ELSEVIER

Blood 142 (2023) 1461–1463

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

612.ACUTE LYMPHOBLASTIC LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Role of Allogeneic Stem Cell Transplantation in Preventing Relapse in Adult BCR::ABL1-like Acute Lymphoblastic Leukemia

Jordi Ribera, PhD[1], *Mireia Morgades*[1], *Isabel Granada, MD*[1], *Teresa González, PhD*[2], *Ricardo Sánchez*[3], *Rosa Ayala, MD PhD*[4], *Esperanza Such, PhD*[5], *Gayane Avetisyan, MSC*[6], *Susana Barrera*[7], *Beatriz Soriano*[7], *Anna Torrent*[8], *Cristina Gil, MD*[9], *Carmen Botella*[10], *Clara Maluquer Artigal, MD*[11], *Pere Barba, MD*[12], *Pau Montesinos, PhDMD*[13], *José González-Campos, MD*[14], *Pilar Martínez-Sánchez*[15], *Rosa Coll*[16], *Jordi Esteve, MD PhD*[17], *Maria Rocio Benito Sanchez, PhD*[2], *Thaysa Lopes*[1], *Celia González Gil*[18], *Eulàlia Genescà*[1], *Joaquin Martínez-López*[19], *Jesús María Hernández-Rivas, PhD*[2], *Alberto Orfao, MD PhD*[20], *Josep-Maria Ribera, MD PhD*[1]

[1] ICO-Hospital Germans Trias i Pujol, Institut de Recerca contra la Leucèmia Josep Carreras (IJC), Universitat Autònoma de Barcelona, Badalona, Spain
[2] University of Salamanca, IBSAL, IBMCC, CSIC, Cancer Research Center, Department of Hematology - Hospital Universitario de Salamanca, Salamanca, Spain
[3] Department of Hematology, Hospital Universitario 12 De Octubre, Universidad Com, Madrid, ESP
[4] Hospital Universitario 12 de Octubre, I+12, CNIO, Complutense University, CIBERONC, Madrid, Spain
[5] Department of Hematology, Hospital Universitari i Politecnic La Fe, Valencia, Spain
[6] Hematology Research Group, Instituto De Investigación Sanitaria La Fe, Valencia, Spain
[7] Department of Medicine, Universidad de Salamanca, Institute of Biomedical research of Salamanca (IBSAL), Biomedical Research Networking Centre Consortium of Oncology (CIBERONC), Instituto de Salud Carlos III, IBMCC, CSIC-USAL, Cytometry Service NUCLEUS, Salamanca, Spain
[8] Institut Català D'oncologia-Hospital Germans Trias I Pujol. Josep Carrera, Badalona, ESP
[9] Hospital General Universitario de Alicante, Alicante, ESP
[10] Hospital General Universitario de Alicante, Alicante, Spain
[11] Hematology Department. Institut Català d'Oncologia, Hospital Duran i Reynals. Institut d'Investigació Biomèdica de Bellvitge (IDIBELL), L'Hospitalet de Llobregat, Barcelona, Spain
[12] Deparment of Hematology, Vall D'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall D'Hebron, La Garriga, Spain
[13] Hospital Universitari i Politecnic la Fe, Valencia, Spain
[14] Hospital Universitario Virgen del Rocío, Sevilla, ESP
[15] Hospital Doce De Octubre, Madrid, ESP
[16] ICO-Hospital Universitari Josep Trueta, Girona, Spain
[17] Hematology Department, Hospital Clínic Barcelona, Barcelona, Spain
[18] ICO-Hospital Germans Trias i Pujol, Institut de Recerca contra la Leucèmia Josep Carreras (IJC), Universitat Autònoma de Barcelona, Badalona, ESP
[19] Department of Hematology, Hospital Universitario 12 de Octubre, Spanish National Cancer Research Center (CNIO), Complutense University Madrid, Madrid, Spain
[20] Cancer Research Center (IBMCC-CSIC/USAL-IBSAL), Cytometry Service (NUCLEUS) and Department of Medicine, University of Salamanca, Salamanca, Spain

Background

Philadelphia-like acute lymphoblastic leukemia (Ph-like ALL) is characterized by the activation of several kinase pathways that promote treatment resistance leading to poor survival of patients at all ages. Despite the use of tyrosine kinase inhibitors in the Ph-like ABL-class subtype (15% Ph-like ALL), there is not a consensus approach for treatment of most patients (JAK-class especially), and the role of allogeneic stem cell transplantation (alloSCT) has scarcely been explored so far (i.e., mandatory vs. MRD-oriented).

