

t(1;19)(q23;p13) TCF3-PBX1 may not be an intermediate-risk subtype in adult B-cell precursor acute lymphoblastic leukemia patients treated with MRD-oriented protocols from the PETHEMA Group

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Background

In adult BCP ALL there is a debate regarding the impact of t(1:19)(q23;p13). While the MD Anderson Group suggests it may be a low risk subtype (1), the German (2), English (3) and French (4) study groups have shown no differential outcome, and Italian (5) and SWOG (6) groups have reported poor outcomes.

Objective

Analyze the frequency and clinical impact of t(1;19) in a series of adult BCP ALL patients.

Materials & Methods

A retrospective review of adolescent and adult Ph-negative BCP ALL patients (15 to 60 years) treated within MRD-oriented protocols of the PETHEMA Group and diagnosed between 2003 and 2017 was done. Outcome results from these protocols have been published previously (7-9).

Cytomorphology, flow cytometry, G-banding cytogenetics, FISH and PCR were used for ALL diagnosis. High-risk was defined by: age>30 years, WBC>30x10⁹/L or 11q23/KMT2A rearrangements. Measurable residual disease (MRD) was centrally assessed by multi-parametric flow cytometry. Patients with MRD levels ≥0.01% at end consolidation received alloHSCT, while patients with good MRD clearance were allocated to maintenance therapy.

Overall survival (OS) was estimated using Kaplan-Meier method and curves were compared by log-rank test. Estimates of cumulative incidence of relapse (CIR) and non-relapse mortality were calculated using cumulative incidence rates to accommodate competing risks and were compared by Gray's test.

Results

- From a series of 385 Ph-negative BCP ALL, 26 patients with **t(1;19)/TCF3-PBX1** were identified **(7%)**

- **Comparison of patients' characteristics at baseline**

		TCF3-PBX1 (n=26)	Remaining (n=333)	P
Age	Median [range]	36 [17; 60]	35 [15 ; 60]	0.675
Gender	Male	7 (27%)	197 (55%)	0.006
	Female	19 (73%)	162 (45%)	
ECOG	0	5/22 (23%)	107 (32%)	0.623
	1	14/22 (64%)	175 (52%)	
	≥2	3/22 (14%)	51 (16%)	
WBC count	Median [range]	16.2 [0 ; 199.5]	12 [0.2 ; 638]	0.144
Mediastinal mass	No	22/22 (100%)	326 (98%)	1.000
	Yes	0	7 (2%)	
CNS	No	21/24 (88%)	309 (93%)	0.417
	Yes	3/24 (12%)	24 (7%)	
Phenotype	Pro-B	0	60 (18%)	<0.001
	Common B	9/24 (37%)	227 (68%)	
	Pre-B	15/24 (63%)	46 (14%)	

- **Response to Induction treatment (d+35)**

	TCF3-PBX1 (n=23)	Remaining (n=333)	p
MRD<0.01%	16/23 (70%)	169/277 (61%)	0.417
MRD≥0.01%	7/23 (30%)	108/277 (39%)	

