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Real-World Patient Characteristics and Treatment Patterns in Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia Patients with Long-Term Survivorship

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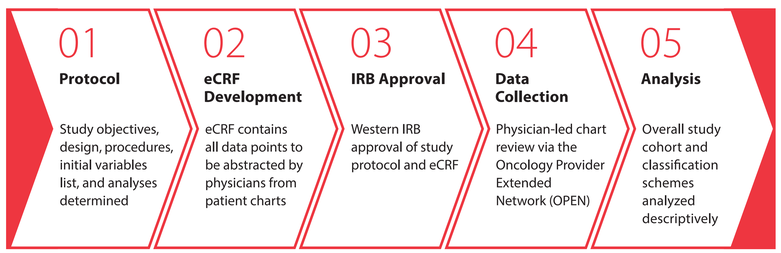
BACKGROUND

- Acute lymphoblastic leukemia (ALL) is an aggressive type of leukemia and in 2025, an estimated 6,100 people will be diagnosed with ALL and 1,400 people will die from ALL.[1,2]
- Five-year overall survival (OS) estimates among adolescents/young adults (20-39 years of age) are 59%, decreasing to <30% among adults >60 years of age.[3]
- Approximately 7-22% of patients receiving first-through-third salvage therapies have refractory disease.[4]
- Recent clinical trial data indicate that even among adults with ALL who achieve post-hematopoietic cell transplantation (HCT) remission, nearly half will experience relapse,[5] and standard first salvage therapies have been shown to result in poor outcomes among numerous subgroups of relapsed or refractory ALL (R/R ALL).[6]
- Real-world patient characteristics and treatment patterns in recently diagnosed R/R ALL -- in particular, clinical characteristics resulting in "long-term" survival in R/R ALL, defined in prior research as survival for ≥3 years after initial diagnosis (3YS) -- are an area of clinical interest.
- OBJECTIVE: This study describes real-world characteristics/treatments among R/R ALL patients and long-term survival.

METHODS

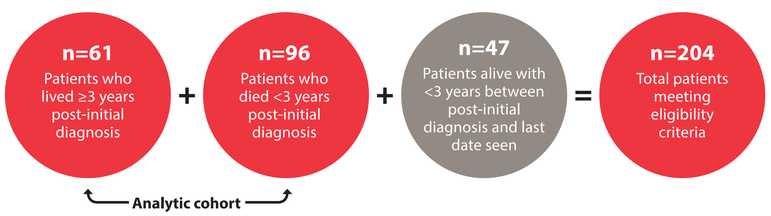
- This is a non-interventional, retrospective, physician-reported, multi-site, community oncology-based medical chart review using existing data from medical records of patients with R/R ALL being managed at community oncology clinics in the United States (US).
- Physicians from Oncology Provider Extended Network (OPEN), a community of over 7,000 oncologists, hematologists, and urologists from across the US, abstracted medical record data into electronic case report forms (June-July 2023).
- Eligible patients were adults with R/R ALL diagnosed September 1, 2017-March 1, 2022, with >12 months of follow-up available for patients alive at abstraction.
  - Clinical trial participants and T-cell ALL patients were excluded.
- Long-term survivors ("LTS") were defined as patients living ≥3 years from initial diagnosis to death/date last seen.
- LTS patients and patients that died <3 years post-initial diagnosis were compared.
- Descriptive analyses characterized deidentified data including t-tests and chi-square tests for continuous and categorical variables, and their non-parametric counterparts. No adjusted analyses were completed, analyses were unadjusted.

Figure 1. Study milestones



Abbreviations: IRB, Internal Review Board

Figure 2. Patient selection from full study-eligible sample (N=204) to patients with R/R B-cell ALL living ≥3 years or <3 years post-initial ALL diagnosis



Abbreviations: ALL, acute lymphoblastic leukemia; R/R, relapsed/refractory

RESULTS

Table 1. Physician demographics

	Physicians (N=24)
Practice setting, n (%)	
Community-based	16 (67)
Academic medical center or affiliated	8 (33)
U.S. region of practice, n (%)	
South	8 (33)
West	8 (33)
North	4 (17)
Midwest	4 (17)
Years in practice, median (p25-p75)	15 (10-18)
Specialty in hematology/oncology, n (%)	24 (100)

*Abbreviations: CAR-T center, Chimeric Antigen Receptor- T cell therapy center; US, United States

Baseline characteristics (Table 2)

Factors favoring LTS:

- Lower age at R/R diagnosis (median: 43 vs. 64 years, *P*<.001)
- Commercially-insured (70% vs. 36%, *P*<.001)
- Residing in the Southern (34% vs. 20%, *P*=0.026) and Midwestern US (25% vs. 15%, *P*=0.026)

Table 2. Baseline characteristics

	Lived ≥3 yrs post-initial diagnosis (n=61)	Died <3 yrs post-initial diagnosis (n=96)	P-value
Age at R/R ALL diagnosis, yrs, median (p25-p75)	43 (37-50)	64 (51-69)	<.001
Male sex at birth, n (%)	27 (44)	49 (51)	0.407
White race, n (%)	45 (74)	68 (71)	0.690
Non-Hispanic / non-Latino(a) ethnicity, n (%)	48 (79)	79 (82)	0.576
Commercially-insured payer at data collection, n (%)	43 (70)	35 (36)	<.001
US state of residence, n (%)			0.026
Northeast	7 (11)	16 (17)	
Midwest	15 (25)	14 (15)	
South	21 (34)	19 (20)	
West	18 (30)	47 (49)	

