MÆDICA - a Journal of Clinical Medicine

JOURNAL CLUB

For Patients with Acute Promyelocytic Leukemia the Arsenic Trioxide Improves Event-free and Overall Survival

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10 to 15% of acute myeloid leukemia cases are patients with acute promyelocytic leukemia (APL). There are unique features of APL as reciprocal translocation between the long arms of chromosomes 15 and 17, younger age of onset, and severe consumptive coagulopathy with a high incidence of early fatal hemorrhage.

Current treatment of APL combines all-trans-retinoic acid (ATRA) with anthracycline-based chemotherapy to induce remission, followed by consolidation chemotherapy and ATRA maintenance.

Arsenic trioxide (As2O3) was approved for treatment of patients with relapsed APL

481 patients (age >15 years) with untreated APL were randomized to either a standard induction regimen of tretinoin, cytarabine, and daunorubicin, followed by 2 courses of consolidation therapy with tretinoin plus daunorubicin, or to the same induction and consolidation regimen plus two 25-day courses of As2O3 consolidation immediately after induction. After consolidation, patients were randomly assigned to one year of maintenance therapy with either tretinoin alone or in combination with methotrexate and mercaptopurine. Ninety percent of patients on each arm achieved remission and were eligible to receive their assigned consolidation therapy.

Event-free survival (EFS), the primary end point, was significantly better for patients assigned to receive As2O3 consolidation, 80% compared with 63% at 3 years (stratified log-rank test, $P < .0001$). Survival, a secondary end point, was better in the As2O3 arm, 86% compared with 81% at 3 years ($P = .059$). Disease-free survival (DFS), a secondary end point, was significantly better in the As2O3 arm, 90% compared with 70% at 3 years ($P < .0001$). The addition of As2O3 consolidation to standard induction and consolidation therapy significantly improves event-free and disease-free survival in adults with newly diagnosed APL.

This study shows that the addition of As2O3 as initial consolidation therapy for adult patients with newly diagnosed APL significantly improves EFS and DFS and enhances overall survival. These improvements are especially impressive considering the use of an intention-to-treat analysis.

The addition of As2O3 to consolidation therapy clearly improves outcome with minimal additional toxicity for patients with APL. However, unanswered questions remain, such as the optimal timing for the As2O3 therapy in the overall treatment regimen and the best approach to decrease early deaths especially in patients with high risk disease.

Comment on a paper:
B. L. Powell, B. Moser, W. Stock, et al. – Arsenic trioxide improves event-free and overall survival for adults with acute promyelocytic leukemia: North American Leukemia Intergroup Study C9710. *Blood* 2010; 116:3751-57.