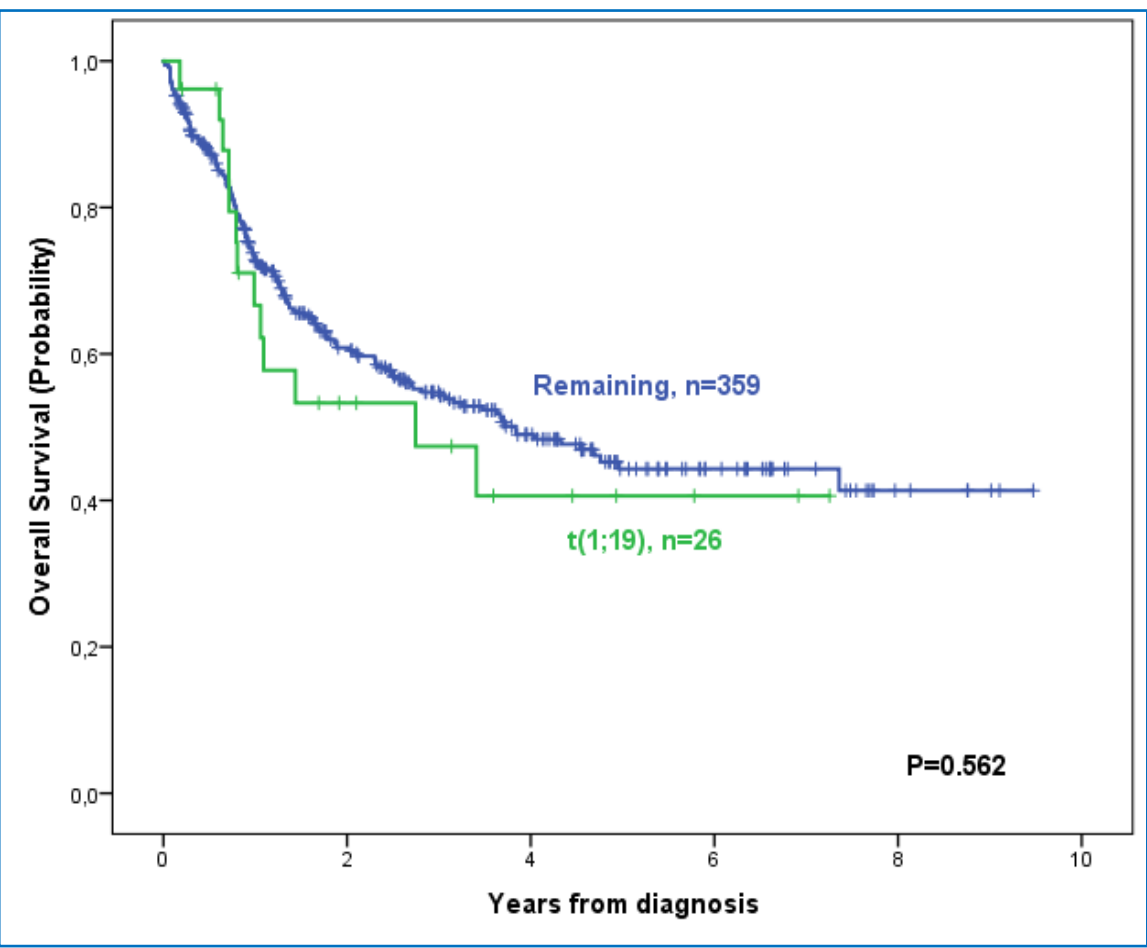
- **Post-induction treatment**

	TCF3-PBX1 (n=26)
On treatment at consolidation	1
Withdrawal at consolidation	1
Exitus at consolidation	1
Relapse at consolidation	5
Consolidation +/- maintenance	16
Allogeneic HSCT	2

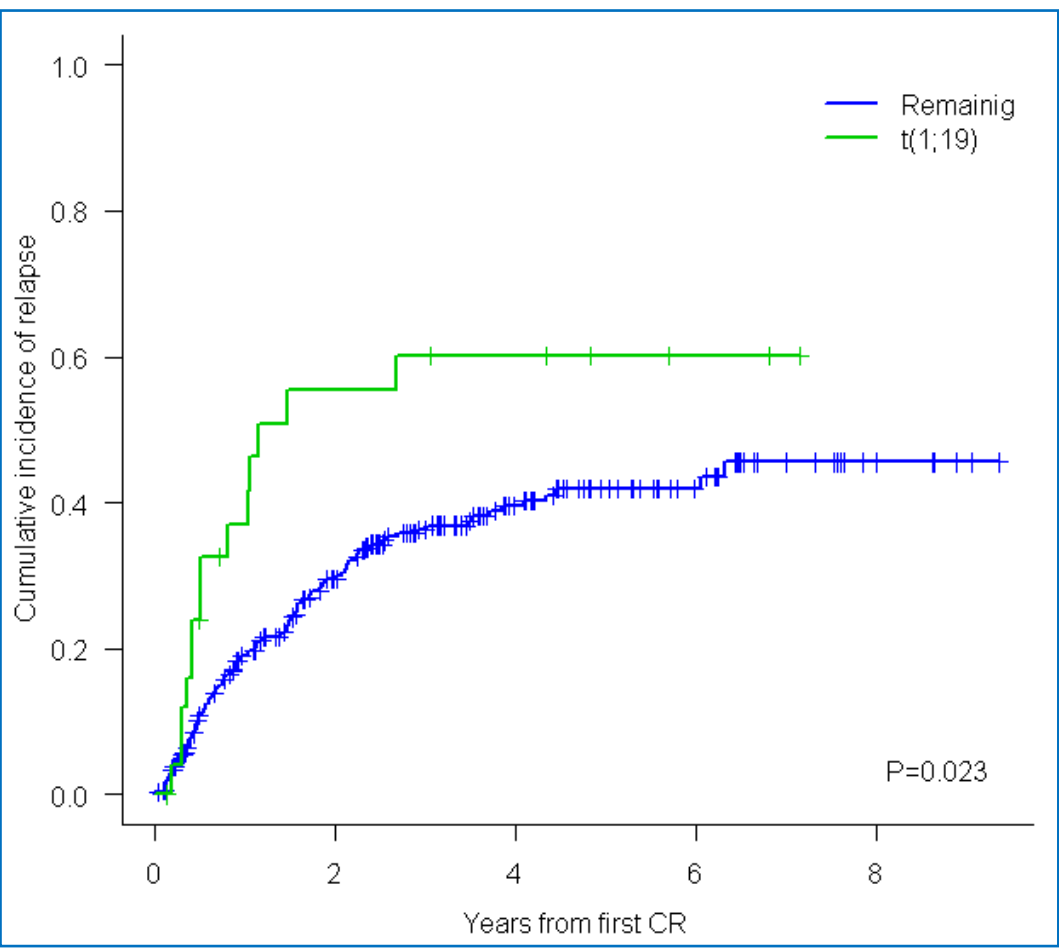
- **Cause of death**

	TCF3-PBX1 (n=13)	Remaining (n=160)	P
Relapse/disease progression	10 (77%)	94 (59%)	0.213
Treatment-related (Chemotherapy/AlloHSCT)	2 (15%)	61 (38%)	
2 nd neoplasm	1 (8%)	5 (3%)	

