PBX1* had a significantly higher CIR than the remaining BCP ALL cases [5-year CIR of 60% (95% CI 36–77%) for *TCF3-PBX1* vs. 42% (95% CI 35–48%) respectively;  $P = 0.023$ ] (Fig 1B). The higher relapse propensity seen in patients with *TCF3-PBX1* was mainly observed in those with ACA (5-year CIR 69% [33–89%] vs. 28% [3–63%],  $P = 0.137$ ) (Fig 1C). In addition, younger patients had a trend for lower CIR than those aged  $\geq 35$  years [2-year CIR 40% (95% CI 11–69%) vs. 70% (95% CI 31–90%),  $P = 0.073$ ]. Patients with both adverse prognostic factors (aged  $\geq 35$  years with ACA, nine patients) showed a trend for higher CIR compared with the remaining 13 patients [2-year CIR 67% (95% CI 20–90%) vs. 36% (95% CI 10–63%),

$P = 0.089$ ]. All patients aged  $\geq 35$  years with ACA relapsed, which correlated with poorer OS for this subgroup [2-year OS 22% (95% CI 0–49%) vs. 74% (95% CI 48–100%),  $P = 0.020$ ]. The Fine–Gray model showed that age was the only predictor for CIR in patients with *TCF3-PBX1* (hazard ratio 4.433, 95% CI 1.014–19.380;  $P = 0.048$ ).

The outcome of the 14 relapsing patients was poor, despite six of them being rescued with blinatumomab (three) or inotuzumab (three), followed by CART19 in two of them. Currently, four patients are alive. The OS of the patients with *TCF3-PBX1* after first relapse was not different from that of the other patients with BCP ALL (data not shown).

Disease progression was the main cause of death among patients with *TCF3-PBX1* (10/13, 77%), while three of 13 patients (23%) died from NRM. In the remaining BCP ALL, death by disease progression was observed in 94/160 (59%) and 66/160 (41%) died from NRM (transplant-related mortality in 13 of them).

## Discussion

The present analysis of adolescent and adult patients treated with MRD-oriented protocols shows that patients with *TCF3-PBX1* have a high probability of relapse, especially those aged  $>35$  years with ACA, despite excellent response to treatment and scarce need of alloHSCT according to the MRD status. The relapse-associated mortality in these patients might counteract the higher NRM registered in the non-*TCF3-PBX1* group, explaining the similar OS of these groups.

Age was a prognostic factor for patients with *TCF3-PBX1*, as shown in any ALL subtype. The median age of the patients with *TCF3-PBX1* in our present series (36 years) was older than that of other similar studies<sup>2,3,5</sup> and the frequency of alloHSCT was lower,<sup>4</sup> as alloHSCT indication was exclusively based on MRD-status after induction and consolidation.

The presence of ACA showed a trend for higher relapse, as has also been shown in patients with Ph<sup>+</sup>-ALL treated within PETHEMA trials.<sup>12</sup> Unfortunately, detailed genomic data are not available, although the ACA could indicate the presence of recurrent abnormalities with potential poor outcome (i.e. *MYB*, *CDKN2A/B* and *RB1*).<sup>13,14</sup> Besides MRD, genetic differences at the molecular level might contribute, at least in part, to the different outcomes observed among patients with *TCF3-PBX1*.

In addition to the lack of genomic data, the main limitation of the present study, and others showing similar frequency, is the low number of patients, despite including FISH analysis to ensure full detection of patients with *TCF3-PBX1* when available. Given the low incidence of this ALL subtype and the conflicting data in the literature, a pooling of data from several studies or a meta-analysis might help to give more reliable results. From our present results, patients with *TCF3-PBX1* aged  $>35$  years with ACA might benefit from consolidation with immunotherapy followed or not by alloHSCT. In addition, targeted therapies with kinase

inhibitors and/or phosphatidylinositol-3 kinase (PI3K)/protein kinase B (Akt) inhibitors may also be of special interest for this subset of patients.<sup>15</sup>

