Meta-Analysis of Oral versus Intravenous Arsenic in Acute Promyelocytic Leukemia: Treatment Effectiveness and Safety Profile

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Introduction

Acute promyelocytic leukemia (APL) is a highly curable subtype of acute myeloid leukemia. For non–high-risk APL, intravenous arsenic trioxide (ATO) plus all-trans-retinoic acid (ATRA) is standard. Oral Realgar-Indigo naturalis formula (RIF) has emerged as a potentially more convenient alternative, but comparative data remain limited.

Aim

To evaluate and compare the therapeutic efficacy and safety profile of oral arsenic versus intravenous arsenic trioxide, both in combination with all-trans-retinoic acid, for the treatment of non–high-risk acute promyelocytic leukemia. The analysis focuses on key clinical outcomes, including remission rates, survival, relapse, and treatment-related adverse events.

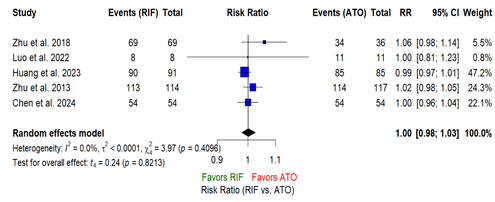
Methods

A systematic literature search of PubMed and Scopus databases was conducted from inception till May 2025 to identify eligible randomized controlled trials comparing oral and intravenous arsenic in APL patients. The primary outcomes included overall survival (OS) and relapse-free survival (RFS). Secondary outcomes included adverse events. Effect estimates were pooled using the Mantel-Haenszel method under a fixed- or random-effects model, and results were reported as risk ratios (RRs) with 95% confidence intervals (CIs). The study adhered to PRISMA (2020) guidelines and statistical analysis was performed using R software version 4.3.2.

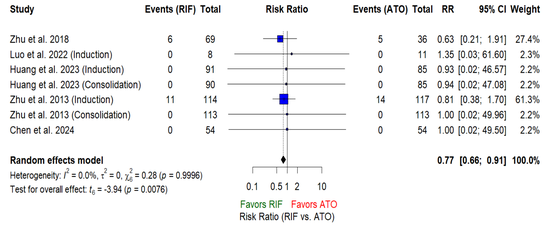
Results

Five randomized controlled trials were included. There was no significant difference in complete remission rates between oral RIF and intravenous ATO (RR: 1.00; 95% CI: 0.98–1.03). Similarly, overall survival (RR: 1.01; 95% CI: 0.99–1.03), event-free survival (RR: 1.01; 95% CI: 0.99–1.03), and 30-day mortality (RR: 0.42; 95% CI: 0.12–1.45) showed no statistically significant differences. The risk of relapse (RR: 1.17; 95% CI: 0.71–1.94), differentiation syndrome (RR: 0.78; 95% CI: 0.43–1.42), infections (RR: 0.84; 95% CI: 0.62–1.12), and bleeding events (RR: 1.05; 95% CI: 0.58–1.88) were also comparable. However, oral RIF was associated with a lower risk of grades 3–4 liver toxicity (RR: 0.77; 95% CI: 0.66–0.91) and fewer cardiac complications (RR: 0.64; 95% CI: 0.35–1.18).

A) complete remission



B) risk of grades 3–4 liver toxicity



Summary

Oral arsenic (RIF) appears as effective as intravenous ATO in non–high-risk APL, with a favorable safety profile and potential for reduced toxicity, supporting its use as a viable alternative.

The authors declare no competing interests