

SAFETY AND FEASIBILITY OF THE CALGB 10403 PEDIATRIC-INSPIRED REGIMEN IN ADULTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA OLDER THAN 40 YEARS



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INTRODUCTION

Pediatric-inspired regimens have transformed outcomes for adolescents and young adults (AYA) with acute lymphoblastic leukemia (ALL). The CALGB 10403 (C10403) regimen has traditionally been limited to patients <40 years, an arbitrary cutoff with limited biological justification. Whether patients aged ≥40 years can safely receive this regimen with comparable efficacy remains debatable.

AIM

Primary endpoints were overall survival (OS) and relapse-free survival (RFS); secondary endpoints included CR, induction mortality, after-induction MRD (<0.1%), and toxicity.

METHOD

Retrospective, single-institution cohort study of **123 patients** with newly diagnosed B-ALL treated with C10403, stratified by age: **<40 years (n=103)** and **≥40 years (n=20)**. In patients >50 years, modifications included delayed and dose-reduced asparaginase (pegaspargase 1000 IU/m² day 18), and prednisone (60 mg/m² for 22 days) instead of dexamethasone.

RESULTS

Table 1. Adverse events

Adverse events	Total N = 123 (%)	<40 years N = 103 (%)	≥40 years N = 20 (%)	P - value
Hepatotoxicity	87 (71)	73 (71)	14 (70)	>0.9
Hypertriglyceridemia	62 (50)	54 (52)	8 (40)	0.3
Critical care admission on induction	28 (22.7)	22 (21.4)	6 (30)	0.39
Sepsis on induction	92 (74.7)	75 (73)	17 (85)	0.4
Mechanical ventilation	11 (8.9)	9 (8.7)	2 (10)	1
Induction mortality	5 (4.1)	4 (3.9)	1 (5)	>0.9

CONCLUSIONS

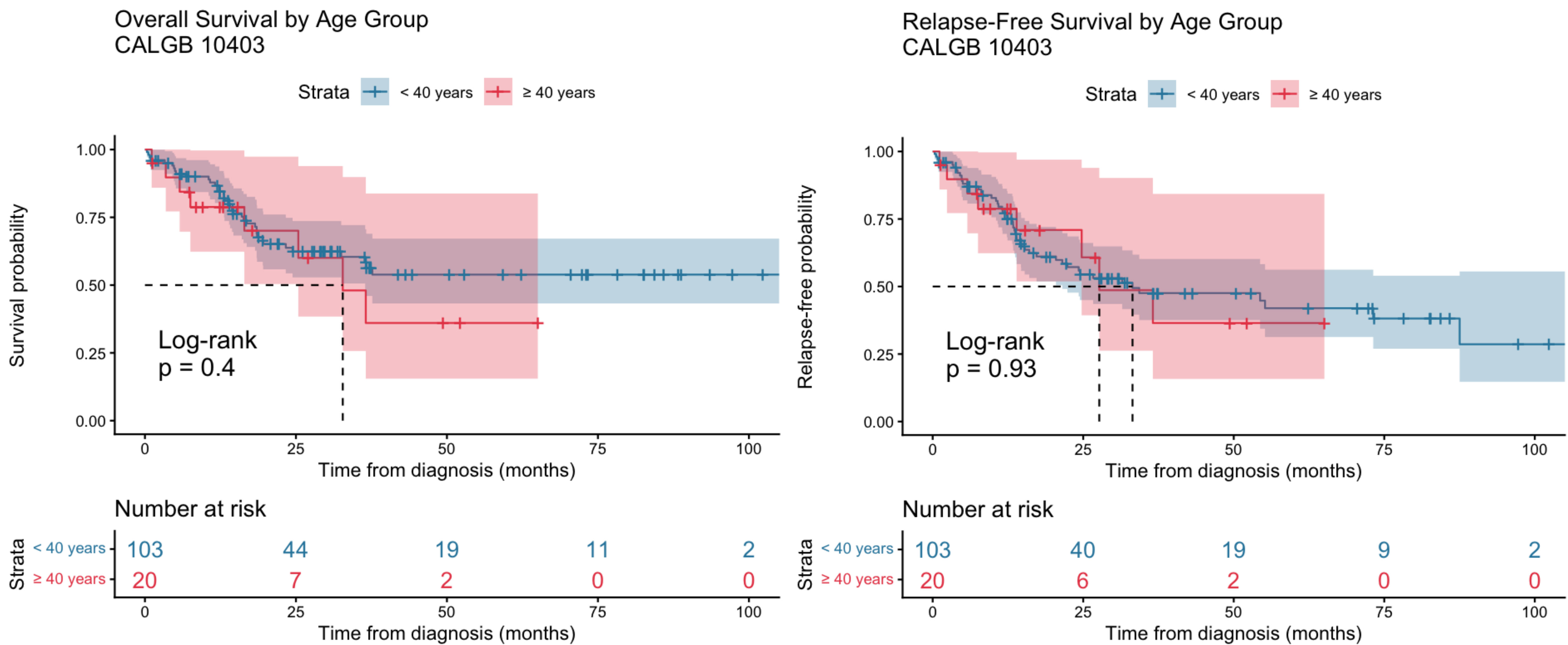
Despite a higher comorbidity burden, patients aged ≥40 years treated with C10403 achieved outcomes equivalent to younger AYA patients across all efficacy and safety endpoints. These findings support extending pediatric-inspired ALL therapy beyond the traditional age cutoff and challenge the validity of 40 years as an upper boundary. Prospective studies are warranted to confirm these results.

RESULTS

Median age was 24 years (17-39) in the <40 group and 48 years (40 - 64) in the ≥40 group. Baseline characteristics were otherwise balanced, except for higher rates of **diabetes** (30% vs. 6.8%, p=0.007), **hypertension** (30% vs. 3.9%, p=0.001), and **CNS involvement** (15% vs 2%, p =0.014) in the ≥40 cohort, and lower WBC at diagnosis (3 vs. 17 ×10³/μL, p=0.047) in the ≥40 cohort. **No significant differences were observed in OS** (HR 1.39, 95% CI 0.65–2.99, p=0.40) **or RFS** (HR 1.03, 95% CI 0.49–2.19, p=0.93). OS at 12/24 months was 86.8%/63.8% vs. 78.8%/70.1%, and RFS 77.4%/57.2% vs. 78.8%/70.9%, respectively (**Figure 1**). CR rates were 90.9% vs. 100% (p=0.35), MRD negativity 57.3% vs. 63.2% (p=0.80), and induction mortality 3.9% vs. 5.0% (p=1.00). **Toxicity rates were comparable between the <40 and ≥40 years groups across all measured parameters** (all p>0.05), including

hepatotoxicity (71% vs. 70%), hypertriglyceridemia (52% vs. 40%), sepsis during induction (72.8% vs. 85%), mechanical ventilation (8.7% vs. 10%), and critical care admission during induction (21.4% vs. 30%). Asparaginase omission was more frequent in the ≥40 group (35% vs. 3.9%, p=0.0002).

Figure 1. Overall survival and relapse free survival



TAKE HOME MESSAGE:

In patients ≥40 years, C10403 achieves survival, response, and toxicity outcomes comparable to younger AYA patients, challenging age 40 as an arbitrary upper limit for pediatric-inspired ALL therapy.

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