Objective

To assess the outcome of Ph-like patients enrolled in the ongoing ALL19 trial from the Programa Español de Tratamientos en Hematología (PETHEMA) for adults (18-60y) with Ph-negative ALL, and to evaluate the effectiveness of alloSCT in first complete remission (CR).

Methods

In the ALL19 trial, patients are allocated to alloSCT according both to the end of induction (EOI) measurable residual disease (MRD) level and to high-risk genetic markers such as low-hypodiploidy, KMT2A rearrangement, TP53 biallelic alteration and concomitant deletion of IKZF1 and CDKN2A/B. Therefore, BCR::ABL1-like subtype was not a criteria for early transplantation unless meeting either poor MRD clearance at EOI or concomitant deletion of IKZF1+CDKN2A/B. Patients with MRD≥0.01% on day+35 (EOI) and/or high-risk genetics were assigned to early alloSCT (preceded by 1 cycle of consolidation chemotherapy) while those with good MRD clearance and standard risk genetics received early and delayed consolidation (3 cycles each) and maintenance therapy. Bone marrow or peripheral blood samples were analyzed by G-banding+FISH, SNP array (750K Affymetrix, Thermo Fisher) and next generation sequencing (NGS, with a custom DNA gene panel, Illumina) at diagnosis in 4 reference laboratories. MRD was centrally assessed by next generation flow cytometry with a sensitivity up to $2x10^{-6}$.

Results

Twenty-four Ph-like out of 248 adult BCP ALL (10%) were detected. Baseline characteristics were similar between Ph-like and the remaining BCP-ALL. Most Ph-like ALL patients showed the JAK-class profile (20/24 [83%]: 17/24 CRLF2 rearrangement[r], 1/24 JAK2r, 1 BLNK::DNTT and 1 JAK2 R683 mutation), 3/24 belonged to the ABL-class subtype (2 ABL2r, 1 NUP214::ABL1) and 1 patient was identified by RNAseq (gene expression profiling similar to BCR::ABL1 ALL) without identifying any rearrangement. Regarding secondary genetic alterations, 17/24 (71%) patients showed the IKZF1 *plus* profile, 10/23 (43%) harbored JAK2 R683 mutation, 4/23 N/KRAS mutations, 2/23 CRLF2 mutation and 1/23 showed mutations in several genes such as IKZF1, NR3C1 or FLT3, among others.

There were no significant differences in the probability of achieving CR between Ph-like and the remaining BCP ALL (15/20 [75%] vs. 137/162 [85%], p=0.334). However, EOI MRD level of Ph-like individuals was significantly poorer (MRD<0.01% Ph-like 4/15 [27%] vs. other BCP-ALL 85/136 [63%], p=0.007). By intention to treat, most Ph-like patients (17/19, 89%) were allocated to alloSCT (vs. 91/153 [59%] in the other BCP-ALL, p=0.011) due to either EOI MRD≥0.01% (9/18), IKZF1+CDKN2A/B concomitant deletions (3/18) or both (6/18). The 2-y overall survival (OS) in both groups was not significantly different (57% [95% CI, 27%-78%] vs. 67% [55%-77%, p=0.304]) (Figure 1). Interestingly, most Ph-like patients died due to treatment-related toxicity (2 transplant-related mortality, 1 CART-related, 1 during induction, 1 in CR and 1 by COVID-19 infection). The 2-y cumulative incidence of relapse (CIR) was also similar (Ph-like 27% [8%-50%] vs. other BCP-ALL 35% [25%-45%], p=0.946) (Figure 1).

Conclusions

Despite the short follow up of this series, our results show that Ph-like ALL patients have poorer EOI MRD clearance and higher rate of alloSCT realization than the remaining BCP ALL patients, without significant differences in outcome. This suggests that early alloSCT in first CR might overcome the poor prognosis of Ph-like ALL patients.

