Outcomes by age in pediatric and adolescent patients treated for de novo Hodgkin lymphoma on contemporary Children's Oncology Group trials

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Introduction

Population-level studies suggest that adolescent/young adults (AYAs, defined by the National Cancer Institute as 15 – 39 years) with Hodgkin lymphoma (HL) have worse outcomes than younger patients. Recent guidelines from the American Society of Clinical Oncology and Friends of Cancer Research call for including patients ≥12 years of age on late phase trials spanning children and adults. We examined whether, in pediatric and adolescent patients receiving risk-based, response-adapted therapy for HL on contemporary Children's Oncology Group (COG) trials, age ≥12 years (vs. younger) would define a group with inferior outcomes.

Methods

This was a pooled analysis of individual patient-level data from three Phase 3 COG trials for intermediate, low, high-risk HL (AHOD0031, AHOD0431, AHOD0831). Five-year relapse rate, event free survival (EFS) and overall survival (OS) by age were estimated via Kaplan Meier method. Cox regression models examined the influence of age on EFS and OS, adjusted for race/ethnicity, sex, insurance, histology, Ann Arbor stage, B symptoms, bulk disease, study, and radiation therapy.

Results

Median follow-up was 6.9 years. A total of 1,733 patients were included in the study cohort. Mean age was 14.6 years (± 3.5) with 55% of patients ≥15 years (N= 956) and 82% ≥ 12 years (N= 1,417). Five-year cumulative incidence of relapse was higher in patients ≥12 years vs. <12 years (18% vs. 11%, p=0.008) as well as in those ≥15 years, vs. < 15 years (19% vs. 13%, p=0.003). In unadjusted analyses age ≥12 years vs. younger was associated with significantly worse EFS (87% vs. 80%, p= 0.01), as was age ≥15 years vs. younger (87% vs. 80%, p= 0.008). Multivariable modeling revealed that age was an independent risk factor for EFS using thresholds of both 12 and 15 years. Age ≥ 15 years was also an independent risk factor for all-cause mortality (hazard ratio: 2.6, 95% confidence interval: 1.2, 5.4).

Conclusion

In patients treated for HL with response-based therapy on contemporary COG trials, age ≥12 years (vs. younger) was associated with inferior EFS and age ≥15 years was significantly associated with higher hazard of death. These findings provide rationale for including patients ≥ 12 years in clinical trials evaluating novel agents in the up-front setting for HL. Analyses examining early response to therapy, treatment-related toxicities, treatment delays and post-relapse survival by age are ongoing.