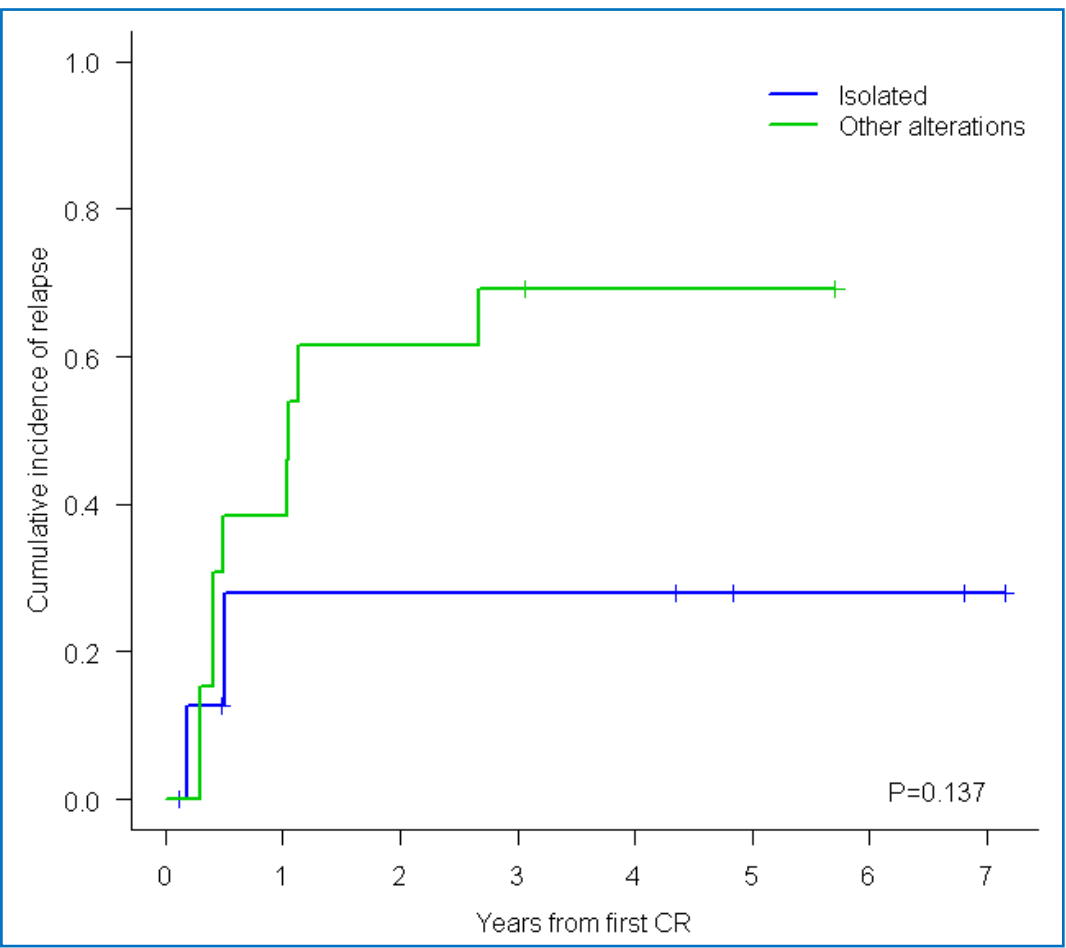
Overall Survival



Cumulative Incidence of Relapse (CIR)



CIR within TCF3-PBX1 patients



Discussion

- TCF3-PBX1 patients have a high probability of relapse, especially those patients over 35 years with additional alterations to t(1;19)(q23;p13).

- Regarding OS, the higher toxicity seen in the non-TCF3-PBX1 group possibly counteracted the higher relapse rate of TCF3-PBX1 individuals.

- The median age of TCF3-PBX1 patients from our series (36 years) was higher than that of other similar studies (2,3,4), while the frequency of alloHSCT was lower in our series than in others (3).

Conclusions

- TCF3-PBX1 patients do not show different survival to other BCP ALL.

- However, CIR is significantly higher in TCF3-PBX1 patients.

- Age, but also ACA , have an impact on patients' outcome.

- An immunotherapeutic approach at CR1 ± allogeneic HSCT could be useful to reduce the risk of relapse of patients with ACA, specially those over 35 years.

References

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