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613. ACUTE MYELOID LEUKEMIA: CLINICAL STUDIES | NOVEMBER 29, 2018

The Real-World Incidence of Relapse in Acute Myeloid Leukemia (AML): A Systematic Literature Review (SLR)

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Abstract

Background: AML is a hematologic malignancy with a high rate of treatment failure due in part to high relapse of the disease following initial or subsequent therapy. Numerous studies have reported AML relapse rates in clinical trials and real-world settings, but systematic review and synthesis of these data are very limited. This study used a SLR to assess the real-world cumulative incidence of relapse in adult patients with AML across various treatment settings.

Methods: A SLR focused on observational studies published in the past 5 years was conducted using MEDLINE, EMBASE, and the Cochrane Database of Systematic Reviews. Additionally, proceedings from the past 2 years of selected clinical conferences were searched. Publications prior to January 2013 were excluded to ensure studies were generalizable to the current clinical context, given the rapidly changing nature of AML risk classification, genotyping, and treatment. Predefined selection criteria were employed to ensure studies were comparable and generalizable to the overall AML population. Key study exclusion criteria included: < 50 participants, selection for special populations or risk-specific populations using defined risk criteria, pediatric- or adolescent-only populations, and lack of reported follow-up time point for relapse. Key patient demographic characteristics, clinical characteristics, and cumulative incidence of relapse were extracted and explored using scatterplots.

Results: Forty-six observational studies were included. There were 29 journal articles (1 reported on 2 studies) and 16 conference abstracts; 45 studies were retrospective cohort studies and 1 was prospective. Thirty studies enrolled patients at the time of receipt of allogeneic stem cell transplant (allo-SCT), 4 at the time of autologous SCT (auto-SCT), 11 at the time of induction chemotherapy (CT), and 1 that reported a mix. The majority of studies (n = 20) were conducted in Europe, with 13 in Asia, 11 in North America, 1 in South America, and 1 defined as worldwide. The final year of study participant data collection ranged from 2008 to 2017. Study sample size range was 51-4,997, average age range was 31-68 years, and male proportion range was 41-64%.

Only 5 studies provided a clinical definition of relapse, and 5 studies clearly reported that relapse was measured only in those who achieved complete remission (4 of which were CT studies). No study reported the incidence of refractory disease. Relapse incidence ranged widely from 9% to 78%, which could be explained by high heterogeneity across the interventions received, differences in the time at which relapse was reported, or differences in the study and baseline population demographics and clinical characteristics, such as differences in mean/median (depending on study) age, prior lines of therapy, or baseline risk (e.g. studies of SCT varied widely with respect to whether patients were in first complete remission [CR1], CR2, CR3+, or had active disease at the time of SCT). The incidence of relapse is presented by continuous follow-up time (Figure), while accounting for intervention received (colors), sample size (bubble size), and mean/median age ≥ 60 years (black outline). Although relapse does not appear to be influenced by continuous follow-up time, the median relapse rate in studies with ≤ 24 months follow-up time was 32% versus 42% for studies with > 24 months follow-up. Relapse was higher in studies with a mean/median age ≥ 60 years, and was higher in studies of induction CT compared with SCT (allo-SCT in particular); however, CT studies included older patients and followed patients across subsequent lines of therapy (e.g. followed patients through transplantation). Whether baseline risk can explain some of the heterogeneity in relapse incidence beyond age or other factors will be explored further.

Conclusions: The real-world burden of relapse is substantial in patients following SCT and CT. Heterogeneity in interventions received, line of therapy/baseline risk, patient demographics and clinical characteristics, and a lack of clear definitions for relapse present challenges when comparing relapse incidence across studies, and result in a wide range of reported relapse rates. Authors of real-world studies should aim to clearly define relapse and its measurement. Future work will explore the impact of baseline risk such as cytogenetic risk classification on relapse.

Disclosures

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