Abbreviations: ALL, acute lymphoblastic leukemia; R/R, relapsed/refractory; p25, 25th percentile; p75, 75th percentile; US, United States; yrs, years

Clinical characteristics (Table 3)

Factors favoring LTS:

- Longer interval from initial to R/R diagnosis (median: 35 vs. 8 months, *P*<.001)
- Lower NCI comorbidity index at R/R diagnosis (median: 0.0 [25th-75th percentile: 0-0.1] vs. median: 0.1 [25th-75th percentile: 0-1], *P*= 0.004)
- BMI at R/R diagnosis (≥25: 46% vs. 69%, *P*= 0.002)
- ECOG at R/R diagnosis (0 or 1: 90% vs. 67%, *P*<.001), KPS (≥80: 57% vs. 30%, *P*=0.002)
- Disease biology:
  - Philadelphia chromosome positive (31% vs. 23%)
  - Not having ≥1 high-risk cytogenetic abnormality (59% vs. 72%)

Table 3. Clinical characteristics

	Lived ≥3 yrs post-initial diagnosis (n=61)	Died <3 yrs post-initial diagnosis (n=96)	P-value
B-cell Ph-positive at initial diagnosis, n (%)	19 (31)	22 (23)	0.253
High-risk cytogenetic abnormalities at initial diagnosis, n (% with ≥1)	36 (59)	69 (72)	0.095
Duration from initial to R/R ALL diagnosis, months, median (p25-p75)	34 (23-41)	8 (5-12)	<.001
BMI, median (p25-p75)	25 (23-27)	28 (24-32)	0.004
NCI comorbidity index score at R/R diagnosis, median (p25-p75)	0 (0-0.1)	0.1 (0-1)	0.004
ECOG performance status at R/R diagnosis, n (%)			0.002
0-1	55 (90)	64 (67)	
2	6 (10)	32 (33)	

Abbreviations: BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; NCI, National Cancer Institute; R/R, relapsed/refractory; p25, 25th percentile; p75, 75th percentile; PH-positive, Philadelphia-chromosome positive; yrs, years

RESULTS

Treatment characteristics prior to relapsed/refractory setting (Table 4)

Factors favoring LTS:

- Treatment regimen
  - Lower proportion receiving "hyper-CVAD plus" (57% vs. 67%, *P*<.001)
- Treatment phase
  - Receiving consolidation (79% vs. 24%, *P*<.001)
  - Receiving allogeneic stem cell transplantation as consolidation (23% vs. 2%, *P*<.001)
  - Receiving maintenance (67% vs. 21%, *P*<.001)
- Response to frontline treatment
  - Post-frontline MRD negative (71% vs. 28%, *P*<.001)

Table 4. Treatments prior to relapsed/refractory setting

	Lived ≥3 yrs post-initial diagnosis (n=61)	Died <3 yrs post-initial diagnosis (n=96)	P-value
Frontline treatment regimen received, n (%)			<.001
Hyper CVAD plus	35 (57)	26 (67)	
CALGB 8811 Larson	10 (16)	7 (7)	
Dasatinib plus prednisone	0 (0)	10 (10)	
Linker <60yrs*	4 (7)	1 (1)	
Other	12 (20)	14 (15)	
Frontline treatment phases received, n (%)			
Induction	57 (93)	92 (96)	0.712
Consolidation	48 (79)	23 (24)	<.001
Allogeneic SCT used as consolidation	14 (23)	2 (2)	<.001
Maintenance	41 (67)	20 (21)	<.001
MRD negative post-frontline treatment, n (%)	43 (70)	27 (28)	<.001

*Linker protocol based on 2002 prospective cohort study by Linker et al.

Abbreviations: ALL, acute lymphoblastic leukemia; BMI, body mass index; CVAD, cyclophosphamide, vincristine sulfate, doxorubicin hydrochloride/adriamycin, dexamethasone, methotrexate, cytarabine; ECOG, Eastern Cooperative Oncology Group; MRD, minimal residual disease; NCI, National Cancer Institute; R/R, relapsed/refractory; PH-positive, Philadelphia-chromosome positive; SCT, stem cell transplantation; yrs, years

Notes: "Plus" in "hyper CVAD plus" includes imatinib, ponatinib, dasatinib, and rituximab

CONCLUSIONS

- This real-world evidence study of a considerable number of R/R B-cell ALL patients (primarily in the community setting) suggests that:
- LTS was prevalent among younger patients with fewer comorbidities and higher performance status achieving MRD.
- Such patients were more likely to receive allogeneic stem cell transplantation as consolidation therapy and more likely to receive maintenance therapy.
- Given the index period, limited observations were available for some newer therapeutics, the earlier use of which among poorer-prognostic patients may contribute to LTS.
- The ongoing challenge of transitioning from LTS to a definitive cure in ALL remains a focal point for future research.
- Analyses were unadjusted. Adjusted analyses are needed to elucidate the impact of potential confounding factors.

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