Funding

Funded in part by: PI10/01417 y FIS PI19/01183 Ministerio de Salud Carlos III, JCyL_SA118P20, FMM21/002_AP176752021, "La Caixa" Foundation, Pfizer Spain, Fundación PETHEMA. This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No IMI001-07. The JU receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

Disclosures Ayala: *Novartis:* Consultancy, Speakers Bureau; *Incyte:* Consultancy; *Astellas, BMS:* Speakers Bureau. **Barba:** *Jazz Pharmaceutical:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Miltenyi Biotech:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Nektar:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Incyte:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Novartis:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Pierre-Fabre:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Kite/Gilead:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *BMS:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Amgen:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Allogene:* Consultancy, Membership on an entity's Board of Directors or advisory committees. **Montesinos:** *Menarini-Stemline:* Consultancy, Research Funding; *Ryvu:* Consultancy; *Kura oncology:* Consultancy; *Jazz pharma:* Consultancy, Research Funding, Speakers Bureau; *Celgene:* Consultancy; *NERVIANO:* Consultancy; *INCYTE:* Consultancy; *BEIGENE:* Consultancy; *GILEAD:* Consultancy; *OTSUKA:* Consultancy; *Astellas:* Consultancy, Speakers Bureau; *Novartis:* Consultancy, Research Funding; *Takeda:* Consultancy, Research Funding; *Janssen:* Speakers Bureau; *Abbvie:* Consultancy, Research Funding, Speakers Bureau; *Pfizer:* Consultancy, Research Funding, Speakers Bureau; *BMS:* Consultancy, Other, Research Funding; *Daiichi Sankyo:* Consultancy, Research Funding. **Esteve:** *Astellas:* Consultancy; *Jazz Pharmaceuticals:* Consultancy, Research Funding; *Abbvie:* Consultancy; *Gilead:* Consultancy; *Pfizer:* Research Funding; *Kronos Bio:* Research Funding. **Hernández-Rivas:** *Novartis:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Pfizer:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Celgene/BMS:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *GSK:* Consultancy, Honoraria, Speakers Bureau; *Amgen:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau. **Ribera:** *Pfizer:* Consultancy, Research Funding; *Bristol Myers Squibb:* Consultancy; *Novartis:* Consultancy; *Takeda:* Consultancy; *Incyte:* Consultancy, Research Funding; *AMGEN:* Research Funding.

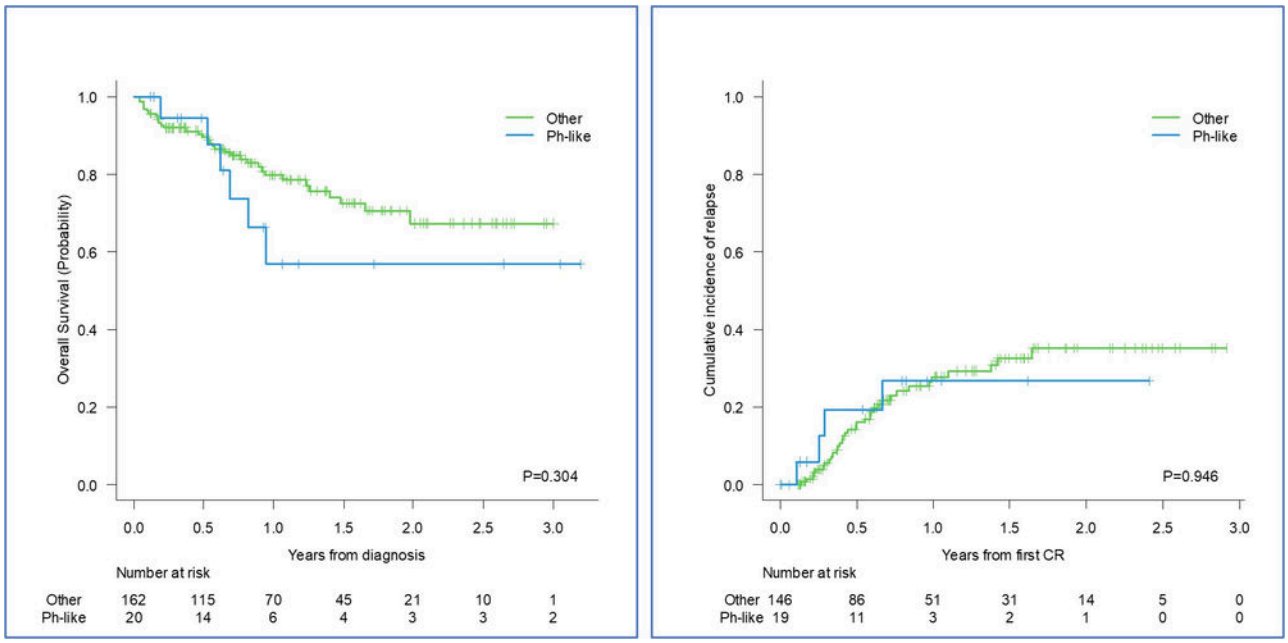

Figure 1

https://doi.org/10.1182/blood-2023-186265