

Age-Based Disparities in Clinical Trials Supporting Food and Drug Administration Approval of Therapies for Hematologic Malignancies

Yolaine Jeune-Smith, PhD¹; Marjorie E. Zettler, PhD, MPH²; Eli G. Phillips Jr, PharmD, JD¹; Bruce A. Feinberg, DO¹; Ajeet Gajra, MD¹

¹Cardinal Health Specialty Solutions, Dublin, OH; ²Regor Pharmaceuticals, Inc.

Background

- Older patients (age ≥65) make up the largest proportion of patients diagnosed with hematologic malignancies.
- Underrepresentation of older adults in oncology clinical trials has been previously described.
- There has been an effort to enroll older adults on trials based on FDA and NIH guidelines.
- Older patient data specific to hematologic malignancy trials are sparse.

Objective

- To evaluate the median age of clinical trial participants and compare it to the real-world age distribution for each respective hematologic malignancy for recently approved agents.

Materials & Methods

- Median age of clinical trial participants were obtained from the prescribing information for novel hematologic malignancy therapies first approved for an adult indication between 2015 and 2019.
- Adult median age estimates for each indication were obtained from the SEER database.
- Difference in median age was calculated by subtracting disease population median age from trial median age as described by Ludmir et al.¹
- Additional trial protocol details were obtained from FDA package labels. Data are presented using descriptive statistics.

Results

Table 1: Trial Characteristics

Trial and Patient Characteristics, n (%)	Trials n=26	Patients n=6,033
Phase		
1	1 (4%)	174 (3%)
1-2	6 (23%)	569 (9%)
2	9 (35%)	914 (15%)
3	10 (38%)	4,376 (73%)
Randomized		
Yes	11 (42%)	4,491 (74%)
No	15 (58%)	1,542 (26%)

Table 2: Supporting Clinical Trial Requirements

Trial Requirements, n (%)	n=26
Upper age limit	
59	1 (4%)
75	1 (4%)
None	24 (92%)
ECOG PS limit	
Yes	11 (42%)
No	15 (58%)
Comorbidity or organ/hematopoietic function restriction	
Yes	26 (100%)
No	0 (0%)

Table 3: Difference in Median Age

DMA (Trial Age – SEER Median Age), mean years	
All trials (n=26)	-3.8 (95% CI: -6.0 to -1.6 years, p<0.01)
Follicular lymphoma trials (n=2)	-1
Mantle cell lymphoma trials (n=3)	-2.7
Myeloma trials (n=6)	-4.4
Large B-cell lymphoma trials (n=3)	-7.0
Acute myeloid leukemia trials (n=5)	-7.8

- Twenty-two hematologic malignancy therapies were approved based on 26 trials, with 6,033 patients in the evaluable populations.
 - Less than half of the trials were phase III (10; 38%) or were randomized with a control group (11; 42%), **Table 1**.
- Protocols for most of the trials (24; 92%) did not specify upper age limits.
- Most required an ECOG PS ≤2, with only 2 trials (8%) permitting ECOG status 0-3.
- All trials had eligibility restrictions related to comorbidities, organ function, or hematopoietic function, **Table 2**.
- The median age of the trial participants was younger (mean 3.8 years) than the median age of the real-world populations (95% CI: –6.0 to –1.6 years; p<0.01).
 - AML trials most often enrolled younger participants (mean DMA -7.8 years), followed by LBCL trials (mean DMA -7.0 years), **Table 3**.

Conclusion

- The median age of trial participants was nearly 4 years younger than their respective disease populations, despite no age-based exclusions in most protocols.
- The differences were particularly striking in LBCL and AML trials.
- Poor performance status, comorbidities, or organ impairment likely contributed to older patients’ ineligibility.
- Adequate representation in clinical trials is critical to evaluate the safety and efficacy of new therapies in the patient population who will eventually receive them.
- Post-approval real-world research can help understand the effect of these therapies on older adults.

REFERENCE: Ludmir EB, Mainwaring W, Lin TA, et al. Factors Associated With Age Disparities Among Cancer Clinical Trial Participants. *JAMA Oncol*. 2019;5(12):1769-1773.