## Acknowledgements

This work was supported in part by CERCA/Generalitat de Catalunya SGR 2017 288 (GRC), a restricted grant from ‘La Caixa’ and Healthcare Alliance for Resourceful Medicine Offensive against Neoplasms (HARMONY). We are very grateful to the following authors for their contribution to this multicentric study: Lurdes Zamora (Josep Carreras Leukaemia Research Institute, ICO-Hospital Germans Trias i Pujol, Universitat Autònoma de Barcelona), Anna Torrent (Josep Carreras Leukaemia Research Institute, ICO-Hospital Germans Trias i Pujol, Universitat Autònoma de Barcelona), Susana Barrena (Cancer Research Center (IBMCC-CSIC/USAL-IBSAL), Cytometry Service (NUCLEUS) and Department of Medicine, University of Salamanca), Beatriz Soriano (Cancer Research Center (IBMCC-CSIC/USAL-IBSAL), Cytometry Service (NUCLEUS) and Department of Medicine, University of Salamanca), Pau Montesinos (Hospital Universitari i Politècnic La Fe), Eulàlia Genescà (Josep Carreras Leukaemia Research Institute, ICO-Hospital Germans Trias i Pujol, Universitat Autònoma de Barcelona), Celia González-Gil (Josep Carreras Leukaemia Research Institute, ICO-Hospital Germans Trias i Pujol, Universitat Autònoma de Barcelona), Francisco Fuster-Tormo (Josep Carreras Leukaemia Research Institute, ICO-Hospital Germans Trias i Pujol, Universitat Autònoma de Barcelona), Clara Maluquer (ICO-Hospital Duran i Reynals), Laura Blanco (Josep Carreras Leukaemia Research Institute, Hospital de Sant Pau), Josep Nomdedéu (Josep Carreras Leukaemia Research Institute, Hospital de Sant Pau), Margarita Ortega (Hospital Universitari Vall d’Hebrón), Jordi Esteve (Haematology Department, Hospital Clínic Barcelona, IDIBAPS, Josep Carreras Leukaemia Research Institute), Marina Díaz-Beyá (Haematology Department, Hospital Clínic Barcelona, IDIBAPS, Josep Carreras Leukaemia Research Institute), Pilar Martínez-Sánchez (Hospital Universitario Doce de Octubre), Andrés Novo (Hospital Universitari Son Espases), M<sup>a</sup> Paz Queipo de Llano (Hospital Clínic Virgen de la Victoria), Ana Batlle (Hospital Universitario Marqués de Valdecilla), Juan Bergua (Hospital San Pedro Alcántara), M<sup>a</sup> Teresa Olave (Hospital Clínic Universitario Lozano Blesa), Beatriz de Rueda (Hospital Universitario Miguel Servet), Pilar Herrera (Hospital Universitario de Donostia), M<sup>a</sup> Teresa Artola (Hospital Universitario de Donostia), Jesús M<sup>a</sup> Hernández-Rivas (Hospital Universitario de Salamanca, Universidad de Salamanca, IBMCC (CSIC/USAL), IBSAL and CIBERONC).

## Conflicts of interest

The authors have no competing interests.

