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POSTER ABSTRACTS

612.ACUTE LYMPHOBLASTIC LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Achievement of Undetectable BCR::ABL1 (uBCR::ABL1) Is Predictive of Improved Survival in Philadelphia Chromosome Positive (Ph+ve) Acute Lymphoblastic Leukemia (ALL) Patients Not Receiving Allogeneic Stem Cell Transplantation

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Background

With the advent of tyrosine kinase inhibitor (TKI)-based therapy the outcome of Philadelphia chromosome-positive (Ph $^{+}$) acute lymphoblastic leukemia (ALL) has significantly improved. Moreover, patients (pts) who achieved undetectable (u) BCR::ABL1 at 3 months (mo) from the time of initiating therapy, tend to have improved outcomes (Short et al. Blood 2016; 128 [4];504-507). We conducted a retrospective multicenter study to analyze the predictors of achieving uBCR::ABL1 in adult (> 18 years) Ph $^{+}$ ALL pts.

Methods

A total of 458 adult Ph $^{+}$ ALL pts from 10 US academic institutions, who were diagnosed between May 2003 and April 2023, were evaluated to assess the rates of uBCR::ABL1 at 3 mo after initiating therapy and factors that predict the achievement of molecular response. Continuous variables were summarized as median (range), while categorical variables were reported as frequency (percentage). Unadjusted comparisons of patient/ treatment related characteristics and molecular response were made using a non-parametric test (continuous variables) or Fisher's exact test (categorical variables). Survival curves were estimated using the Kaplan-Meier method and compared between molecular responses via the log-rank test.

Results

Baseline characteristics

The median age of the pts was 53 years (range [R] 19-85), median white blood cell count (WBC) was 17.6 (10 ^{9}/L) (R, 1.2-571), 249 (55%) pts had additional cytogenetic (CG) abnormalities, 98 (22%) pts had p210 fusion protein, and 35 (8%) pts had CNS disease at diagnosis. A higher proportion of pts received TKI in combination with intensive chemotherapy (IC) (69%), than

TKI + steroids (15%), TKI + low intensity chemotherapy (LC; combination of vincristine, steroids +/- rituximab) (9%), TKI + blinatumomab (3%) and IC without TKI (4%) during induction. During induction, the highest proportion of pts received 2 nd generation TKI combinations (67%; majority dasatinib 98%), compared to imatinib (19%) or ponatinib (10%): 4% of pts did not receive TKI with induction. The complete remission (CR) rate was 94%; measurable residual disease (MRD) negative by flow cytometry 51% (181/352 evaluable pts) and 58.5% (209/354 evaluable pts) of pts had uBCR::ABL1 by PCR at 3 mo from induction. A total of 212 (46%) pts received allogeneic stem cell transplantation (allo-HCT) in CR1, among them 61% of pts received TKI maintenance post allo-HCT.

Predictors of uBCR::ABL1 at 3 months

Predictors for uBCR::ABL1 at 3 mo are summarized in **Table 1**. The proportion of pts with WBC > 100 (45% vs 60%, p= 0.04), p210 fusion protein (35% vs 85%, p= <0.001), additional CG abnormality with monosomy 7 (40% vs 61%, p= 0.03), additional somatic myeloid co-mutation (39% vs 61%, p= 0.09; 94 pts evaluable), received induction with steroid plus TKI (41% vs 63%, p= 0.002) or received imatinib based induction (47% vs 61%,p= 0.07) had inferior uBCR::ABL1 rates at 3 mo. Conversely pts who received ponatinib based induction had significantly better uBCR::ABL1 rates (79% vs 57%, p= 0.009).

Survival

The median relapse free survival (RFS) was 72.3 mo (95% CI; 50.1-94.4), RFS was numerically higher among pts who achieved uBCR::ABL1 at 3 mo but not statistically significant (84.2 mo vs 62.9 mo, p= 0.20). The median overall survival (OS) was 129.2 mo (95% CI; 81.2-177.2), OS was not significantly different among pts who achieved uBCR::ABL1 at 3 mo (129.2) versus no uBCR::ABL1 (not reached; 50% alive at 94 mo), p= 0.47. In sub-set analysis, among non-transplanted pts, RFS was not statistically significant between those who achieved uBCR::ABL1 vs those who did not (38.9 vs 22.0 mo, respectively p= 0.24). However, the median OS was significantly higher in pts who achieved uBCR::ABL1 at 3 mo compared to pts who did not achieve uBCR::ABL1 at 3 mo: 149.3 vs 77.5 mo, p= 0.04 (**Figure 1**).

Conclusion

In this large multicenter study, we observed significantly inferior uBCR::ABL1 rates among pts with WBC > 100, p210 fusion protein, monosomy 7 CG abnormality, pts receiving induction with steroid plus TKI or imatinib based induction. Conversely, uBCR::ABL1 rates were significantly better in pts receiving ponatinib based induction therapy. Overall, we did not see significant impact of uBCR::ABL1 at 3 mo, on RFS or OS. It is likely subsequent therapies and allo-HCT abrogates the negative impact of not achieving uBCR::ABL1 at 3 mo. However, among non-transplanted pts achievement of uBCR::ABL1 at 3 mo showed a significantly improved OS.

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Table 1. Predictors of uBCR::ABL1 at 3 months		
Variables	uBCR::ABL1 at 3 months, (%)	P value
WBC (10^9/L) > 100 vs < 100	45% vs 60%	0.04
p210 vs p190 (fusion protein)	35% vs 85%	<0.001
CNS disease at diagnosis vs no CNS disease	59% vs 58%	>0.99
Additional cytogenetic abn. vs none	65% vs 51%	0.01
Monosomy 7 abn. vs others	40% vs 61%	0.03
Somatic myeloid mutation vs none (N= 94 evaluable)	39% vs 61%	0.09
Treatment regimen		
IC plus TKI vs others	62% vs 53%	0.10
LC plus TKI vs others	63% vs 59%	0.71
Steroids plus TKI vs others	41% vs 63%	0.002
Blinatumomab plus TKI vs others	80% vs 58%	0.20
TKI combination		
Imatinib vs others	47% vs 61%	0.07
Dasatinib vs others	59% vs 59%	>0.99
Ponatinib vs others	79% vs 57%	0.009
u; undetectable, WBC; white blood cell count, abn.; abnormality, IC; intensive chemotherapy, LC; low intensity chemotherapy, TKI; tyrosine kinase inhibitor		

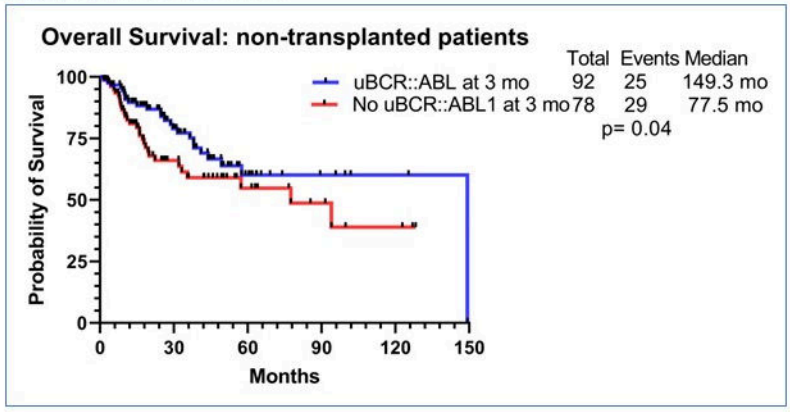

Figure 1

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