(PS1657) REDUCED DOSE ALL-TRANS RETINOIC ACID AND ARSENIC TRIOXIDE TO DECREASE EARLY DEATHS IN OLDER ACUTE PROMYELOCYTIC LEUKEMIA (APL) PATIENTS. POST-HOC ANALYSIS OF PATIENTS >60 YEARS IN THE EA9131 TRIAL

Topic: 04. Acute myeloid leukemia - Clinical

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Background

Clinical trials have reported >95% durable remissions in patients with (APL). In contrast, population studies from national registries report one-year survival less than 70%. The conflicting rates are due to enrollment of younger patients in trials (median age early 40s) and exclusion of patients with co-morbid conditions. Of particular importance is the under appreciation among physicians of a high rate of Early Deaths (ED) of 17-29% in the general population and more than 50% in patients >60 years within the first 30 days of treatment. ED is the commonest cause of treatment failure in APL. Contributory factors are older age, comorbid conditions, complexity at diagnosis, lack of institutional treatment pathways and provider inexperience given the rarity of the disease. In the EA9131multi-center cooperative group prospective trial, we proposed that use of a treatment algorithm and access to APL experts at academic centers to provide remote guidance to community centers (CC) would decrease ED. Of 201 enrolled patients, there were 6 deaths with an ED rate of 3% and a 1-year survival of 94.5% (Jillella et al 2025). We herein report the care approach and exploratory analysis of outcome in patients >60 years.

Methods

We used a treatment algorithm developed by 7 APL experts at 6 academic lead centers (LC). The trial was opened at 6 LC and 293 CC. Patients who presented to one of the 6 LC were managed with input from the local expert. Physicians at the CC contacted one of the 7 experts when a patient presented with suspected APL. Expert support was available 24/7 and the patient was eligible if the contact was made within 3 days of starting APL therapy. There were no exclusion criteria. A workup and treatment plan was provided to the CC physician based on standard of care with dose reductions for patients >60. For patients >60, ATRA at 25 mg/m2/day was suggested with addition of 50% dose reduced ATO after 10 days and patients >70 further reduction was made with ATRA at 10mg/m2/day and ATO added later or only during consolidation. Communication was maintained throughout induction. OS data was evaluated using the method of Kaplan-Meier (KM) and one-month and one-year OS rates estimated based on the KM estimate.

Results

Of 201 patients enrolled, 72 were >60; of these 41(56.9%) were 60-69, 22 (30.6%) 70-79 and 9 (12.5%) >80. 36 (50%) were male and 62 white, 7 African American, 2 Asian, 1 unknown; 7 identified as Hispanic. 15 patients (20.8%) were high-risk, 42 (58.3) obese and 49 (68%) had a Charlson comorbid index of >3. In 5 patients the dose of ATRA was not available. In 67 with reported doses, 20 started ATRA on day 1 at 45mg/m2/day with dose reduction to 25mg/m2/day in 15 by day 5. 39 started at 25mg/m2/day on day 1 and 8 at <25mg/m2/day. In 20 patients ATRA was decreased further, held and restarted for leukocytosis or differentiation syndrome (DS). 21 patients did not receive ATO during induction and 44 started around day 10 with most receiving 50% dose reduction. There were 5 deaths (ages 70, 71, 76, 79 and 81) all from DS with a one-month survival of 93.1% and a 1-year survival of 87.5%. There were 4 relapses; 3 were non-compliant/declined consolidation.

Summary/Conclusion

In this elderly cohort with multiple comorbid conditions, reduced dose ATRA and ATO, late initiation of ATO, algorithm use and expert support decreased ED. Full doses of ATRA and ATO are poorly tolerated by the elderly and further studies are needed in this highly curable malignancy.

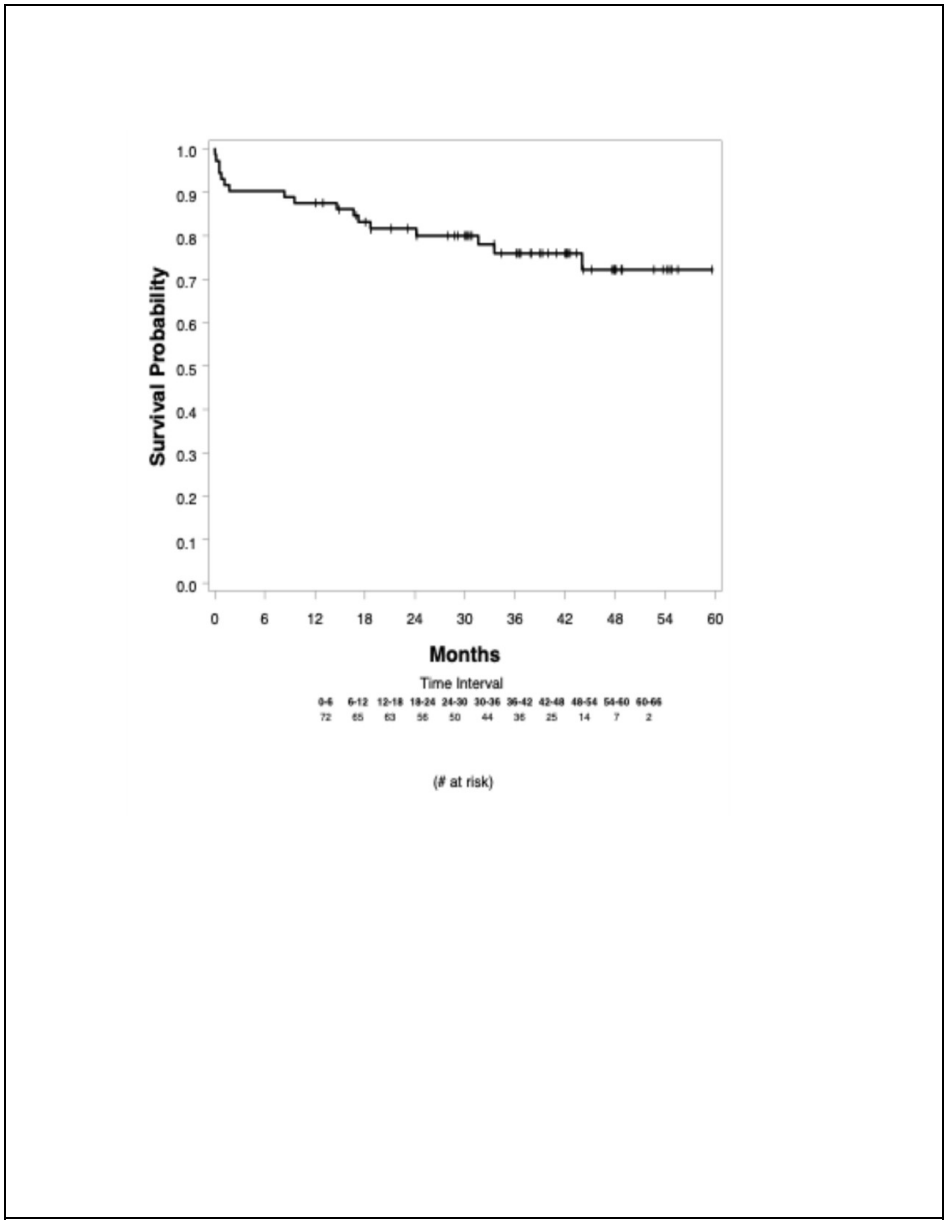

Figure 1. Survival plot for patients 60+ years of age One-month: 93.1% 95% CI (84.1%, 97.0%) One-Year:87.5%, 95% CI (77.3%, 93.3%)