## References

- Paietta E, Roberts KG, Wang V, Gu Z, Buck G, Pei D, et al. Molecular classification improves risk assessment in adult BCR-ABL1-negative B-ALL. *Blood*. 2021. <https://doi.org/10.1182/blood.2020010144>.
- Yilmaz M, Kantarjian HM, Toruner G, Yin CC, Kanagal-Shamanna R, Cortes JE, et al. Translocation t(1;19)(q23;p13) in adult acute lymphoblastic leukemia - a distinct subtype with favorable prognosis. *Leuk Lymphoma*. 2021;62:224–8.
- Burmeister T, Gokbuget N, Schwartz S, Fischer L, Hubert D, Sindram A, et al. Clinical features and prognostic implications of TCF3-PBX1 and ETV6-RUNX1 in adult acute lymphoblastic leukemia. *Haematologica*. 2010;95:241–6.
- Lafage-Pochitaloff M, Baranger L, Hunault M, Cuccuini W, Lefebvre C, Bidet A, et al. Impact of cytogenetic abnormalities in adults with Ph-negative B-cell precursor acute lymphoblastic leukemia. *Blood*. 2017;130:1832–44.
- Moorman AV, Harrison CJ, Buck GAN, Richards SM, Secker-Walker LM, Martineau M, et al. Karyotype is an independent prognostic factor in adult acute lymphoblastic leukemia (ALL): analysis of cytogenetic data from patients treated on the Medical Research Council (MRC) UKALL-XII/Eastern Cooperative Oncology Group (ECOG) 2993 trial. *Blood*. 2007;109:3189–97.
- Mancini M, Scappaticci D, Cimino G, Nanni M, Derme V, Elia L, et al. A comprehensive genetic classification of adult acute lymphoblastic leukemia (ALL): analysis of the GIMEMA 0496 protocol. *Blood*. 2005;105:3434–41.
- Pullarkat V, Slovak ML, Kopecky KJ, Forman SJ, Appelbaum FR. Impact of cytogenetics on the outcome of adult acute lymphoblastic leukemia: results of Southwest Oncology Group 9400 study. *Blood*. 2008;111:2563–72.
- Yan CH, Jiang Q, Wang J, Xu LP, Liu DH, Jiang H, et al. Superior survival of unmanipulated haploidentical hematopoietic stem cell transplantation compared with chemotherapy alone used as post-remission therapy in adults with standard-risk acute lymphoblastic leukemia in first complete remission. *Biol Blood Marrow Transplant*. 2014;20:1314–21.
- Ribera J-M, Oriol A, Morgades M, Montesinos P, Sarrà J, González-Campos J, et al. Treatment of high-risk Philadelphia chromosome-negative acute lymphoblastic leukemia in adolescents and adults according to early cytologic response and minimal residual disease after consolidation assessed by flow cytometry: final results of the PETHEMA ALL-AR-03 trial. *J Clin Oncol*. 2014;32:1595–604.
- Ribera JM, Morgades M, Ciudad J, Montesinos P, Esteve J, Genescà E, et al. Chemotherapy or allogeneic transplantation in high-risk Philadelphia chromosome-negative adult lymphoblastic leukemia. *Blood*. 2021;137:1879–94.
- Ribera J-M, Morgades M, Montesinos P, Tormo M, Martínez-Carballeira D, González-Campos J, et al. A pediatric regimen for adolescents and young adults with Philadelphia chromosome-negative acute lymphoblastic leukemia: results of the ALLRE08 PETHEMA trial. *Cancer Med*. 2020;9:2317–29.
- Motlló C, Ribera JM, Morgades M, Granada I, Montesinos P, Mercadal S, et al. Frequency and prognostic significance of additional cytogenetic abnormalities to the Philadelphia chromosome in young and older adults with acute lymphoblastic leukemia. *Leuk Lymphoma*. 2018;59:146–54.
- González-Gil C, Ribera J, Ribera JM, Genescà E. The Yin and Yang-like clinical implications of the *CDKN2A/ARF/CDKN2B* gene cluster in acute lymphoblastic leukemia. *Genes (Basel)*. 2021;12:79.
- Messina M, Chiaretti S, Fedullo AL, Piciocchi A, Puzzolo MC, Lauretti A, et al. Clinical significance of recurrent copy number aberrations in B-lineage acute lymphoblastic leukaemia without recurrent fusion genes across age cohorts. *Br J Haematol*. 2017;178:583–7.
- Eldfors S, Kuusanmäki H, Kontro M, Majumder MM, Parsons A, Edgren H, et al. Idelalisib sensitivity and mechanisms of disease progression in relapsed TCF3-PBX1 acute lymphoblastic leukemia. *Leukemia*. 2017;31:51–7.